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Protocol

Insomnia as an Unmet Need in Patients With Chronic Hematological Cancer: Protocol for a Randomized Controlled Trial Evaluating a Consumer-Based Meditation App for Treatment of Sleep Disturbance

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Abstract

Background: To address the need for long-term, accessible, nonpharmacologic interventions targeting sleep in patients with chronic hematological cancer, we propose the first randomized controlled trial to determine the effects of a consumer-based mobile meditation app, Calm, on sleep disturbance in this population.

Objective: This study aims to test the efficacy of daily meditation delivered via Calm compared with a health education podcast control group in improving the primary outcome of self-reported sleep disturbance, as well as secondary sleep outcomes, including sleep impairment and sleep efficiency; test the efficacy of daily meditation delivered via Calm compared with a health education podcast control group on inflammatory markers, fatigue, and emotional distress; and explore free-living use during a 12-week follow-up period and the sustained effects of Calm in patients with chronic hematological cancer.

Methods: In a double-blinded randomized controlled trial, we will recruit 276 patients with chronic hematological cancer to an 8-week *app-based wellness* intervention—the active, daily, app-based meditation intervention or the health education podcast app control group, followed by a 12-week follow-up period. Participants will be asked to use their assigned app for at least 10 minutes per day during the 8-week intervention period; complete web-based surveys assessing self-reported sleep disturbance, fatigue, and emotional distress at baseline, 8 weeks, and 20 weeks; complete sleep diaries and wear an actigraphy device during the 8-week intervention period and at 20 weeks; and complete blood draws to assess inflammatory markers (tumor necrosis factor-α, interleukin-6, interleukin-8, and C-reactive protein) at baseline, 8 weeks, and 20 weeks.

Results: This project was funded by the National Institutes of Health National Cancer Institute (R01CA262041). The projects began in April 2022, and study recruitment is scheduled to begin in October 2022, with a total project duration of 5 years. We anticipate that we will be able to achieve our enrollment goal of 276 patients with chronic hematological cancers within the allotted project time frame.

Conclusions: This research will contribute to broader public health efforts by providing researchers and clinicians with an evidence-based commercial product to improve sleep in the long term in an underserved and understudied cancer population with a high incidence of sleep disturbance.

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International Registered Report Identifier (IRRID): PRR1-10.2196/39007

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KEYWORDS

hematological cancers; mobile health; mHealth; meditation; sleep disturbance; mobile phone

Introduction

Symptom Burden and Sleep Disturbance Among Patients With Chronic Hematological Cancer

Hematological cancers, a group of cancer subtypes that include blood- and lymph-related disorders, account for 11% of all cancer diagnoses in the United States [1], with an estimated 1.9 million patients with hematological cancer currently living in the United States [1]. New noncurative therapies have led to improved survival for many hematological cancers; however, these maintenance medicines leave patients in a state of chronic disease. Approximately 60% of chronic hematological cancers, which include chronic leukemias (chronic lymphocytic and chronic myelogenous leukemia), low-grade lymphomas (follicular lymphomas), myeloma, myelodysplastic syndrome, and myeloproliferative neoplasms (MPNs), are incurable and typically follow unpredictable remitting-relapsing pathways associated with varying needs for treatment, which may be distressing for patients [2]; thus, these patients have distinct needs from those of patients with solid tumors (eg, breast cancer) [3]. Patients with chronic hematological cancers experience ongoing disease-induced symptoms that are frequently not resolved by medical therapy and chronic maintenance therapy-associated toxicities. This chronic symptom burden (eg, sleep disturbance, inflammation, fatigue, and emotional distress) persists into survivorship and re-emerges over time, despite the best available pharmacological therapy [1].

In particular, sleep disturbance (eg, difficulty falling asleep, difficulty staying asleep, nonrestorative sleep, or insomnia disorder) [4] is highly prevalent among patients with chronic hematological cancer [5]. Across studies, 50% to 80% of patients with hematological cancer have reported sleep disturbance [6-8]. Findings for the treatment of sleep disturbance in other highly studied cancer populations, such as breast cancer, may not be generalizable to patients with chronic hematological cancer, given their unique needs and disease course [9,10]. There is a pressing need for evidence-based, accessible treatments to improve *sleep* specifically in patients with chronic hematological cancers.

In addition, in patients with chronic hematological cancer, sleep disturbance is a predictor of increased inflammatory cytokine levels [10,11]; increased fatigue [10]; and poorer emotional functioning or emotional distress [10], including depressive symptoms [10]. In both noncancer and solid tumor cancer populations, sleep disturbance increases inflammation through persistent activation of the hypothalamic-pituitary-adrenal axis, which can, in turn, induce glucocorticoid resistance in immune cells, ultimately leading to a state of chronically elevated proinflammatory cytokines [12]. Sleep disturbance has also been shown to induce fatigue [13,14] and emotional distress [15-17]. The joint occurrence of sleep disturbance, fatigue, and emotional distress is referred to as symptom clustering [18] or grouping of interrelated symptoms. Such clusters have been shown to have a negative impact on patient survival [14,19]. These factors are also known to interact in complex ways, potentially leading to negative feedback loops that further affect symptom clustering (eg, as inflammation increases, further decrements in sleep and fatigue may be observed) [20].

Current Approaches to Addressing Sleep Disturbance

Medications are the most commonly prescribed treatment for patients with cancer experiencing sleep disturbances; however, to date, there is insufficient evidence to conclude that they are truly effective, particularly when considering long-term treatment of sleep problems [4,21]. In addition, medication may exacerbate symptoms associated with chronic hematological cancer, such as increased severity of insomnia, fatigue, and pain [22]. Potential deleterious side effects, along with the poor long-term success of pharmacological treatment for managing sleep disturbance, may outweigh any potential effectiveness for improving sleep and related quality of life in patients with chronic hematological cancer, indicating a need for alternative, safe, and effective sleep management strategies.

Nonpharmacologic behavioral interventions are promising strategies for treating sleep disturbance because of their (1) limited side effects, (2) targeting of specific psychological and behavioral factors that interfere with sleep, and (3) potential for long-lasting effects [23]. Currently, cognitive behavioral therapy for insomnia (CBT-I) is the most widely available, evidence-based, nonpharmacological treatment strategy for managing sleep disturbances in patients with and survivors of cancer [24]. However, CBT-I is intensive and time consuming for patients, requiring frequent in-person meetings with therapists and physicians at sites or clinics [21]. Remote delivery of CBT-I may be an alternative approach; however, studies assessing remotely delivered CBT-I have not been conducted for patients with cancer [21]. Even app-based CBT-I requires considerable effort and time to be effective [21]. Specifically, cognitive behavioral therapy apps require both clinician involvement and support, along with high adherence on the patient's side, to be effective [25]. Patients with chronic hematological cancer need less burdensome intervention strategies for long-term sleep management. Currently, patients with chronic hematological cancer have limited options for easily accessible, evidence-based treatments for sleep disturbance, exacerbating the diminished quality of life and resulting in poorer cancer outcomes.

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Evidence and Previous Literature Supporting Meditation

Meditation is a sleep disturbance treatment strategy recommended by the American Cancer Society and the National Center for Complementary and Integrative Health. Mindfulness meditation is the practice of moment-to-moment awareness, in which a person purposefully focuses on the present without judgment [26]. Several reviews and meta-analyses have demonstrated the positive effects of mindfulness-based interventions for general sleep complaints and sleep parameters associated with sleep quality (eg, total sleep time, sleep efficiency, and sleep onset latency) [27-29], yielding moderate effect sizes comparable with those of standard of care treatments for insomnia [28]. Individual studies have also demonstrated effects on specific sleep disorders, including insomnia [30], narcolepsy [31], restless leg syndrome [32], and sleep apnea [33]. Ong et al [34] suggested that meditation promotes balanced appraisals, cognitive flexibility, equanimity, and recommitment to values, which can, in turn, allow sleep-related arousal to subside and normal sleep patterns to re-emerge. Shallcross et al [27] further posited that sleep disturbance involves five processes: (1) rumination, (2) primary arousal, (3) secondary arousal, (4) sleep monitoring and selective attention and effort, and (5) distorted perceptions. The core processes involved in mindfulness (ie, experiential awareness, attentional control, and acceptance) have the potential to target each of the 5 processes contributing to sleep disturbance [27].

Meditation also has a dose-response relationship with reductions in inflammation for both those with solid tumors and those without cancer [35-37]. One review found that mindfulness-based interventions had no effect on cytokines in healthy populations but improved cytokine levels in patients with cancer [38]. Mindfulness-based interventions aid the recovery of the immune system, and the resulting immune changes show a shift from a carcinogenic cytokine profile to a more normalized profile. Meditation and other mindfulness-based practices have improved inflammatory biomarker levels common in patients with chronic hematological cancer (eg, tumor necrosis factor-α [TNF-α], interleukin [IL]–6 [IL-6], IL-8, and C-reactive protein [CRP]), as well as in populations such as patients with insomnia disorder, survivors of cancer, and older adults [39-42]. These specific cytokines and proteins are the most common inflammatory cytokines closely associated with chronic hematological cancer disease progression, symptoms, and sleep disturbances across all hematologic malignancy subtypes [11,43,44]. The calming effects of meditation on the autonomic nervous system and the hypothalamic-pituitary-adrenal axis may reduce proinflammatory gene expression and signaling via the downregulation of the proinflammatory transcription factor necrosis factor κβ pathway [35,45].

Meditation has previously demonstrated improvements in both sleep disturbance and fatigue among a subset of patients with chronic hematological cancer (MPN), with patients reporting that their reductions in fatigue were because of better sleep quality [46,47]. Several other studies have established the effects of mindfulness interventions in reducing fatigue in patients with cancer [48-50]. For example, Ikeuchi et al [51] found that mindfulness affected fatigue both directly and indirectly through anxiety, depression, pain, loneliness, and sleep disturbances. Randomized controlled trials (RCTs) have also shown that meditation reduces sleep disturbance by reducing emotional distress (eg, anxiety and depression) in patients with and survivors of cancer [52] and reducing sleep-interfering cognitive processes (eg, ruminating thoughts) [53,54]. Mindfulness meditation may reduce stress, worry, intrusive thoughts, and presleep arousal, which may, in turn, reduce sleep disturbance [55]. In particular, patients with chronic hematological cancer are more likely to experience such issues as their disease is never cured.

Although the Society for Integrative Oncology Clinical Practice Guidelines [56] suggests that meditation is a safe technique for decreasing the burden of a variety of cancer-related symptoms and comorbidities, few studies have investigated the effects of mindfulness meditation on sleep disturbance, specifically in patients with chronic hematological cancer [57]. In 2 recent RCTs with patients with leukemia, meditation interventions were delivered in person in hospital settings by trained clinicians [58,59], thereby limiting accessibility and use, especially in patients who were fatigued, had inflexible schedules, or had transportation difficulties [60]. Traditional in-person meditation programs for patients with cancer are lengthy and potentially burdensome (eg, 30- to 60-minute sessions on a single day of the week [58]), especially for patients with chronic hematological cancer and high chronic symptom burden [61]. Of note, meditation studies with patients with leukemia had short durations (only 5 weeks in length), were conducted at a specific time during treatment and in a clinical inpatient setting (eg, during chemotherapy treatment sessions [58] or in the hospital [59]), and did not measure sustained practice or effects outside of the clinic setting. Prior studies of meditation in limited cancer settings have supported extending and testing flexible and effective modes of delivering meditation to understudied groups with cancer.

Mobile App Use Among Patients With Chronic Hematological Cancer

Research further demonstrates that patients with chronic hematological cancer are interested in smartphone apps as a means of self-managing their health [38-40]. As of April 2020, there were approximately 55 mobile apps marketed to patients with or survivors of cancer available in the Google Play and Apple App stores, offering mostly educational content and information for caregivers. Of these, 4 included some form of meditation. No commercially available meditation apps for cancer populations have been rigorously evaluated for their feasibility, safety, or effectiveness [41,42]. A review identified only 2 meditation studies for patients with cancer delivered via mobile apps; both focused on breast cancer, and only 1 tested a consumer-based app [62]. In one of these studies, an adapted mindfulness-based stress reduction (MBSR) program was delivered via an iPad, resulting in significant improvements in psychological status and quality of life among MBSR participants compared with a usual care control group [63]. However, this study was conducted over 6weeks without any follow-up [63]. The other study assessed a consumer-based app, Headspace, and found an increased quality of life and

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mindfulness in Headspace participants compared with the control group but did not obtain app use data in most participants [64]. Meinlschmidt et al [65] suggested that there is more value in identifying and testing popular and currently available tools that have a committed user base and are likely to remain in use in the near future. To date, few interventions have tested the effects of consumer-based, commercially available meditation apps for sleep, and none have been tested to reduce sleep disturbances in chronic hematological cancer. A summary of key takeaways from current literature in this area is presented in Textbox 1.

Textbox 1. Key takeaways from current literature.

Key points regarding sleep disturbance in chronic hematological cancer

- Sleep disturbance is a long-term and serious problem for patients with hematological cancer and warrants distinct treatment.
- Patients with chronic hematological cancer lack effective, long-term treatment options for sleep disturbance.
- Mindfulness meditation has been rigorously tested as a nonpharmacological complementary therapy that leads to the amelioration of sleep disturbances and specific sleep disorders.
- Mindfulness meditation consistently improves factors associated with sleep disturbance in populations with cancer: inflammation, fatigue, and emotional distress.
- Current meditation interventions do not meet the diverse and unique needs of patients with chronic hematological cancer; more flexible options are needed.
- Consumer-based apps have great potential to deliver meditation interventions; however, more rigorous studies are needed.

This Trial

Therefore, leveraging a unique academic-industry partnership, we propose a 20-week RCT (8-week intervention+12-week follow-up) to rigorously test the consumer-based app Calm to effectively deliver a meditation intervention to patients with chronic hematological cancer (N=276; 138 per group) as compared with a health education podcast control group. Calm was chosen for this study as our research team had rigorously tested the app among patients with chronic hematological cancer previously, and we have demonstrated its preliminary efficacy and preference among patients with chronic hematological cancer over another popular meditation app, Headspace [47]. This study aims to (1) test the efficacy of daily meditation (≥10 minutes per day) delivered via Calm compared with a health education podcast control group in improving the primary outcome of self-reported sleep disturbance, as well as secondary sleep outcomes, including sleep impairment and sleep efficiency; (2) test the efficacy of daily meditation (≥10 minutes per day) delivered via Calm compared with a health education podcast control group on inflammatory markers (TNF-α, IL-6, IL-8, and CRP), fatigue, and emotional distress (anxiety and depressive symptoms); and (3) explore free-living use during a 12-week follow-up period and sustained effects at 20 weeks from the baseline of Calm in patients with chronic hematological cancer.

Methods

Ethics Approval

All study procedures and materials were approved by the Biomedical Research Alliance of New York Institutional Review Board (study 21-136-955) and conducted in accordance with the Declaration of Helsinki. This study has been registered at ClinicalTrials.gov (NCT05294991). Written informed consent will be obtained from all participants.

Study Design

This study is a double-blind RCT in which eligible and consenting study participants will be randomly assigned to one of two groups: (1) the daily Calm meditation intervention group or (2) health education podcast control group.

Recruitment

Patients with chronic hematological cancers will be nationally recruited using previously established organizational partners (eg, Leukemia and Lymphoma Society, MPN Research Foundation, Patient Empowerment Network, Banner Health, and Mays Cancer Center at UT Health San Antonio MD Anderson). Recruitment materials will be developed specifically for each organizational partner to advertise the study to potential participants via social media (eg, Facebook, Instagram, and Twitter), email listservs, website postings, and postings in clinics or waiting rooms. The study will be advertised as an *app-based wellness* study to blind study participants to the intended Calm intervention group.

Enrollment and Randomization

Interested patients with chronic hematological cancer will be directed to complete a web-based eligibility screening questionnaire via REDCap (Research Electronic Data Capture; Vanderbilt University; see Textbox 2 for a detailed list of the eligibility criteria). Ineligible participants will be sent an email notifying them of their ineligibility status and providing resources for patients with cancer, which will include an educational sleep handout and a discount code for Calm. Eligible participants will be sent an email notifying them of their eligibility; asked to review a video-based overview of the study (including the informed consent); and sent a link to electronically sign the informed consent via REDCap, a secure web-based data collection and management platform. Participants will be offered the option of scheduling a call with a member of the research team to review any questions related to the study before providing their consent. Once consent is signed, participants will be (1) asked to complete the baseline

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questionnaire via REDCap, (2) blindly and randomly assigned to either the Calm intervention or health education podcast control arm, and (3) emailed the study materials (eg, app download instructions, blood draw instructions, and welcome email with important dates and study milestones). As part of the study instructions, all participants will be asked not to participate in any similar interventions, including other meditation apps, medications, or nonpharmacological sleep interventions during the study period. Participants will be blocked or stratified by biological sex and then randomly allocated (with a 1:1 allocation ratio) within the male-female strata to treatments using a pseudorandom number algorithm provided by the study statistician. Research personnel who assign participants to a group will not be the same as those who enroll participants or download and clean data. The group allocation status will be restricted so that statisticians and researchers will remain blind to treatment assignment.

After randomization, all participants will be offered an app download coaching and tutorial call with a study team member to review their assigned app, including a review of (1) the general app layout and basic functionalities (eg, look, feel, and types of content found on the app), (2) where to find content and how the content is organized, (3) how to view participation-tracking statistics, (4) how to set reminders to meditate or view podcasts, and (5) how to share participation statistics on social media. Following the call, the participants will receive an email containing a phone number for continued support using the app.

In addition, the participants will receive blood draw instructions. Participants will have a blood draw request placed to obtain a blood draw from their local Quest Diagnostics Patient Service Center and instructed on the time of day to receive their blood draw and the forms of identification they will need to obtain the blood draw. Participants will have access to a study team member's phone number and email for further support while receiving a blood draw throughout the study.

Finally, participants will receive a mailed package containing (1) an Actiwatch Spectrum device; (2) instructions detailing the wear, care, and use of the device; and (3) instructions for shipping the device back to the research team at the study conclusion. The participants will not proceed with the intervention until the previous steps are fully completed.

Textbox 2. Study eligibility criteria.

Inclusion criteria

- Diagnosis of chronic hematological cancer on stable maintenance management (chronic hematological cancer subtypes include: chronic lymphocytic leukemia, follicular lymphoma, smoldering myeloma, myeloma, myeloproliferative neoplasm subtypes [polycythemia vera, essential thrombocythemia, and myelofibrosis], systemic mastocytosis, chronic myelomonocytic leukemia, and myelodysplastic syndrome) by a treating physician:
- On stable medical therapy or observation (ie, no changes in disease-targeted medications [or their dose] for the past 2 months)
- Not currently participating in a therapeutic pharmacologic clinical trial
- Has not received and is not planning to receive an allogeneic stem cell transplantation
- Self-identifying as sleep disturbed (Pittsburgh Sleep Quality Index score of >5, indicating moderate sleep disturbance)
- Owning and able to operate a mobile smartphone (iPhone with iOS 9.0 or later or an Android 4.1 or later)
- Willing to download and able to operate a mobile app
- Able to understand written and spoken English
- Aged ≥18 years
- Willing to be randomized
- Willing to drive to Quest Diagnostics Patient Service Center 3 times during the study in the morning
- No change in sleep medication use (if any) over the past 6 weeks

Exclusion criteria

- Meditation or meditative movement practice (ie, yoga, tai chi, and qi gong) of ≥60 minutes per month in the past 6 months
- Use of any consumer-based meditation app
- Residing outside of the United States
- Any planned change in pharmacological therapy (ie, new drug) during the study time frame (ie, 20 weeks)
- Self-reporting sleep-disordered breathing or sleep movement disorder
- Taking sleep medications or supplements ≥3 times per week
- Self-reporting any other diagnosed and uncontrolled medical or psychiatric condition

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Intervention Group (Calm)

Calm does not provide its users with a specific prescription for how often to use the app (frequency) or how long to use the app (dose); users self-select the frequency, dose, and timing of engagement, as well as which content and features to use. The Calm intervention participants will be asked to complete a minimum of 10 minutes per day of meditation via Calm, at any time of day for 8 weeks. During weeks 1 to 4, participants will be asked to complete the introductory 30-day program *How to Meditate* comprising 30 days of 10-minute daily meditation along with education about what mindfulness is, how to practice and achieve it with meditation, the seated or reclining positions to use for meditation, and how to monitor and guide their breathing. During weeks 5 to 8, participants will be asked to complete one daily meditation that may include the *Daily Calm*, a different 10-minute mindfulness meditation each day, or a meditation from various series of meditations (eg, loving-kindness and 7 days of managing stress). Participants will have complete autonomy over choosing the meditation, which includes options for at least 10 minutes (meditation periods are tracked). After completing their daily meditation, participants will also be able to use the app content more broadly (ie, nonmeditative content, including Sleep Stories and Daily Move) based on their preference.

Calm meditation focuses on mindfulness components [66], breathing techniques, and body scans, all of which are consistent with core mindfulness practices, such as MBSR (nonjudgmental moment-to-moment awareness) [67] and one of Vipassana's principles—objective observation of physical sensations in the body [68]. As an ideal dose for mindfulness meditation interventions has not been established because of considerable variability in intervention prescription [69], the 10-minute daily dose was chosen, as Calm currently offers 10-minute meditations (daily and series meditations), which corresponds to how long users typically meditate using the app. Practical guides recommend that beginners start with short daily meditations lasting between 10 and 30 minutes per session [26,70]; thus, the intervention prescription will be a minimum of 10 minutes per day of meditation to be effective but not overly burdensome.

Participants will be allowed to choose the time of day when they meditate. Giving participants autonomy over choosing the time of day for meditation mirrors the way in which Calm's paying subscribers use the app, thus yielding benefits (eg, ecological validity and participant satisfaction) that likely outweigh those of imposing strict controls over the timing of use, which could lead to lower adherence (eg, missed or truncated practice). Participation (meditations completed, time of day, length of time, and nonmeditative content used) will be tracked using the Calm app throughout the study and addressed in sensitivity analyses.

After completion of the 8-week study intervention period, the Calm intervention participants will no longer have to complete daily meditations but will continue to have access to the app for 12 additional weeks during the follow-up period. Participation in the Calm app will continue to be tracked during this time.

Control Group (Health Education Podcast)

Similar to the Calm intervention group, podcast group participants will listen to a minimum of 10 minutes per day of a health education podcast delivered via a mobile app for 8 weeks (Tables 1 and 2). A library of health education podcasts will be available on the app, with carefully chosen content that excludes any recommendations for sleep, meditation, or mindfulness-like principles or practice. Participants will be able to select the podcast based on title, time, or both in an effort to mirror the delivery of meditations in the Calm intervention group. Podcast group participants will also be encouraged to use other components of the podcast. Participation (podcasts completed, time of day, length of time, and components used) will be tracked on the app throughout the study period. After completion of the 8-week sham intervention period, the podcast group participants will no longer be asked to listen to daily podcasts but will continue to have access to the app for 12 additional weeks during the follow-up period. Participation in the podcast app will still be tracked during this period. Upon completion of the entire 20-week study period, podcast group participants will be given a discount code for 6 months of free access to the Calm app.

Table 1. Calm and podcast group prescriptions.

Week	Calm intervention group	Podcast group[a]
Week 1: total 7 days	Daily introductory 10-minute meditation	Daily 10-minute health education podcasts
Weeks 2-4: total 21 days	Daily 10-minute exploration of mindfulness meditation	Daily 10-minute health education podcasts
Weeks 5-20: Full access	Full library of individual and series of 10-minute meditations	Full library of podcasts available

[a]Podcasts will be uploaded weekly, except during weeks 5-20 when the remaining full library will be uploaded.

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Table 2. Examples of Calm and podcast group prescriptions.

Group and examples	Minutes
Ca lm intervention group	
Returning to the Here and Now	10
Acceptance	11
Paying Attention	10
Podcast group	
Alcohol and Cancer	10
Community Gardening	10
10 Ways to Have a Better Conversation	12

Retention and Adherence Strategies

We will use self-determination theory (SDT) and SDT-based strategies to guide our protocol and promote adherence [71]. The SDT postulates that the initiation and maintenance of behavior is influenced by three basic needs:(1) competence, or the need to produce desired outcomes and to experience mastery; (2) autonomy, or the need to feel ownership of one's behavior; and (3) relatedness, or the need to feel connected to others [72]. Participants will be encouraged to use the features built into the Calm intervention or podcast, which are designed to help maintain engagement and adherence in their assigned app. All these features are consistent with practices that help individuals participate in health behaviors [71], and these features are identical in both apps. To promote autonomy, a feature of the Calm and podcast apps includes time spent meditating or listening to podcasts—participants can go to their Calm profile and they are automatically provided the total time they have spent meditating or listening (time from the first meditation or podcast to present), total sessions, and longest streak after each use. To promote competence, the Calm and podcast apps include a reminder that participants can set in the app that will send them a push notification to meditate or listen to a podcast at a set time each day. To promote relatedness, the final feature of the Calm and podcast apps includes *Share Your Stats*, which allows participants to share summaries of their meditation or podcast listening use with others via SMS text messages, emails, or social media (eg, Facebook, Pinterest, or Instagram).

In addition to the above app features, EZTexting (a commercial SMS text messaging–based platform) will be used to send a brief, automated phone call, email, or SMS text message (based on participant preference) at the beginning of the week to encourage continued participation, with the message and conversation grounded in the 3 tenets of SDT (ie, autonomy, competence, and relatedness). Participants who are not meditating or listening to the podcast episodes for at least 10 minutes per day or 70 minutes per week for >3 consecutive days will receive a midweek phone call, email, or text (based on participant preference) through EZTexting. Participants could opt out of these follow-up messages at any time during the intervention. Research staff will track adherence information throughout the study and determine whether the patterns of use are similar across arms. Furthermore, both the Calm intervention and podcast will automatically show the user their time spent in meditation or listening for the day, the total time since the start of the study, and the longest streak as a reinforcing self-management technique. Finally, the Calm intervention and podcast also include reminder tools in which participants can set reminders on their phones to participate [73]. All study participants will receive a monetary incentive for completion of the baseline (US $15), postintervention (US $25), and follow-up (US $35) assessments, including blood draws, for a total incentive opportunity of US $75 paid in one lump sum at the end of the study if all 3 outcome time points are completed.

Study Outcomes and Measures

Overview

Table 3 presents the study outcomes and measures. All study participants will be asked to complete web-based questionnaires via REDCap at 3 time points: baseline (week 0), postintervention (week 8), and follow-up (week 20). In addition, participants will complete a weekly web-based sleep diary via REDCap from weeks 1 to 8 and at the end of week 20. Participants will also complete a weekly log via REDCap regarding their satisfaction with the study and whether there have been any changes in their cancer therapy, sleep medication and supplement use, and disease status. The weekly satisfaction logs will specifically include questions to assess the participants' overall perceptions of their meditation or podcast sessions. If the participant meditates or listens to a podcast, they will be asked about their likes, dislikes, facilitators, and barriers. If they do not meditate or listen to a podcast, they will be asked what would help them.

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Table 3. Summary of data collection.

Data, outcomes, and measures	Week 1	Weekly	Week 8	Week 20
Aim 1				
Sleep disturbance (subjective)				
Insomnia Severity Index	✓		✓	✓
PROMIS[a] Sleep Disturbance	✓		✓	✓
PROMIS Sleep-Related Impairment	✓		✓	✓
Sleep diary		✓		✓
Sleep disturbance (objective)				
Actiwatch		✓[b]		✓
Aim 2				
Inflammation				
Serum cytokines and proteins (TNF-α[c], interleukin-6, interleukin-8, and CRP[d])	✓		✓	✓
Fatigue				
PROMIS Adult Cancer Fatigue	✓		✓	✓
Depression				
PROMIS Depression	✓		✓	✓
Anxiety				
PROMIS Anxiety	✓		✓	✓
Demographics				
Biological sex				
Self-report	✓			
Age				
Self-report	✓			
Race and ethnicity				
Self-report	✓			
Income				
Self-report	✓			
Education				
Self-report	✓			
Marital status				
Self-report	✓			
Occupation				
Self-report	✓			
Disease and treatment variables				
Comorbidity condition				
Charlson Comorbidity Index	✓			
Blood counts				
Complete blood count	✓		✓	✓
Sleep medications				
Self-reported		✓		✓
Cancer therapy changes				
Self-reported		✓		✓

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Data, outcomes, and measures	Week 1	Weekly	Week 8	Week 20
BMI				
Self-reported height and weight	✓			
Fidelity and process				
Meditation participation				
Self-report log		✓		
Calm-provided data		✓		
Podcast participation				
Self-report log		✓		
App-provided data		✓		
Satisfaction				
Self-report log		✓		
Check-ins and reminders				
Email, SMS text message, and phone call		✓		

[a]PROMIS: Patient-Reported Outcomes Measurement Information System.

[b]Assessed daily during the intervention period (weeks 0-8) and for a 7-day period at week 20.

[c]TNF-α: tumor necrosis factor-α.

[d]CRP: C-reactive protein.

Demographics

Demographic characteristics will be self-reported at baseline and will include biological sex, age, race, ethnicity, marital status, income, education, and occupation.

Clinical Data

Clinical characteristics will include a comprehensive assessment of cancer-specific disease information (eg, comorbidities and complete blood count); other comorbidities (Charlson Comorbidity Index) [74]; self-reported weight and height; and current pharmacological treatment information, including sleep medication.

Primary Outcomes (Sleep)

The primary outcome of changes in sleep disturbance will be assessed using the Insomnia Severity Index (ISI). The ISI, a 7-item measure of reported insomnia symptom severity over the past 2 weeks, has been validated among patients with cancer (Cronbach α=.90) [75]. Total scores range from 0 to 28, with scores of 8 to 14 and ≥15 indicating subclinical and moderate to severe insomnia symptom severity, respectively [75]. An ISI change score >7 is considered a clinically meaningful response to treatment [75]. Sleep will secondarily be assessed using the National Institutes of Health (NIH) Patient-Reported Outcomes Measurement Information System (PROMIS) Sleep Disturbance Short Form 8b, PROMIS Sleep Impairment Scale, actigraphy, and sleep diaries. The PROMIS Sleep Disturbance Short Form 8b comprises 8 items assessing various aspects of sleep on a 1 to 5 Likert scale. The measure generates a total summed score, which is then converted to a standardized *t* score for analysis [76]. The NIH PROMIS Sleep Disturbance Short Form 8b is a reliable and valid measure for assessing sleep disturbance in patients with cancer (Cronbach α=.86) [76]. The PROMIS Sleep-Related Impairment Short Form 8a comprises 8 items assessing various aspects of sleep-related impairment (self-reported perceptions of alertness, sleepiness, and tiredness during usual waking hours and perceived functional impairments during wakefulness associated with sleep problems or impaired alertness) on a 1 to 5 Likert scale. The measure generates a total summed score, which is then converted to a standardized *t* score for use in analyses [77,78]. The PROMIS Sleep-Related Impairment Short Form 8a is a reliable and valid measure for assessing impairments associated with sleep across a range of healthy and patient populations reporting sleep disturbance and sleep impairments (Cronbach α=.85-.91) [77,78].

Sleep will also be assessed objectively via wrist-worn actigraph, specifically, via an Actiwatch Spectrum Plus device (Philips Respironics, Inc). Participants will wear the Actiwatch daily throughout the 8-week intervention period, mail it back to research personnel after week 8 (the Actiwatch has a maximum battery life of 68 days), and receive an Actiwatch to wear again for a 7-day period during the follow-up period or week 20. The Actiwatch Spectrum Plus is a valid, reliable, and objective assessment of sleep to be worn on the nondominant wrist 24 hours a day and 7 days a week. This assesses the motion and ambient light data used to analyze the sleep and circadian rhythm parameters. Actigraphy data of ≥5 nocturnal periods recorded per week during the intervention period (ie, week 0-8) and during the 7-day follow-up or week 20 will be considered valid, and the actigraphy data will be binned weekly. The sleep-wake status in each 30-second epoch during the rest intervals will be determined with the Actiware version 6.1.2 (Phillips) scoring algorithm at the medium wake sensitivity threshold. The Actiware software contains automatic off-wrist detection and scoring. All main and minor rest intervals will be verified, with participants entering the rest interval onset and offset times, which are marked at the epoch level when the participant pushes a corresponding button on the device. If these

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event markers are absent, then the rest intervals will be verified using a daily sleep diary.

Finally, sleep will be further assessed using the Consensus Sleep Diary (CSD). The CSD will be used to assess reported bedtimes and wake times to determine the sleep and wake windows of the main and minor sleep periods [79]. Similar to the actigraphy data, sleep data from the CSD will also be binned weekly. The following night-level and averaged sleep metrics will be derived from both sleep diaries and actigraphy: bedtime, wake time, time in bed, total sleep time, sleep onset latency, wakefulness after sleep onset, number of awakenings, and sleep efficiency ([total sleep time/time in bed]×100%). Sleep efficiency from both sleep diaries and actigraphy will be the main secondary sleep outcome of interest.

Secondary Outcomes

Inflammatory biomarkers with serum cytokines and proteins (TNF-α, IL-6, IL-8, and CRP) will be objectively assessed from participant blood samples. The participants' blood draw instructions will include the address of the nearest Quest Diagnostics Patient Service Center (there are approximately 2200 centers located across the United States). Participants will be instructed to have their blood *drawn in the morning before 10 AM* within 2 weeks of notifying research personnel that they received their package and to repeat their blood draw at postintervention (8 weeks) and follow-up (20 weeks) time points. Participants will not need to fast and follow any other *day-of* procedures. In our prior work, we had high compliance with this method (92.6% at baseline and 70.4% at the postintervention time point) despite offering no incentives for completion of the blood draws [80]. A certified phlebotomist will perform all blood tests, drawing 3 mL of blood. Blood will be transferred into a plastic screw-cap vial and stored on cold packs. The Patient Service Center will mail the drawn blood to the Clinical Laboratory Improvement Amendments–-certified laboratory at the Quest Diagnostics Nichols Institute (San Juan Capistrano, California) for analysis. There will be no cost to the participants. Quest Diagnostics will provide test results to research staff via a secure web-based platform.

Fatigue and emotional distress (ie, anxiety and depression) will be assessed using the NIH PROMIS Adult Cancer Fatigue 7a (7 items), NIH PROMIS Emotional Distress-Anxiety Short Form 7a (7 items), and NIH PROMIS Emotional Distress-Depression Short Form 8a (8 items). Each of these measures asks participants questions on a 1 to 5 Likert scale and generates a total summed score, which is then converted to a standardized *t* score for use in the analyses. These NIH PROMIS instruments are reliable and valid measures of fatigue (Cronbach α>.86), anxiety (Cronbach α=.90), and depression (Cronbach α=.91) in patients with cancer [76].

Statistical Analysis

Sample Size and Power

All estimates presented here are conservatively based on a generalized linear mixed model analytic approach, in which the focal effect is an arm (Calm vs podcast) × time (baseline vs 8 or 20 weeks) interaction. A generalized linear mixed model approach affords lower power than the preferred analysis of covariance (ANCOVA) approach, which will be pursued if the model's homogeneity of effect assumption is met (see the *Analytic Approach* section). Assuming a sample SD for ISI scores of 6.0 (derived from the literature on sleep disturbance among patients with cancer [81-85]) and Cronbach α=.05, a complete-case sample size of 28 (n=14 pee arm) would afford a power of 0.80 to detect a clinically meaningful between-arm (Calm vs podcast) differences in ISI scores of >7 points (ie, a standardized between-arm difference of Cohen *d*=1.33). However, anticipated effects on other sleep measures and measures of well-being are generally much more modest; accordingly, the study sample size was determined based on anticipated intervention effects on these outcomes rather than those on the ISI. In our previous work, we found moderate effects of meditation on self-reported psychological well-being (aim 2; Cohen d_s=0.31-0.44), self-reported sleep disturbance assessed via the PROMIS Sleep Disturbance questionnaire (Cohen *d*=0.47), and inflammation biomarkers (Cohen d_s=0.41-0.50) [39]. The meta-analysis by Duong et al [86] suggests somewhat stronger effects of mindfulness (standardized mean difference 0.50) and relaxation (standardized mean difference 0.94) interventions on fatigue. Assuming an effect size typical of those observed across these various outcomes (Cohen *d*=0.45), a conservative estimate of the pre-post correlation for outcome scores (*r*=0.30) and Cronbach α=0.05, a complete-case sample (at 8 weeks) of 220 (n=110 per arm) should afford a power of 0.80 to detect significant between-arm differences in secondary outcomes (and power >0.99 to detect a clinically meaningful difference in ISI scores). Anticipating up to 20% attrition at 8 weeks, we will enroll and randomize 276 participants (n=138 per arm). For aim 3, anticipating up to 30% attrition by week 20 (yielding 194 complete cases; n=97 per arm), tests of intervention effects should have power=0.80 to detect the effects of Cohen *d*≥0.48. Multivariable linear regression analyses of potential dose-response effects on outcomes will take two forms: (1) analysis of all available cases with a dose coded as 0 for the podcast group and (2) analysis using data from the Calm group only. These analyses should have a power of 0.80 to detect small (r^2≥0.039) and moderate (r^2≥0.076) linear dose-response effects.

Analytic Approach

For preliminary analyses, univariate and bivariate statistics and plots will be used to examine the distributions of and associations between study variables, identify potential multivariate outliers and influential cases, explore patterns of missingness, and check for systematic between-arm differences in baseline participant characteristics. Before addressing the study aims, we will estimate multivariable linear regression models predicting week 8 and week 20 values of each outcome from the main effects of the treatment arm (arm) and the corresponding baseline value of the outcome (baseline) and an arm × baseline interaction term. If the interaction is not significant, an ANCOVA-type approach (described in the following paragraphs) will be used. However, if this interaction is significant, a generalized linear mixed model approach will be used, with repeated measurements of outcomes treated as nested within the participants. Preliminary analyses will inform the choice of link function (eg, natural log) and error

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distributions (eg, negative binomial) or the transformation of outcome scores used in the primary analyses. R (version 4.1.2) will be used for all analyses and plots.

To assess intervention effects on sleep quality and sleep-related impairment, we will use multivariable linear regression models (following an ANCOVA-type approach), predicting week 8 values on the ISI and secondary sleep outcomes, including the PROMIS Sleep Disturbance questionnaire and Sleep-related Impairment Scale, and sleep efficiency measured via sleep diaries and actigraphy from the study arm (Calm v podcast), adjusting for corresponding baseline values and relevant background covariates (eg, prestudy sleep medication dosage and BMI). These analyses, which will follow a strict intent-to-treat approach, will be supplemented by parallel analyses in which week 8 outcome values will be predicted from dose (minutes of meditation use), with the dose coded as 0 for the podcast arm, while adjusting for baseline outcome measure values and background covariates. These supplemental analyses will address heterogeneity in intervention exposure without including highly collinear arm and dose terms in the same models.

To address the hypotheses regarding the intervention effects on inflammatory markers (TNF-α, IL-6, IL-8, and CRP), fatigue, anxiety, and depressive symptoms, we will estimate models parallel to those estimated for sleep measures, with week 8 outcome values predicted based on the arm, adjusting for corresponding baseline values on outcome measures and relevant background covariates.

To address the hypotheses regarding longer-term intervention effects at week 20, we will use analytic approaches parallel to those to assess differences in change at week 8, with outcomes being predicted from arm or dose (minutes spent meditating), adjusting for corresponding baseline outcome values and background covariates.

To address the hypotheses regarding associations between dose and sustained meditation use (number of weeks with ≥4 days of meditation use) and longer-term change in outcomes within only the Calm intervention arm, we will examine bivariate plots and estimate a variety of multivariable regression models (eg, polynomial linear regression, piecewise linear function, and generalized additive models) to understand the forms of the associations of dose and sustained use and change in outcomes.

If preliminary analyses indicate significant arm × baseline interactions, we will use (instead of an ANCOVA approach) a generalized linear mixed model approach in which a cross-level arm (Calm vs podcast) × time (eg, baseline vs week 8) interaction term is the focal effect for predicting repeated measurements of the outcome measure. This interaction term will capture between-arm differences in changes from baseline to week 8 (or week 20). Differences in change as a function of the intervention dose will be captured using dose × time interaction terms. Although the generalized linear mixed model approach generally does not provide as much statistical power as the ANCOVA approach, generalized linear mixed models (estimated using maximum likelihood) have the advantage of drawing on the strength of all available covariate and outcome data to produce unbiased parameter estimates and SEs in the presence of outcome data that are missing at random.

All preliminary analyses will be supplemented by analyses exploring the interactions between biological sex (male vs female) and the focal effect in each model (eg, sex × arm in ANCOVAs or sex × arm × time in generalized linear mixed models) to determine whether these effects differ by sex. Furthermore, we will conduct sensitivity analyses by examining associations between time of day (eg, proportion of meditation bouts occurring within 2 hours of bedtime) and the proportion of sessions using nonmeditative content and outcomes at 8 and 20 weeks, adjusting for baseline outcome values. As these variables will be highly collinear with the study arm because podcast users will not have any recorded in-app meditation use, sensitivity analyses gauging the potential impact of these variables will parallel the dose-response analyses described previously. Further sensitivity analyses will be conducted to assess the potential impact of (1) changes in the chronic hematological cancer treatment regimen and (2) sleep disorder diagnoses that occur after randomization. For these, analyses of intervention effects will be repeated, excluding data from individuals who experience either of these events, and the results will be compared with those from the full intent-to-treat sample. To maintain the type I error rates at a nominal Cronbach α=.05, we will use *P* values adjusted using the Hommel approach [87].

Missing Data

If an ANCOVA-type approach is pursued, we will use multiple imputation to impute missing data by including all the variables from a given analytic model (ie, the variables with missingness will be included in the imputation model) in the imputation model, as well as potentially important auxiliary variables that are predictive of missingness or found to be associated with variables that have missingness [88]. With the *mice* package in R, we will use the fully conditional specification to generate 100 imputed data sets to be analyzed, as described previously [89]. Although generalized linear mixed models are robust to missingness in the response variable, data from participants with incomplete data on ≥1 covariate will be excluded from the analyses. Therefore, where warranted, we will use multiple imputation to generate imputed data sets to be analyzed via linear mixed models.

Results

This project is funded by the NIH National Cancer Institute (R01CA262041). The projects kicked off in April 2022, and study recruitment is scheduled to begin in October 2022, with the total project duration lasting 5 years. We anticipate that we will be able to achieve our enrollment goal of 276 patients with chronic hematological cancer within the allotted project time frame.

Discussion

Principal Findings

The purpose of this study is to leverage an academic-industry partnership with the consumer-based app Calm to rigorously evaluate Calm for the effective delivery of a meditation

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intervention to patients with chronic hematological cancer via a 20-week RCT. Specifically, in this study, we aimed to (1) test the efficacy of daily meditation (≥10 minutes per day) delivered via Calm compared with a health education podcast control group on self-reported sleep disturbance, sleep impairment, and sleep efficiency; (2) test the efficacy of daily meditation (≥10 minutes per day) delivered via Calm compared with a health education podcast control group on inflammatory markers, fatigue, and emotional distress; and (3) explore the sustained effects at 20 weeks from the baseline of Calm in patients with chronic hematological cancer. This study will be the first RCT to determine the effects of a consumer-based mobile meditation app on sleep disturbances in patients with chronic hematological cancer. If our findings demonstrate a significant clinical impact on sleep disturbance in patients with chronic hematological cancer, we will have an inexpensive, easily accessible, nonpharmacological intervention that can readily be prescribed by cancer care providers for sleep disturbance in chronic hematological cancer. Our rigorous RCT will fill a knowledge and rigor gap regarding the delivery of smartphone-based meditation as an intervention for sleep and provide new data on sustained effects.

Comparison With Prior Work

There is limited understanding of the effects of meditation on sleep-related outcomes in patients with cancer, with no research to date examining these outcomes in hematological cancers (1.9 million in the United States) [28,57]. Existing research using apps has focused on emotional measures or cancer-specific biological changes as outcomes but not sleep disturbance [90-94] in survivors of solid tumors with minimal residual disease or those with short survival times (eg, patients with metastatic solid tumors). The different and distinct long-term disease courses of patients with chronic hematological cancer and the associated maintenance therapy toxicities and symptoms warrant innovative interventions that support the self-management of symptoms [3]. Patients with chronic hematological cancer are often geographically dispersed, with substantial variability in their proximity to cancer centers because of the rarity of certain subtypes (eg, MPNs) [95], limiting opportunities for community-based local programs to help manage symptoms. Remote delivery of meditation via a mobile app will improve reach and scalability in this understudied population.

In addition, previous studies on meditation in cancer have focused primarily on White women with breast cancer [57]. This study presents an opportunity to study meditation in older adults, men, and minorities who present with chronic hematological cancer. Our prior successful recruitment strategies for patients with cancer will specifically recruit representative samples from these populations. Furthermore, we previously established that Calm is acceptable and appealing to a wide population group, which can expand the reach of traditional research interventions. For example, in a cross-sectional survey of Calm subscribers (N=12,151), 20% were male, 19% were people of color, and 15% were older adults (aged >65 years).

Prior studies using meditation to reduce sleep disturbance in patients with cancer did not have follow-up periods beyond 12 weeks [53]. In the 2 meditation-based interventions conducted in patients with chronic hematological cancer, both were delivered for a very short period (ie, 5 sessions of 1 hour per week). No product could be used continually and accessed beyond study completion [58,59]. As most evidence-based apps are developed within the context of research studies and are not sustained at the end of the study [96], the scalability and viability of the widespread distribution of mobile app–based interventions in these studies are not possible. As Calm is consumer based, the intervention never truly *ends*. Calm is available and can be used whenever a patient desires or feels it is needed (eg, when they feel overwhelmed, fatigued, anxious, or lying down to go to sleep). The patient can choose when and how frequently Calm is used, increasing the likelihood that patients will use Calm to alleviate sleep disturbance in the long term. This study can uniquely measure and explore time and dose effects and will advance the evidence for a consumer-based meditation app that patients with chronic hematological cancer can use for symptom self-management in the long term. This research will contribute to broader public health efforts by providing researchers and clinicians with an evidence-based commercial product to improve sleep in the long term in an underserved and understudied population with cancer and a high incidence of sleep disturbance.

Future Directions

If it is demonstrated that Calm is an efficacious intervention for patients with chronic hematological cancer, future work will aim to disseminate Calm as an evidence-based option for health care providers to recommend or prescribe to patients with chronic hematological cancer. Consideration will be made to apply for a NIH Small Business Innovation Research grant to help with the dissemination of Calm or to receive Food and Drug Administration approval for Calm as a nonpharmacological intervention for the treatment of sleep in patients with chronic hematological cancer.

Conclusions

In summary, this study will contribute to the mindfulness and cancer literature at large, with a unique focus on filling the much-needed gap by examining remote mindfulness-based interventions in patients with chronic hematological cancer.

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Data Availability

All data gathered in this study will be kept private. A reasonable request can be made by researchers and physicians to have access to deidentified data when data collection is complete.

Conflicts of Interest

JH discloses that she receives an annual salary from Calm and holds stock in the company. However, her salary and equity do not depend on the results of her research.

References

1. Facts and statistics. Leukemia and Lymphoma Society. URL: https://www.lls.org/facts-and-statistics/facts-and-statistics-overview [accessed 2022-06-23]
2. Howell DA, McCaughan D, Smith AG, Patmore R, Roman E. Incurable but treatable: understanding, uncertainty and impact in chronic blood cancers-a qualitative study from the UK's Haematological Malignancy Research Network. PLoS One 2022 Feb 10;17(2):e0263672 [FREE Full text] [doi: 10.1371/journal.pone.0263672] [Medline: 35143569]
3. McCorkle R, Ercolano E, Lazenby M, Schulman-Green D, Schilling LS, Lorig K, et al. Self-management: enabling and empowering patients living with cancer as a chronic illness. CA Cancer J Clin 2011;61(1):50-62 [FREE Full text] [doi: 10.3322/caac.20093] [Medline: 21205833]
4. Ancoli-Israel S. Sleep disturbances in cancer: a review. Sleep Med Res 2015 Dec 01;6(2):45-49. [doi: 10.17241/smr.2015.6.2.45]
5. Scherber R, Dueck AC, Johansson P, Barbui T, Barosi G, Vannucchi AM, et al. The Myeloproliferative Neoplasm Symptom Assessment Form (MPN-SAF): international prospective validation and reliability trial in 402 patients. Blood 2011 Jul 14;118(2):401-408 [FREE Full text] [doi: 10.1182/blood-2011-01-328955] [Medline: 21536863]
6. Gowin KL, Langlais BT, Kosiorek HE, Dueck A, Millstine D, Huberty J, et al. Sleep and psychiatric disturbance in chronic Philadelphia negative myeloproliferative neoplasms. Blood 2017 Dec 7;130(Supplement 1):4189. [doi: 10.1182/blood.V130.Suppl_1.4189.4189]
7. Luskin M, Zhou E, Zhang Z, DeAngelo DJ, Stone R, Wadleigh M, et al. Sleep disturbance among patients with myelodysplastic syndromes and acute leukemia. Blood 2019 Nov 13;134(Supplement_1):4786. [doi: 10.1182/blood-2019-125147]
8. Luskin MR, Cronin AM, Owens RL, DeAngelo DJ, Stone RM, Wadleigh M, et al. Self-reported sleep disturbance and survival in myelodysplastic syndromes. Br J Haematol 2017 May;177(4):562-566. [doi: 10.1111/bjh.14573] [Medline: 28272741]
9. Oerlemans S, Mols F, Issa DE, Pruijt JH, Peters WG, Lybeert M, et al. A high level of fatigue among long-term survivors of non-Hodgkin's lymphoma: results from the longitudinal population-based PROFILES registry in the south of the Netherlands. Haematologica 2013 Mar;98(3):479-486 [FREE Full text] [doi: 10.3324/haematol.2012.064907] [Medline: 22929981]
10. Geyer HL, Dueck AC, Emanuel RM, Cannon K, Kiladjian JJ, Slot S, et al. Insomnia, quality of life and MPN symptom burden: an analysis by the MPN quality of life international study group (MPN-QOL ISG). Blood 2013 Nov;122(21):4087. [doi: 10.1182/blood.v122.21.4087.4087]
11. Geyer HL, Dueck AC, Scherber RM, Mesa RA. Impact of inflammation on myeloproliferative neoplasm symptom development. Mediators Inflamm 2015;2015:284706 [FREE Full text] [doi: 10.1155/2015/284706] [Medline: 26538823]
12. Irwin MR. Sleep and inflammation: partners in sickness and in health. Nat Rev Immunol 2019 Nov;19(11):702-715. [doi: 10.1038/s41577-019-0190-z] [Medline: 31289370]
13. Anderson KO, Getto CJ, Mendoza TR, Palmer SN, Wang XS, Reyes-Gibby CC, et al. Fatigue and sleep disturbance in patients with cancer, patients with clinical depression, and community-dwelling adults. J Pain Symptom Manage 2003 Apr;25(4):307-318 [FREE Full text] [doi: 10.1016/s0885-3924(02)00682-6] [Medline: 12691682]
14. Fox RS, Ancoli-Israel S, Roesch SC, Merz EL, Mills SD, Wells KJ, et al. Sleep disturbance and cancer-related fatigue symptom cluster in breast cancer patients undergoing chemotherapy. Support Care Cancer 2020 Feb;28(2):845-855 [FREE Full text] [doi: 10.1007/s00520-019-04834-w] [Medline: 31161437]
15. Lee J, Youn S, Kim C, Yeo S, Chung S. The influence of sleep disturbance and cognitive emotion regulation strategies on depressive symptoms in breast cancer patients. Sleep Med Res 2019 Jun 30;10(1):36-42. [doi: 10.17241/smr.2019.00388]
16. Peltz JS, Rogge RD, Pugach CP, Strang K. Bidirectional associations between sleep and anxiety symptoms in emerging adults in a residential college setting. Emerg Adulthood 2016 Nov 04;5(3):204-215. [doi: 10.1177/2167696816674551]
17. Khurshid KA. Bi-directional relationship between sleep problems and psychiatric disorders. Psychiatr Ann 2016 May 31;46(7):385-387. [doi: 10.3928/00485713-20160531-01]
18. Kwekkeboom KL, Tostrud L, Costanzo E, Coe CL, Serlin RC, Ward SE, et al. The role of inflammation in the pain, fatigue, and sleep disturbance symptom cluster in advanced cancer. J Pain Symptom Manage 2018 May;55(5):1286-1295 [FREE Full text] [doi: 10.1016/j.jpainsymman.2018.01.008] [Medline: 29360570]

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19. Souza RC, Dos Santos MR, das Chagas Valota IA, Sousa CS, Costa Calache AL. Factors associated with sleep quality during chemotherapy: an integrative review. Nurs Open 2020 Sep;7(5):1274-1284 [FREE Full text] [doi: 10.1002/nop2.516] [Medline: 32802348]
20. Alvaro PK, Roberts RM, Harris JK. A systematic review assessing bidirectionality between sleep disturbances, anxiety, and depression. Sleep 2013 Jul 01;36(7):1059-1068 [FREE Full text] [doi: 10.5665/sleep.2810] [Medline: 23814343]
21. Zhou ES, Partridge AH, Syrjala KL, Michaud AL, Recklitis CJ. Evaluation and treatment of insomnia in adult cancer survivorship programs. J Cancer Surviv 2017 Feb;11(1):74-79 [FREE Full text] [doi: 10.1007/s11764-016-0564-1] [Medline: 27495283]
22. Paltiel O, Marzec-Boguslawska A, Soskolne V, Massalha S, Avitzour M, Pfeffer R, et al. Use of tranquilizers and sleeping pills among cancer patients is associated with a poorer quality of life. Qual Life Res 2004 Dec;13(10):1699-1706. [doi: 10.1007/s11136-004-8745-1] [Medline: 15651540]
23. Winbush NY, Gross CR, Kreitzer MJ. The effects of mindfulness-based stress reduction on sleep disturbance: a systematic review. Explore (NY) 2007;3(6):585-591. [doi: 10.1016/j.explore.2007.08.003] [Medline: 18005910]
24. National Institutes of Health. URL: https://www.nih.gov/ [accessed 2022-06-23]
25. Wright JH, Mishkind M. Computer-assisted CBT and mobile apps for depression: assessment and integration into clinical care. Focus (Am Psychiatr Publ) 2020 Apr;18(2):162-168 [FREE Full text] [doi: 10.1176/appi.focus.20190044] [Medline: 33162853]
26. McDonald K. How to Meditate: A Practical Guide. New York, NY, USA: Simon and Schuster; 2005.
27. Shallcross AJ, Visvanathan PD, Sperber SH, Duberstein ZT. Waking up to the problem of sleep: can mindfulness help? A review of theory and evidence for the effects of mindfulness for sleep. Curr Opin Psychol 2019 Aug;28:37-41 [FREE Full text] [doi: 10.1016/j.copsyc.2018.10.005] [Medline: 30390479]
28. Rusch HL, Rosario M, Levison LM, Olivera A, Livingston WS, Wu T, et al. The effect of mindfulness meditation on sleep quality: a systematic review and meta-analysis of randomized controlled trials. Ann N Y Acad Sci 2019 Jun;1445(1):5-16 [FREE Full text] [doi: 10.1111/nyas.13996] [Medline: 30575050]
29. Rash JA, Kavanagh VA, Garland SN. A meta-analysis of mindfulness-based therapies for insomnia and sleep disturbance: moving towards processes of change. Sleep Med Clin 2019 Jun;14(2):209-233. [doi: 10.1016/j.jsmc.2019.01.004] [Medline: 31029188]
30. Garland SN, Zhou ES, Gonzalez BD, Rodriguez N. The quest for mindful sleep: a critical synthesis of the impact of mindfulness-based interventions for insomnia. Curr Sleep Med Rep 2016 Sep;2(3):142-151 [FREE Full text] [doi: 10.1007/s40675-016-0050-3] [Medline: 28191449]
31. Jalal B, Moruzzi L, Zangrandi A, Filardi M, Franceschini C, Pizza F, et al. Meditation-relaxation (MR therapy) for sleep paralysis: a pilot study in patients with narcolepsy. Front Neurol 2020 Aug 12;11:922 [FREE Full text] [doi: 10.3389/fneur.2020.00922] [Medline: 32903364]
32. Bablas V, Yap K, Cunnington D, Swieca J, Greenwood KM. Mindfulness-based stress reduction for restless legs syndrome: a proof of concept trial. Mindfulness 2016;7(2):396-408. [doi: 10.1007/s12671-015-0457-9]
33. Huberty JL, Green J, Puzia ME, Larkey L, Laird B, Vranceanu A, et al. Testing a mindfulness meditation mobile app for the treatment of sleep-related symptoms in adults with sleep disturbance: a randomized controlled trial. PLoS One 2021 Jan 7;16(1):e0244717 [FREE Full text] [doi: 10.1371/journal.pone.0244717] [Medline: 33411779]
34. Ong JC, Moore C. What do we really know about mindfulness and sleep health? Curr Opin Psychol 2020 Aug;34:18-22. [doi: 10.1016/j.copsyc.2019.08.020] [Medline: 31539830]
35. Bower JE, Crosswell AD, Stanton AL, Crespi CM, Winston D, Arevalo J, et al. Mindfulness meditation for younger breast cancer survivors: a randomized controlled trial. Cancer 2015 Apr 15;121(8):1231-1240 [FREE Full text] [doi: 10.1002/cncr.29194] [Medline: 25537522]
36. Shete SU, Verma A, Kulkarni DD, Bhogal RS. Effect of yoga training on inflammatory cytokines and C-reactive protein in employees of small-scale industries. J Educ Health Promot 2017 Aug 9;6:76 [FREE Full text] [doi: 10.4103/jehp.jehp_65_17] [Medline: 28856165]
37. Pace TW, Negi LT, Sivilli TI, Issa MJ, Cole SP, Adame DD, et al. Innate immune, neuroendocrine and behavioral responses to psychosocial stress do not predict subsequent compassion meditation practice time. Psychoneuroendocrinology 2010 Feb;35(2):310-315 [FREE Full text] [doi: 10.1016/j.psyneuen.2009.06.008] [Medline: 19615827]
38. Sanada K, Alda Díez M, Salas Valero M, Pérez-Yus MC, Demarzo MM, Montero-Marín J, et al. Effects of mindfulness-based interventions on biomarkers in healthy and cancer populations: a systematic review. BMC Complement Altern Med 2017 Feb 23;17(1):125 [FREE Full text] [doi: 10.1186/s12906-017-1638-y] [Medline: 28231775]
39. Irwin MR, Olmstead R, Breen E, Witarama T, Carrillo C, Sadeghi N, et al. Tai chi, cellular inflammation, and transcriptome dynamics in breast cancer survivors with insomnia: a randomized controlled trial. J Natl Cancer Inst Monogr 2014 Nov;2014(50):295-301 [FREE Full text] [doi: 10.1093/jncimonographs/lgu028] [Medline: 25749595]
40. Irwin MR, Olmstead R, Breen EC, Witarama T, Carrillo C, Sadeghi N, et al. Cognitive behavioral therapy and tai chi reverse cellular and genomic markers of inflammation in late-life insomnia: a randomized controlled trial. Biol Psychiatry 2015 Nov 15;78(10):721-729 [FREE Full text] [doi: 10.1016/j.biopsych.2015.01.010] [Medline: 25748580]

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41. Black DS, Cole SW, Irwin MR, Breen E, St Cyr NM, Nazarian N, et al. Yogic meditation reverses NF-κB and IRF-related transcriptome dynamics in leukocytes of family dementia caregivers in a randomized controlled trial. Psychoneuroendocrinology 2013 Mar;38(3):348-355 [FREE Full text] [doi: 10.1016/j.psyneuen.2012.06.011] [Medline: 22795617]
42. Creswell JD, Irwin MR, Burklund LJ, Lieberman MD, Arevalo JM, Ma J, et al. Mindfulness-based stress reduction training reduces loneliness and pro-inflammatory gene expression in older adults: a small randomized controlled trial. Brain Behav Immun 2012 Oct;26(7):1095-1101 [FREE Full text] [doi: 10.1016/j.bbi.2012.07.006] [Medline: 22820409]
43. Birgegard G, Samuelsson J, Ahlstrand E, Ejerblad E, Enevold C, Ghanima W, et al. Inflammatory functional iron deficiency common in myelofibrosis, contributes to anaemia and impairs quality of life. From the Nordic MPN study Group. Eur J Haematol 2019 Mar;102(3):235-240. [doi: 10.1111/ejh.13198] [Medline: 30472746]
44. Craver BM, El Alaoui K, Scherber RM, Fleischman AG. The critical role of inflammation in the pathogenesis and progression of myeloid malignancies. Cancers (Basel) 2018 Apr 03;10(4):104 [FREE Full text] [doi: 10.3390/cancers10040104] [Medline: 29614027]
45. Bower JE, Ganz PA, Irwin MR, Kwan L, Breen EC, Cole SW. Inflammation and behavioral symptoms after breast cancer treatment: do fatigue, depression, and sleep disturbance share a common underlying mechanism? J Clin Oncol 2011 Sep 10;29(26):3517-3522 [FREE Full text] [doi: 10.1200/JCO.2011.36.1154] [Medline: 21825266]
46. Huberty J, Puzia M, Eckert R, Larkey L. Cancer patients' and survivors' perceptions of the calm app: cross-sectional descriptive study. JMIR Cancer 2020 Jan 25;6(1):e16926 [FREE Full text] [doi: 10.2196/16926] [Medline: 32039812]
47. Huberty J, Eckert R, Larkey L, Kurka J, Rodríguez De Jesús SA, Yoo W, et al. Smartphone-based meditation for myeloproliferative neoplasm patients: feasibility study to inform future trials. JMIR Form Res 2019 Apr 29;3(2):e12662 [FREE Full text] [doi: 10.2196/12662] [Medline: 31033443]
48. Gok Metin Z, Karadas C, Izgu N, Ozdemir L, Demirci U. Effects of progressive muscle relaxation and mindfulness meditation on fatigue, coping styles, and quality of life in early breast cancer patients: an assessor blinded, three-arm, randomized controlled trial. Eur J Oncol Nurs 2019 Oct;42:116-125. [doi: 10.1016/j.ejon.2019.09.003] [Medline: 31520865]
49. Eyles C, Leydon GM, Hoffman CJ, Copson ER, Prescott P, Chorozoglou M, et al. Mindfulness for the self-management of fatigue, anxiety, and depression in women with metastatic breast cancer: a mixed methods feasibility study. Integr Cancer Ther 2015 Jan;14(1):42-56 [FREE Full text] [doi: 10.1177/1534735414546567] [Medline: 25161198]
50. Carlson LE, Garland SN. Impact of mindfulness-based stress reduction (MBSR) on sleep, mood, stress and fatigue symptoms in cancer outpatients. Int J Behav Med 2005;12(4):278-285. [doi: 10.1207/s15327558ijbm1204_9] [Medline: 16262547]
51. Ikeuchi K, Ishiguro H, Nakamura Y, Izawa T, Shinkura N, Nin K. The relation between mindfulness and the fatigue of women with breast cancer: path analysis. Biopsychosoc Med 2020 Feb 10;14:1 [FREE Full text] [doi: 10.1186/s13030-020-0175-y] [Medline: 32071613]
52. Piet J, Würtzen H, Zachariae R. The effect of mindfulness-based therapy on symptoms of anxiety and depression in adult cancer patients and survivors: a systematic review and meta-analysis. J Consult Clin Psychol 2012 Dec;80(6):1007-1020. [doi: 10.1037/a0028329] [Medline: 22563637]
53. Gong H, Ni CX, Liu YZ, Zhang Y, Su WJ, Lian YJ, et al. Mindfulness meditation for insomnia: a meta-analysis of randomized controlled trials. J Psychosom Res 2016 Oct;89:1-6. [doi: 10.1016/j.jpsychores.2016.07.016] [Medline: 27663102]
54. Tang NK, Harvey AG. Effects of cognitive arousal and physiological arousal on sleep perception. Sleep 2004 Feb 01;27(1):69-78. [doi: 10.1093/sleep/27.1.69] [Medline: 14998240]
55. Cincotta AL, Gehrman P, Gooneratne NS, Baime MJ. The effects of a mindfulness-based stress reduction programme on pre-sleep cognitive arousal and insomnia symptoms: a pilot study. Stress Health 2011 Aug;27(3):e299-e305. [doi: 10.1002/smi.1370]
56. Lyman GH, Greenlee H, Bohlke K, Bao T, DeMichele AM, Deng GE, et al. Integrative therapies during and after breast cancer treatment: ASCO endorsement of the SIO clinical practice guideline. J Clin Oncol 2018 Sep 01;36(25):2647-2655. [doi: 10.1200/JCO.2018.79.2721] [Medline: 29889605]
57. Salhofer I, Will A, Monsef I, Skoetz N. Meditation for adults with haematological malignancies. Cochrane Database Syst Rev 2016 Feb 03;2(2):CD011157 [FREE Full text] [doi: 10.1002/14651858.CD011157.pub2] [Medline: 26840029]
58. Zhang R, Yin J, Zhou Y. Effects of mindfulness-based psychological care on mood and sleep of leukemia patients in chemotherapy. Int J Nurs Sci 2017 Oct 10;4(4):357-361 [FREE Full text] [doi: 10.1016/j.ijnss.2017.07.001] [Medline: 31406777]
59. Cole B, Broer K, Hopkins C, Tisak J, Hunt R, McNally C, et al. A randomized controlled trial of spiritually-focused meditation in patients newly diagnosed with acute leukemia. Blood 2010 Nov 19;116(21):1519. [doi: 10.1182/blood.V116.21.1519.1519]
60. van Waart H, van Harten WH, Buffart LM, Sonke GS, Stuiver MM, Aaronson NK. Why do patients choose (not) to participate in an exercise trial during adjuvant chemotherapy for breast cancer? Psychooncology 2016 Aug;25(8):964-970. [doi: 10.1002/pon.3936] [Medline: 26282696]

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61. Ribeiro L, Atchley RM, Oken BS. Adherence to practice of mindfulness in novice meditators: practices chosen, amount of time practiced, and long-term effects following a mindfulness-based intervention. Mindfulness (N Y) 2018 Apr;9(2):401-411 [FREE Full text] [doi: 10.1007/s12671-017-0781-3] [Medline: 30881517]
62. Jongerius C, Russo S, Mazzocco K, Pravettoni G. Research-tested mobile apps for breast cancer care: systematic review. JMIR Mhealth Uhealth 2019 Feb 11;7(2):e10930 [FREE Full text] [doi: 10.2196/10930] [Medline: 30741644]
63. Lengacher CA, Johnson-Mallard V, Post-White J, Moscoso MS, Jacobsen PB, Klein TW, et al. Randomized controlled trial of mindfulness-based stress reduction (MBSR) for survivors of breast cancer. Psychooncology 2009 Dec;18(12):1261-1272. [doi: 10.1002/pon.1529] [Medline: 19235193]
64. Rosen KD, Paniagua SM, Kazanis W, Jones S, Potter JS. Quality of life among women diagnosed with breast cancer: a randomized waitlist controlled trial of commercially available mobile app-delivered mindfulness training. Psychooncology 2018 Aug;27(8):2023-2030. [doi: 10.1002/pon.4764] [Medline: 29766596]
65. Meinlschmidt G, Lee JH, Stalujanis E, Belardi A, Oh M, Jung EK, et al. Smartphone-based psychotherapeutic micro-interventions to improve mood in a real-world setting. Front Psychol 2016 Jul 28;7:1112 [FREE Full text] [doi: 10.3389/fpsyg.2016.01112] [Medline: 27516747]
66. Bower JE, Irwin MR. Mind-body therapies and control of inflammatory biology: a descriptive review. Brain Behav Immun 2016 Jan;51:1-11 [FREE Full text] [doi: 10.1016/j.bbi.2015.06.012] [Medline: 26116436]
67. Carmody J, Baer RA. Relationships between mindfulness practice and levels of mindfulness, medical and psychological symptoms and well-being in a mindfulness-based stress reduction program. J Behav Med 2008 Feb;31(1):23-33. [doi: 10.1007/s10865-007-9130-7] [Medline: 17899351]
68. Gethin R, Miquel P. The Foundations of Buddhism. Oxford, UK: Oxford University Press; 1998.
69. Van Dam NT, van Vugt MK, Vago DR, Schmalzl L, Saron CD, Olendzki A, et al. Mind the hype: a critical evaluation and prescriptive agenda for research on mindfulness and meditation. Perspect Psychol Sci 2018 Jan;13(1):36-61 [FREE Full text] [doi: 10.1177/1745691617709589] [Medline: 29016274]
70. Prasad K, Wahner-Roedler DL, Cha SS, Sood A. Effect of a single-session meditation training to reduce stress and improve quality of life among health care professionals: a "dose-ranging" feasibility study. Altern Ther Health Med 2011;17(3):46-49. [Medline: 22164812]
71. Kinnafick FE, Thøgersen-Ntoumani C, Duda J. The effect of need supportive text messages on motivation and physical activity behaviour. J Behav Med 2016 Aug;39(4):574-586 [FREE Full text] [doi: 10.1007/s10865-016-9722-1] [Medline: 26915963]
72. Ng JY, Ntoumanis N, Thøgersen-Ntoumani C, Deci EL, Ryan RM, Duda JL, et al. Self-determination theory applied to health contexts: a meta-analysis. Perspect Psychol Sci 2012 Jul;7(4):325-340. [doi: 10.1177/1745691612447309] [Medline: 26168470]
73. Cole-Lewis H, Kershaw T. Text messaging as a tool for behavior change in disease prevention and management. Epidemiol Rev 2010;32(1):56-69 [FREE Full text] [doi: 10.1093/epirev/mxq004] [Medline: 20354039]
74. Charlson ME, Carrozzino D, Guidi J, Patierno C. Charlson comorbidity index: a critical review of clinimetric properties. Psychother Psychosom 2022;91(1):8-35 [FREE Full text] [doi: 10.1159/000521288] [Medline: 34991091]
75. Savard J, Simard S, Ivers H, Morin CM. Randomized study on the efficacy of cognitive-behavioral therapy for insomnia secondary to breast cancer, part I: sleep and psychological effects. J Clin Oncol 2005 Sep 01;23(25):6083-6096. [doi: 10.1200/JCO.2005.09.548] [Medline: 16135475]
76. Quach CW, Langer MM, Chen RC, Thissen D, Usinger DS, Emerson MA, et al. Reliability and validity of PROMIS measures administered by telephone interview in a longitudinal localized prostate cancer study. Qual Life Res 2016 Nov;25(11):2811-2823 [FREE Full text] [doi: 10.1007/s11136-016-1325-3] [Medline: 27240448]
77. Yu L, Buysse DJ, Germain A, Moul DE, Stover A, Dodds NE, et al. Development of short forms from the PROMIS™ sleep disturbance and Sleep-Related Impairment item banks. Behav Sleep Med 2011 Dec 28;10(1):6-24 [FREE Full text] [doi: 10.1080/15402002.2012.636266] [Medline: 22250775]
78. Buysse DJ, Yu L, Moul DE, Germain A, Stover A, Dodds NE, et al. Development and validation of patient-reported outcome measures for sleep disturbance and sleep-related impairments. Sleep 2010 Jun;33(6):781-792 [FREE Full text] [doi: 10.1093/sleep/33.6.781] [Medline: 20550019]
79. Carney CE, Buysse DJ, Ancoli-Israel S, Edinger JD, Krystal AD, Lichstein KL, et al. The consensus sleep diary: standardizing prospective sleep self-monitoring. Sleep 2012 Feb 01;35(2):287-302 [FREE Full text] [doi: 10.5665/sleep.1642] [Medline: 22294820]
80. Huberty J, Eckert R, Dueck A, Kosiorek H, Larkey L, Gowin K, et al. Online yoga in myeloproliferative neoplasm patients: results of a randomized pilot trial to inform future research. BMC Complement Altern Med 2019 Jun 07;19(1):121 [FREE Full text] [doi: 10.1186/s12906-019-2530-8] [Medline: 31174535]
81. Mercier J, Ivers H, Savard J. A non-inferiority randomized controlled trial comparing a home-based aerobic exercise program to a self-administered cognitive-behavioral therapy for insomnia in cancer patients. Sleep 2018 Oct 01;41(10):zsy149. [doi: 10.1093/sleep/zsy149] [Medline: 30053196]
82. Savard MH, Savard J, Simard S, Ivers H. Empirical validation of the Insomnia Severity Index in cancer patients. Psychooncology 2005 Jun;14(6):429-441. [doi: 10.1002/pon.860] [Medline: 15376284]

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83. Fleming L, Randell K, Stewart E, Espie CA, Morrison DS, Lawless C, et al. Insomnia in breast cancer: a prospective observational study. Sleep 2019 Mar 01;42(3):zsy245. [doi: 10.1093/sleep/zsy245] [Medline: 30521041]
84. Schieber K, Niecke A, Geiser F, Erim Y, Bergelt C, Büttner-Teleaga A, et al. The course of cancer-related insomnia: don't expect it to disappear after cancer treatment. Sleep Med 2019 Jun;58:107-113. [doi: 10.1016/j.sleep.2019.02.018] [Medline: 31146122]
85. Zaki NF, Sabri YM, Farouk O, Abdelfatah A, Spence DW, Bahammam AS, et al. Depressive symptoms, sleep profiles and serum melatonin levels in a sample of breast cancer patients. Nat Sci Sleep 2020 Feb 13;12:135-149 [FREE Full text] [doi: 10.2147/NSS.S206768] [Medline: 32104121]
86. Duong N, Davis H, Robinson PD, Oberoi S, Cataudella D, Culos-Reed SN, et al. Mind and body practices for fatigue reduction in patients with cancer and hematopoietic stem cell transplant recipients: a systematic review and meta-analysis. Crit Rev Oncol Hematol 2017 Dec;120:210-216. [doi: 10.1016/j.critrevonc.2017.11.011] [Medline: 29198334]
87. Hommel G. A stagewise rejective multiple test procedure based on a modified Bonferroni test. Biometrika 1988 Jun;75(2):383-386. [doi: 10.1093/biomet/75.2.383]
88. Van Buuren S. Flexible Imputation of Missing Data. 2nd Edition. Boca Raton, FL, USA: CRC Press; 2018.
89. van Buuren S, Groothuis-Oudshoorn K. mice: multivariate imputation by chained equations in R. J Stat Soft 2011;45(3):1-67. [doi: 10.18637/jss.v045.i03]
90. Atreya CE, Kubo A, Borno HT, Rosenthal B, Campanella M, Rettger JP, et al. Being present: a single-arm feasibility study of audio-based mindfulness meditation for colorectal cancer patients and caregivers. PLoS One 2018 Jul 23;13(7):e0199423 [FREE Full text] [doi: 10.1371/journal.pone.0199423] [Medline: 30036361]
91. Chambers SK, Occhipinti S, Foley E, Clutton S, Legg M, Berry M, et al. Mindfulness-based cognitive therapy in advanced prostate cancer: a randomized controlled trial. J Clin Oncol 2017 Jan 20;35(3):291-297. [doi: 10.1200/JCO.2016.68.8788] [Medline: 27870567]
92. Henderson VP, Clemow L, Massion AO, Hurley TG, Druker S, Hébert JR. The effects of mindfulness-based stress reduction on psychosocial outcomes and quality of life in early-stage breast cancer patients: a randomized trial. Breast Cancer Res Treat 2012 Jan;131(1):99-109 [FREE Full text] [doi: 10.1007/s10549-011-1738-1] [Medline: 21901389]
93. Kenne Sarenmalm E, Mårtensson LB, Andersson BA, Karlsson P, Bergh I. Mindfulness and its efficacy for psychological and biological responses in women with breast cancer. Cancer Med 2017 May;6(5):1108-1122 [FREE Full text] [doi: 10.1002/cam4.1052] [Medline: 28421677]
94. Milbury K, Tsao AS, Liao Z, Owns A, Engle R, Gonzalez EA, et al. A research protocol for a pilot randomized controlled trial designed to examine the feasibility of a couple-based mind-body intervention for patients with metastatic lung cancer and their partners. Pilot Feasibility Stud 2018 Jan 24;4:37 [FREE Full text] [doi: 10.1186/s40814-018-0231-6] [Medline: 29416870]
95. Huberty J, Eckert R, Gowin K, Mitchell J, Dueck AC, Ginos BF, et al. Feasibility study of online yoga for symptom management in patients with myeloproliferative neoplasms. Haematologica 2017 Oct;102(10):e384-e388 [FREE Full text] [doi: 10.3324/haematol.2017.168583] [Medline: 28596279]
96. Huberty J, Vranceanu AM, Carney C, Breus M, Gordon M, Puzia ME. Characteristics and usage patterns among 12,151 paid subscribers of the calm meditation app: cross-sectional survey. JMIR Mhealth Uhealth 2019 Nov 03;7(11):e15648 [FREE Full text] [doi: 10.2196/15648] [Medline: 31682582]

Abbreviations

ANCOVA: analysis of covariance
CBT-I: cognitive behavioral therapy for insomnia
CRP: C-reactive protein
CSD: Consensus Sleep Diary
IL: interleukin
ISI: Insomnia Severity Index
MBSR: mindfulness-based stress reduction
MPN: myeloproliferative neoplasm
NIH: National Institutes of Health
PROMIS: Patient-Reported Outcomes Measurement Information System
RCT: randomized controlled trial
REDCap: Research Electronic Data Capture
SDT: self-determination theory
TNF-α: tumor necrosis factor-α

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Protocol

Tuberculosis Treatment Compliance Under Smartphone-Based Video-Observed Therapy Versus Community-Based Directly Observed Therapy: Protocol for a Cluster Randomized Controlled Trial

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Abstract

Background: The health care system in Thailand has struggled to cope with the COVID-19 pandemic, resulting in decreased administration of community-based directly observed therapy (DOT) for tuberculosis (TB). As an alternative to failed DOT, video-observed therapy (VOT) or the Thai asynchronous VOT system, "TH VOT," was devised. We developed a protocol for a study to test the superiority of VOT over DOT in ensuring treatment compliance.

Objective: We aim to compare the mean cumulative compliance days of TB patients and their observers under the VOT program with that of individuals under the DOT program during the intensive phase of TB treatment.

Methods: A cluster randomized controlled trial of pulmonary TB patients and their observers will be conducted over a 2-month period. This study will be conducted in the Hat Yai and Meuang Songkhla districts of Songkhla Province, Southern Thailand. A total of 38 observers working at 38 primary care units (PCUs) will be randomized equally into VOT and DOT groups. The TH VOT system will be implemented in 19 PCUs in the VOT group while the other 19 PCUs will continue with the traditional DOT program. Approximately 1-5 TB patients will be under observation, depending on the PCU jurisdiction in which the patients reside. The inclusion criteria for TB patients will be as follows: patients diagnosed with newly active pulmonary TB with a positive acid-fast bacilli sputum smear, aged >18 years, own a smartphone, and are able to use the LINE (Line Corporation) app. The exclusion criteria will be patients with a condition that requires the intervention of a specialist, rifampicin resistance according to a cartridge-based nucleic acid amplification test (GeneXpert MTB/RIF), unable to continue the treatment, and/or alcohol dependence. After the 2-month observation period, all sessions and follow-up clinical outcomes recorded will be retrieved. An intention-to-treat analysis will be performed to assess the compliance of both patients undergoing drug administration and their observers.

Results: The Human Research Ethics Committee, Faculty of Medicine, Prince of Songkla University approved the trial on February 19, 2021 (approval number 64-03618-9). The trial was funded in May 2021. The recruitment period will be from January 2022 to July 2022. The observation is scheduled to end by September 2022.

Conclusions: If the VOT shows superiority in observational compliance among patients and observers, the existing DOT policy will be replaced with VOT.

Trial Registration: Thai Clinical Trials Registry TCTR20210624002; https://www.thaiclinicaltrials.org/show/TCTR20210624002

International Registered Report Identifier (IRRID): DERR1-10.2196/38796

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KEYWORDS

VOT; VDOT; video-enhanced therapy; tuberculosis; health care system; observed therapy; video-observed therapy; treatment compliance; lung disease; randomized trial; digital health; telehealth; telemedicine

Introduction

Thailand is one of the 30 countries worldwide with the greatest tuberculosis (TB) burden [1]. During the past 2 years, Thailand has also been heavily impacted by the COVID-19 pandemic [2-4]. The pandemic led to a reduced frequency of administration of the existing community-based directly observed therapy (DOT) for TB patients and irregularity in its implementation [5-7].

Recently, a new strategy called "video-observed therapy" (VOT) was developed, which enables the provision of remote observation for patients with TB in contrast to conventional DOT. There are two forms of VOT: synchronous VOT (S-VOT) and asynchronous VOT (A-VOT) [8]. With S-VOT, observers video call their patients for real-time observation of drug administration, whereas with A-VOT, observers can review the video sent by patients at any time. Globally, A-VOT is more commonly used than S-VOT because it allows patients to record drug-administration sessions at their convenience; moreover, the video can be watched multiple times [8]. Thus, Thailand uses an A-VOT system to collect video records that can be audited [9]. Instead of a home visit in a community, an observer can flexibly use the A-VOT system to lower their travel costs and risk of SARS-CoV-2 infection.

Previous studies reported that in western countries, A-VOT has better patient compliance, cost utility, and acceptability than DOT [10-13]. However, these studies assessed A-VOT according to the number of observations of clinic-based and comprehensive community-based DOT. The irregular community-based DOT in Thailand cannot be applied to these previous studies that were conducted at an individual patient level. Owing to irregularities of DOT compliance among observers in Thailand [5], it is important to consider observation of therapy at the observer level.

To ensure an unbiased comparison between VOT and DOT, a cluster randomized controlled trial will be conducted based on a series of 2-month observations among pulmonary TB patients and their observers. A cluster randomized controlled trial design is required because in the Thai health system, patients within the same jurisdiction are observed by the same observers working at the primary care unit (PCU) of the jurisdiction.

The primary objective of this trial is to compare the mean cumulative number of compliance days of TB patients and their observers under the A-VOT program with those under the traditional community DOT program. In each jurisdiction, patient compliance with self-reporting daily drug-administration sessions and the number of doses observed will be assessed at an individual level. Patients in the same jurisdiction will represent a cluster and will be observed by the same observer. After 60 days of the intensive phase of TB treatment, the mean cumulative number of the patients' days with self-reporting and being observed in the VOT group and the DOT group will be compared at a cluster level. The secondary objectives include performing a descriptive review of the compliance activities and comparing the clinical outcomes between patients in the VOT and DOT groups. The clinical outcomes of sputum conversion and reporting of adverse events will also be ascertained, and statistically significant differences in the secondary outcomes between the VOT and DOT groups are not expected.

Methods

Study Setting

This study will be conducted in the Hat Yai and Meuang Songkhla districts of Songkhla Province, Southern Thailand, where a robust internet network is available. The study setting is based on 53 PCUs in the province, each including a TB staff member who worked as a DOT observer for at least 2 years. All people in the setting are regular smartphone users.

Background of the Existing A-VOT in Thailand

An A-VOT in Thailand (ie, the "TH VOT" system) was developed to enable remote observation of administration of anti-TB drugs taken by patients with TB [7]. The TH VOT system is a secured web system that allows patients and their observers to make a daily appointment for an observation session [14]. The system is compatible with any mobile web browsers without the requirement for installation of an additional app. A TH VOT app is also available on the Google Play store as an alternative platform that uses the system [15]. The patients and observers can easily register and use this VOT system through user authentication of the LINE (Line Corporation) app, which is the most commonly used app in Thailand [16-18]. With daily autonotification, both patients and observers will be notified about their appointment. The patients record themselves while taking their medication and upload the video to the server. The server then notifies the observer to review the video. Data regarding patient and observer compliance will be assessed according to our previous study protocol [9]. The usability of the system was tested during November 2021. It was found to function well with no technical problems and was usable among both TB patients and observers [9].

Study Design

We will perform a cluster randomized controlled trial. An observer will be assigned a cluster of patients with pulmonary TB that live in the same jurisdiction, either using DOT or VOT. We aim to observe each patient for 60 days during the intensive phase of their TB treatment. Daily compliance will be audited by one auditor who will supervise all observers in the study area according to a standard assessment protocol [9]. The study flow is summarized in Figure 1.

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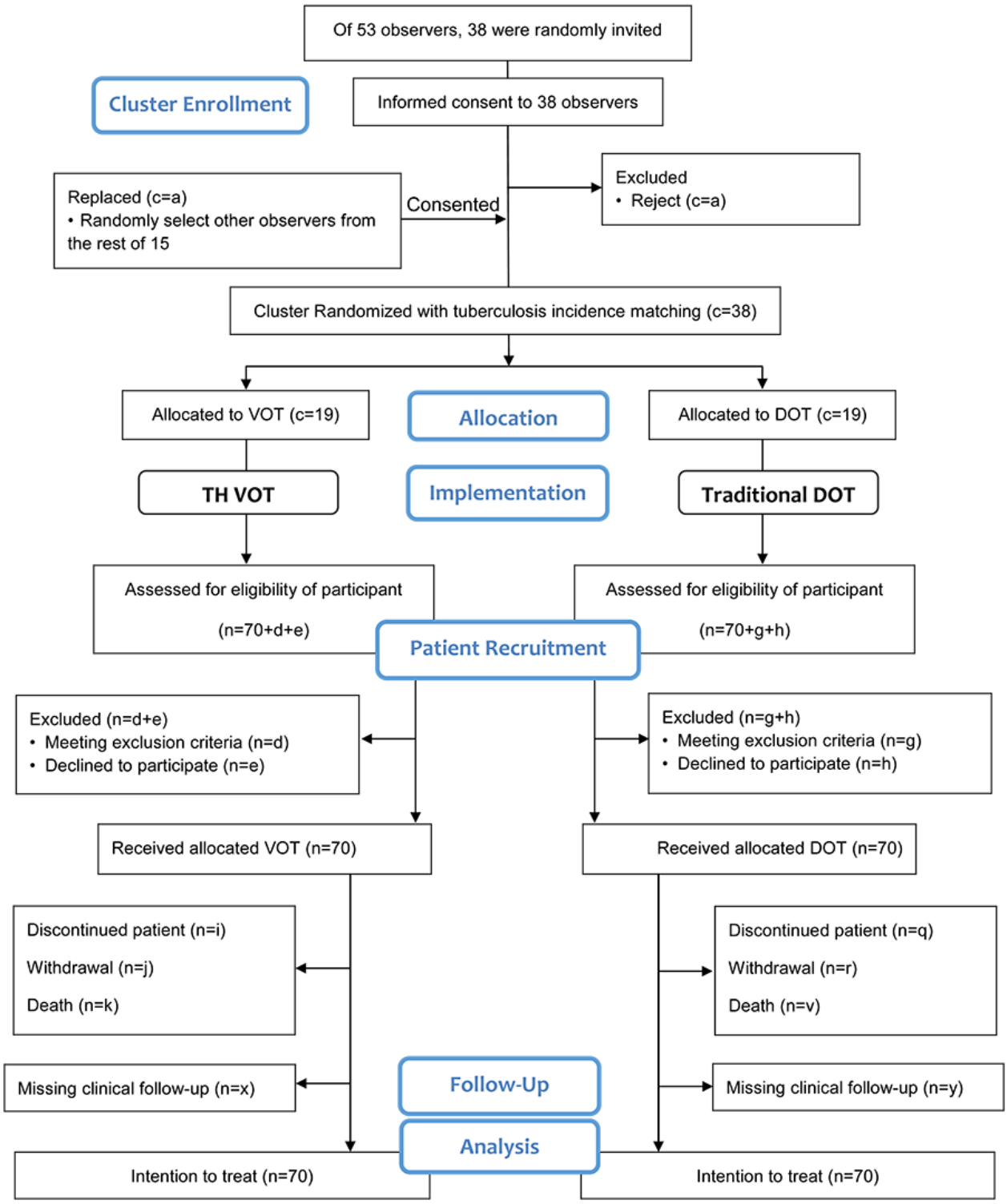
Figure 1. Study flow. c: number of clusters; n: number of patients with tuberculosis; DOT: directly observed therapy; TH VOT: Thailand's asynchronous video-observed therapy system; VOT: video-observed therapy.



Participants

Patients (Individual Level)

Patients will be considered eligible if they have newly active pulmonary TB diagnosed with a positive acid-fast bacilli (AFB) sputum smear, are aged>18 years, own a smartphone, and are able to use the LINE app. Participants are excluded if they have a condition that requires a specialist's intervention, have rifampicin-resistant TB as tested by GeneXpert, unable or ineligible to continue the treatment for 60 days, or have alcohol dependence.

Observers (Cluster Level)

There are 53 PCUs in the study area. Based on a random list of the PCU numbers generated using R software (1-53), the observers in the PCUs numbered 1 to 38 will be randomly allocated to groups. If they refuse to undergo allocation, the

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observers in the PCUs numbered 39 to 53 will be subsequently invited until 38 observers have been allocated.

Cointerventions

The following criteria will be applied to all patients and observers, regardless of their treatment group.

Patients with pulmonary TB will be diagnosed and treated by a general physician at Hat Yai Hospital or Songkhla Hospital. After diagnosis, the patients will be referred to the TB clinic. The patients will be provided zipped bags daily for 60 days, each with a daily dose of their isoniazid, rifampicin, pyrazinamide, and ethambutol (HRZE) drug regimen [7]. Patients who consent will be registered in the database by a TB nurse. The patients will be scheduled to take their medications (HRZE regimen) once a day. After each patient registration, the observer in the jurisdiction where the patient resides will be notified through autonotification on the official LINE app (either DOT or VOT).

For monetary compensation, the patients will receive 300 baht (US $8.68) immediately after registration to cover the cellular internet cost for the first month. Further compensation will be paid once the patients complete their 60-day intensive treatment without discontinuing the assigned intervention. They will receive 300 baht (US $8.68) to reimburse the cellular internet cost for the second month and 400 baht (US $11.57) for transportation of the sputum specimen for 3 consecutive days.

The observers will be compensated 600 baht (US $17.36) if they observe medication administration among patients for at least 15 out of 60 daily sessions. They will also be compensated for the cost of travel to visit their patients (4 baht or US $0.12 per kilometer).

Apart from the assigned intervention, the care of the patients at the TB clinic will remain the same as that during routine clinical practice. In the event of any suspected adverse events, the patients or their families will be able to phone the TB clinic for advice.

Assigned Interventions

Individual Level

VOT for Patients

After registration, TB patients in the VOT jurisdiction will be trained by the TB nurse regarding how to log in to the TH VOT system through the official LINE app, and record and upload a drug-taking video session according to the standard operating procedure (SOP) [7]. Briefly, the patients must set their video frame for clear visibility of their face. All tablets and capsules should also be clearly visible. Patients should pick up the pills from the drug plane (see [7]) and put them on their tongue. Next, they should swallow the pills with clear water from a (clear) glass, raise their tongue to show the sublingual area, and stick out their tongue to show the palate area.

DOT for Patients

For patients in the DOT jurisdiction, the TB nurse will provide a booklet for recording daily drug intake and whether the intake is observed by the assigned observer. The TB nurse will request the patients to return the booklet and all zipped bags on the follow-up day to claim their compensation. Each weekend, the auditor will notify the patients to capture and send the most recent page of the booklet to the official LINE chat, to which the observers do not have access.

Cluster Level

VOT for Observers

To avoid a learning curve on the VOT side, the observers will be trained to demonstrate to the patient on how to correctly record and approve the recorded video according to the SOP [7]. They will be required to undergo real or simulated activities for 1 month before the trial [9].

After being notified about patient recruitment, the observers will visit patients at home on the first day. They will confirm whether the patient can record the video according to the SOP [7]. The observer and the patient will set an appointment time for medication administration. Next, the patient will keep a daily record of the drug-taking session, note any adverse events, and send the video to the observer through the TH VOT system. The observer will review the video, approve the session, and provide any necessary advice through the LINE chat box. The observer will follow up with a phone call if the patient fails to send the video within 30 minutes of the appointment.

DOT for Observers

Based on the guideline provided by the National Tuberculosis Information Program (NTIP) [19], which specifies that only the observer takes notes, we added an instruction regarding TB patients self-recording their daily drug-taking session.

After being notified by the automatic system, the observer will conduct home-visit DOT as routine treatment. To validate the observer's recorded information, every weekend, the patient and the observer will be requested to take a photo of the most recent page of the booklet and send it to the auditor through the TH VOT official LINE system. The auditor will review these and record the number of daily compliant sessions in the database.

Procedures for the Auditor to Review Each Video/Picture Session

Sessions in the VOT Group

"Day" will be used as the time unit for judging compliance, and local times (Greenwich Mean Time+7 hours) will be recorded. The morning will begin at 12 AM (midnight) and the evening will end at 11:59 PM. However, daily compliance will be judged as "achieved within the cut-off time" if the patients take their medication and submit their videos before 6 AM the following day. The auditor will assess daily video sessions for patients within 24 hours of the video upload. Assessment items include whether the VOT has been administered, if the patients followed the SOP, and whether they were observed as per the protocol or properly reminded by their observer. The auditor will interpret each session based on the SOP modified from the previous study [9].

The patient will be considered to have daily compliance if the video is sent within the stipulated time and if its quality meets

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the following criteria: (1) the patient's face and the drug tablets/capsules are clearly visible in the video frame, (2) the pills are picked up from the drug plane and placed on the tongue, (3) the pills are swallowed with water from a (clear) glass, (4) the tongue is raised to show the sublingual area and stuck out to show the palate area, and (5) steps 2 to 4 are repeated until all pills are consumed.

The observers will be considered compliant if they adhere to the following quality standards: (1) correctly assess whether the patient performs the aforementioned steps, (2) note the number of pills consumed by the patient in the video correctly, and (3) follow up with patients via phone calls if they perform any procedure incorrectly. The TH VOT system can detect whether the observers have already made a phone call to their patients.

The daily session scored by the auditor will be recorded as 1 for daily compliance or 0 otherwise. The approval platform of the TH VOT system will automatically save all lists of the steps approved and the daily compliance score to the server database. If a patient does not record a video following the SOP, the auditor will make a phone call to remind the observer to correct the patient's mistakes. If a patient does not send a video for 7 consecutive days, they will be considered to have discontinued the intervention.

Sessions in the DOT Group

The auditor will score the daily compliance weekly based on the booklet photos sent by the TB patients and their observers. The patients will be considered to have daily compliance as reported (no audit). The auditor will make a phone call to the TB patients to confirm if they were observed as reported by their observer and to remind them to safely store the booklet and all zipped bags received from the TB clinic. If the patients report that they were not observed, the auditor will further investigate and record the observer's actions such as making phone calls instead of in-person visits to check patients' daily drug administration, missing patient appointments, or performing activities not included in the in-person DOT protocol.

A daily session reported by the observer will be scored as 1 for daily compliance as confirmed by the patients and 0 otherwise. If a patient misses a phone call twice or loses the booklet and/or the blank zipped bags, they will be discontinued from the intervention and their daily scores of the previous 7 days will be 0. All scored sessions will be recorded in the DOT record system of the server. The activities of observers not included in the in-person DOT will also be recorded.

Follow-ups

Each patient will be scheduled to return to the TB clinic for a follow-up on the 61st day. One day before the scheduled visit, the TB nurse will remind the patient in the DOT group to return the booklet and zipped bags. A deep-cough specimen will be collected early in the morning for 3 consecutive days. The sputum specimens will then be sent for an AFB test. The patients will be requested to notify their doctors about all adverse events occurring from the start of the treatment. The doctors will record the reported adverse events in the electronic health record (EHR) system and suggest appropriate treatment. If a patient misses their follow-up appointment, the responsible TB nurse will contact them and record the reasons in the EHR.

Data Collection

Data regarding observational activities will be recorded in the database, and data regarding clinical outcomes will be documented in the EHR system of the involved hospitals. These records will be retrieved for analysis at the end of the follow-up.

Outcomes

Primary Outcomes

Data recorded by the auditor will be compiled to understand the compliance of patients and observers in each arm. For compliance of the individual TB patients, the daily compliance scores rated by the auditor will be summed and divided by 60 (for the 60 days of observation) to obtain the percentage of cumulative days with compliance. For the whole group of patients, the mean cumulative number of compliance days will be calculated, taking the clusters into account.

Similarly, for compliance of the individual observers, the daily compliance score rated by the auditor will be calculated. The individual compliance unit of an observer will be the number of days each patient is actually observed. A higher number of patient doses observed will increase the overall contribution of the observer to the mean cumulative number of compliance days for the whole group of observers (VOT or DOT).

Secondary Outcomes

The clinical outcomes retrieved from the EHR, conversion of the AFB smear (three negative sputum smears as mentioned above), reporting of adverse events, missing the follow-up visit, and death during the 60-day follow-up period will be compared between the two groups.

For adverse events, information retrieved from the EHR system will be used to compare the reporting of adverse events by the observers in both the VOT and DOT groups.

Sample Size

Each jurisdictional area comprises 1000-5000 individuals. With an approximately annual TB incidence of 130 per 100,000 individuals in Songkhla Province [20], the sample size estimate is based on the assumption that each cluster can recruit approximately 1 to 5 TB patients within 9 months.

This study is designed to detect the cumulative percentage of compliant days of the observers in the VOT group for comparison with those in the DOT group. In development of the VOT, we conducted in-depth interviews of patients with TB and their observers, and discovered that the patients had an actual appointment for DOT only once during the entire follow-up period [7]. According to our previous study [9], the cumulative percentage of compliant days among patients in the VOT group was 65%. We assumed a difference in the cumulative compliance percentage of 64% (65/100–1/60)×100. We accepted 80% statistical power and a significance level of .05 using a one-tailed test. We assumed an intracluster correlation coefficient (ICC) of 0.2. We estimated that each cluster would have approximately three patients during the

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study. The sample size was calculated using the group-randomized control trial calculator [21]. The variance was set to 1.00 as the default. The formula does not require an exact variance estimation in the population as the ICC takes the variance into account. The required number of clusters for each arm was 19. Thus, the number of TB patients in each group would be 19×3=57. With a sample size inflation factor of 20% to compensate for the uncertainty of TB incidence in each jurisdictional area, a sample size of 70 TB patients is required in each arm.

Cluster Randomized Allocation

The observers that consent to participate will be randomly allocated to either VOT or DOT by a file generated using R software (R Foundation for Statistical Computing, Vienna, Austria). The sequence will be stored in the study server. Following the protocol of this trial, the participating observers will register themselves in the study LINE system. After they press the "accept" button, the observers will be informed about their allocated intervention group through the study LINE system.

Implementation of the Trial and Patient Information

The new patients with pulmonary TB will be recruited to the VOT or DOT group by the TB nurse, depending on the jurisdiction of residence of the observer.

The relevant information regarding the study will be provided to potential patients prior to the start of the trial, including highlighting who can observe them taking their medication (ie, their observer and the auditor) along with the possible assigned interventions (VOT or DOT). The observer's intervention group will not be revealed before they consent to participate. If the patients consent to participate, they will be assigned to the same intervention group as the observer of their PCU. They will be free to refuse the intervention at any point, and those who refuse or withdraw from the study will continue with traditional DOT without study data collection.

Blinding

The observers will disclose their assigned intervention to the auditor, TB nurses, and researchers. Next, the researchers will train the VOT observers to familiarize them with the TH VOT system [9]; the DOT observers will be requested to perform traditional DOT as routine care. Thus, none of the researchers or staff involved in the study will be blinded to the assigned interventions.

Statistical Analysis

Background information of patients and observers will be summarized using descriptive statistics.

An intention-to-treat analysis will be performed according to the randomized allocation. Thus, participants will be classified according to the intervention group to which they are assigned, regardless of their actual intervention.

We will compare the percentages of compliance between the two interventions at 60 days after treatment initiation. The 60-day compliance of the individuals will be defined as the percentage calculated using the following formula: (mean cumulative compliance days×100)/60. Our study is a cluster randomized controlled trial; thus, the cumulative number of compliant days of patients and observers will be nested in clusters. We will analyze their 60-day compliance considering that the same observer may monitor more than one patient. The intervention effect will be based on a linear mixed-effects model [22]. According to our study design, the intervention will be a fixed effect, whereas the cluster level will be a random effect.

The number of compliant days of patients and their observers will be visualized using solid green dots indicating the daily compliance of the individual subjects (Y-axis) and the elapsed number of days since starting the medication (X-axis). To investigate the dynamics of compliant days of the patients and observers over time, the mean cumulative number of complaint days within each group will also be plotted. The estimation of mean cumulative compliant days will range between 0 and 60, with 60 indicating that all participants in the group completed their daily sessions for 60 days. The function will be plotted using the mean cumulative number of compliant days (Y-axis) and the elapsed number of days since the start of medication administration (X-axis). Ideally, a steady increase in linear trend with a 45° slope indicates 100% compliance at any point from 0 to 60 days. Flattening of the slope represents a decline in the compliance percentage over time within the group.

Only descriptive statistical methods will be used on the aforementioned clinical outcomes and noncompliance activities of the observers because we may not have sufficient statistical power to detect small differences.

Ethics Approval

The Human Research Ethics Committee, Faculty of Medicine, Prince of Songkla University approved the trial on February 19, 2021 (approval number 64-03618-9).

Data Sharing

Data and programming R codes used in this trial are available in a GitHub repository [23].

Results

This study is being supported by the Fogarty International Center and the US National Institute of Allergy and Infectious Diseases of the US National Institutes of Health under Award Number D43 TW009522 (June 14, 2021). The researchers and Deputy Province Chief Medical Officer of Songkhla Provincial Public Health Office came to an agreement on the implementation of the VOT on June 22, 2021. Recruitment started in January 2022 and will end in July 2022. The observation period is scheduled to end by September 2022.

Discussion

Summary

The DOT program is not sustainable in Thailand, especially during the COVID-19 pandemic period. The VOT program is a good alternative to remotely observe TB patients. The present trial will confirm whether compliance is better in observers assigned to VOT than in observers assigned to standard

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community-based DOT. The cluster randomized superiority trial design will minimize confounding variables and strengthen the evidence base for VOT.

Potential Strengths

This study will assess the compliance effect on both patients and their observers in a cluster, which is more practical than using an individual effect. Compliance of both patients and observers under community-based DOT, which has rarely been studied, will be assessed in this cluster randomized superiority trial. Although treatment group blinding is not possible [24], both groups will be under the same level of monitoring by the auditor. Thus, the Hawthorne effect will be balanced.

Previous VOT versus DOT comparative studies [10,11] have been based on an overall assessment, including ordinary percentage of compliance. Our mean cumulative function analysis will determine periods with weak compliance. This can be used to reinforce observation compliance in the future.

Limitations

Compliance of the patients in the VOT group will be directly recorded in the video records, which are accurate. However, compliance in the DOT group is only based on the patient's report, which is not verifiable. The comparison is limited by the quality of compliance ascertainment in the DOT intervention group. The compliance of the DOT group may be overreported. If the compliance on the DOT side is lower than that on the VOT side, VOT would definitely be superior to DOT. Otherwise, the comparison may not be fully conclusive.

The main limitation is that the TB patients will not be followed up until the end of the treatment. The trial period is limited to the first 2 months of TB treatment (the intensive phase) owing to budget limitations. Sputum conversion is an uncertain surrogate of successful treatment. However, numerous studies have shown that sputum conversion is well-correlated with successful treatment [25-29].

Conclusion

The study should provide evidence to determine whether a new policy for using VOT instead of traditional DOT for TB patients who own smartphones could improve the accountability of TB treatment monitoring. If the VOT intervention is shown to be superior to the community-based DOT intervention, we will advocate for VOT to replace the existing DOT.

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Conflicts of Interest

None declared.

Multimedia Appendix 1
CONSORT-eHEALTH checklist V 1.6.1.
[PDF File (Adobe PDF File), 1298 KB - resprot_v11i7e38796_app1.pdf]

References

1. Global tuberculosis report. World Health Organization. 2020. URL: https://apps.who.int/iris/bitstream/handle/10665/336069/9789240013131-eng.pdf [accessed 2021-04-21]
2. Caren GJ, Iskandar D, Pitaloka DA, Abdulah R, Suwantika AA. COVID-19 pandemic disruption on the management of tuberculosis treatment in Indonesia. J Multidiscip Healthc 2022;15:175-183. [doi: 10.2147/JMDH.S341130] [Medline: 35115781]
3. Fekadu G, Jiang X, Yao J, You JHS. Cost-effectiveness of video-observed therapy for ambulatory management of active tuberculosis during the COVID-19 pandemic in a high-income country. Int J Infect Dis 2021 Dec;113:271-278 [FREE Full text] [doi: 10.1016/j.ijid.2021.10.029] [Medline: 34688946]
4. Katewongsa P, Widyastaria DA, Saonuam P, Haematulin N, Wongsingha N. The effects of the COVID-19 pandemic on the physical activity of the Thai population: evidence from Thailand's Surveillance on Physical Activity 2020. J Sport Health Sci 2021 May;10(3):341-348 [FREE Full text] [doi: 10.1016/j.jshs.2020.10.001] [Medline: 33039655]
5. Pungrassami P, Johnsen SP, Chongsuvivatwong V, Olsen J. Has directly observed treatment improved outcomes for patients with tuberculosis in southern Thailand? Trop Med Int Health 2002 Mar;7(3):271-279 [FREE Full text] [doi: 10.1046/j.1365-3156.2002.00849.x] [Medline: 11903990]
6. Pungrassami P, Chongsuvivatwong V. Are health personnel the best choice for directly observed treatment in southern Thailand? A comparison of treatment outcomes among different types of observers. Trans R Soc Trop Med Hyg 2002;96(6):695-699. [doi: 10.1016/s0035-9203(02)90354-8] [Medline: 12625153]

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7. Kumwichar P, Chongsuvivatwong V, Prappre T. Development of a video-observed therapy system to improve monitoring of tuberculosis treatment in Thailand: mixed-methods study. JMIR Form Res 2021 Jul 27;5(7):e29463 [FREE Full text] [doi: 10.2196/29463] [Medline: 34313602]
8. Garfein RS, Doshi RP. Synchronous and asynchronous video observed therapy (VOT) for tuberculosis treatment adherence monitoring and support. J Clin Tuberc Other Mycobact Dis 2019 Dec;17:100098 [FREE Full text] [doi: 10.1016/j.jctube.2019.100098] [Medline: 31867442]
9. Kumwichar P, Chongsuvivatwong V, Prappre T. Video-observed therapy with a notification system for improving the monitoring of tuberculosis treatment in Thailand: usability study. JMIR Form Res 2022 May 06;6(5):e35994 [FREE Full text] [doi: 10.2196/35994] [Medline: 35522469]
10. Beeler Asay GR, Lam CK, Stewart B, Mangan JM, Romo L, Marks SM, et al. Cost of tuberculosis therapy directly observed on video for health departments and patients in New York City; San Francisco, California; and Rhode Island (2017–2018). Am J Public Health 2020 Nov;110(11):1696-1703. [doi: 10.2105/ajph.2020.305877]
11. Story A, Aldridge RW, Smith CM, Garber E, Hall J, Ferenando G, et al. Smartphone-enabled video-observed versus directly observed treatment for tuberculosis: a multicentre, analyst-blinded, randomised, controlled superiority trial. Lancet 2019 Mar 23;393(10177):1216-1224 [FREE Full text] [doi: 10.1016/S0140-6736(18)32993-3] [Medline: 30799062]
12. Ravenscroft L, Kettle S, Persian R, Ruda S, Severin L, Doltu S, et al. Video-observed therapy and medication adherence for tuberculosis patients: randomised controlled trial in Moldova. Eur Respir J 2020 Aug;56(2):2000493 [FREE Full text] [doi: 10.1183/13993003.00493-2020] [Medline: 32381495]
13. Doltu S, Ciobanu A, Sereda Y, Persian R, Ravenscroft L, Kasyan L, et al. Short and long-term outcomes of video observed treatment in tuberculosis patients, the Republic of Moldova. J Infect Dev Ctries 2021 Sep 29;15(9.1):17S-24S [FREE Full text] [doi: 10.3855/jidc.14601] [Medline: 34609956]
14. Medication adherence interface. THVOT. URL: https://thvot.com/thvotweb/app/ [accessed 2022-04-20]
15. Google Play. URL: https://play.google.com/store?hl=th&gl=TH [accessed 2022-04-20]
16. Choemprayong S, Charoenlap C, Piromsopa K. Exploring usability issues of a smartphone-based physician-to-physician teleconsultation app in an orthopedic clinic: mixed methods study. JMIR Hum Factors 2021 Dec 20;8(4):e31130 [FREE Full text] [doi: 10.2196/31130] [Medline: 34931991]
17. Songsermpong S, Bunluesin S, Khomgongsuwan P, Junthon S, Cazabon D, Moran AE, et al. Innovations to sustain non-communicable disease services in the context of COVID-19: report from Pakkred District, Nonthaburi Province, Thailand. Glob Heart 2021 Jun 10;16(1):44 [FREE Full text] [doi: 10.5334/gh.1003] [Medline: 34211830]
18. Amatavete S, Lujintanon S, Teeratakulpisarn N, Thitipatarakorn S, Seekaew P, Hanaree C, et al. Evaluation of the integration of telehealth into the same-day antiretroviral therapy initiation service in Bangkok, Thailand in response to COVID-19: a mixed-method analysis of real-world data. J Int AIDS Soc 2021 Oct;24(Suppl 6):e25816 [FREE Full text] [doi: 10.1002/jia2.25816] [Medline: 34713623]
19. National Tuberculosis Control Programme guideline, Thailand 2021. Bureau of Tuberculosis, Department of Disease Control Thailand. URL: https://www.tbthailand.org/download/Manual/NTP2018.pdf [accessed 2022-04-20]
20. National Tuberculosis Information Dashboard. Bureau of Tuberculosis, Department of Disease Control Thailand. URL: http://tbcmthailand.ddc.moph.go.th/UIForm/Tableau/TEST_tbcm.php [accessed 2020-12-15]
21. Parallel Group- or Cluster-Randomized Trials (GRTs). Research Methods Resources National Institutes of Health. URL: https://researchmethodsresources.nih.gov/methods/grt [accessed 2022-04-02]
22. Schunck R, Perales F. Within- and between-cluster effects in generalized linear mixed models: a discussion of approaches and the Xthybrid command. Stata J 2017 Mar 01;17(1):89-115. [doi: 10.1177/1536867x1701700106]
23. Cluster_RCT_VOT_vs_DOT. GitHub. URL: https://github.com/ponlagrit/Cluster_RCT_VOT_vs_DOT [accessed 2022-06-17]
24. Dron L, Taljaard M, Cheung YB, Grais R, Ford N, Thorlund K, et al. The role and challenges of cluster randomised trials for global health. Lancet Glob Health 2021 May;9(5):e701-e710 [FREE Full text] [doi: 10.1016/S2214-109X(20)30541-6] [Medline: 33865475]
25. Kayigamba FR, Bakker MI, Mugisha V, Gasana M, Schim van der Loeff MF. Sputum completion and conversion rates after intensive phase of tuberculosis treatment: an assessment of the Rwandan control program. BMC Res Notes 2012 Jul 16;5:357 [FREE Full text] [doi: 10.1186/1756-0500-5-357] [Medline: 22800438]
26. Bisognin F, Amodio F, Lombardi G, Bacchi Reggiani ML, Vanino E, Attard L, et al. Predictors of time to sputum smear conversion in patients with pulmonary tuberculosis under treatment. New Microbiol 2019 Jul;42(3):171-175 [FREE Full text] [Medline: 31157399]
27. Azarkar Z, Sharifzadeh G, Ebrahimzadeh A, Olumi S. Time to sputum smear conversion in smear-positive pulmonary tuberculosis patients and factors for delayed conversion. Iran J Med Sci 2016 Jan;41(1):44-47 [FREE Full text] [Medline: 26722144]
28. Lv L, Li T, Xu K, Shi P, He B, Kong W, et al. Sputum bacteriology conversion and treatment outcome of patients with multidrug-resistant tuberculosis. Infect Drug Resist 2018;11:147-154. [doi: 10.2147/IDR.S153499] [Medline: 29416359]
29. Pefura-Yone EW, Kengne AP, Kuaban C. Non-conversion of sputum culture among patients with smear positive pulmonary tuberculosis in Cameroon: a prospective cohort study. BMC Infect Dis 2014 Mar 11;14(1):138 [FREE Full text] [doi: 10.1186/1471-2334-14-138] [Medline: 24618155]

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Abbreviations

AFB: acid-fast bacilli
A-VOT: asynchronous video-observed therapy
DOT: directly observed therapy
EHR: electronic health record
HRZE: isoniazid, rifampicin, pyrazinamide, and ethambutol
ICC: intracluster correlation coefficient
NTIP: National Tuberculosis Information Program
PCU: primary care unit
SOP: standard operating procedure
S-VOT: synchronous video-observed therapy
TB: tuberculosis
TH VOT: Thai video-observed therapy
VOT: video-observed therapy

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Protocol

Efficacy of Group Exercise–Based Cancer Rehabilitation Delivered via Telehealth (TeleCaRe): Protocol for a Randomized Controlled Trial

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Abstract

Background: Access to rehabilitation to support cancer survivors to exercise is poor. Group exercise–based rehabilitation may be delivered remotely, but no trials have currently evaluated their efficacy.

Objective: We aimed to evaluate the efficacy of a group exercise–based cancer rehabilitation program delivered via telehealth compared to usual care for improving the quality of life of cancer survivors.

Methods: A parallel, assessor-blinded, pragmatic randomized controlled trial with embedded cost and qualitative analysis will be completed. In total, 116 cancer survivors will be recruited from a metropolitan health network in Melbourne, Victoria, Australia. The experimental group will attend an 8-week, twice-weekly, 60-minute exercise group session supervised via videoconferencing supplemented by a web-based home exercise program and information portal. The comparison group will receive usual care including standardized exercise advice and written information. Assessments will be completed at weeks 0 (baseline), 9 (post intervention), and 26 (follow-up). The primary outcome will be health-related quality of life measured using the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire at week 9. Secondary measures include walking capacity (6-minute walk test), physical activity (activPAL accelerometer), self-efficacy (Health Action Process Approach Questionnaire), and adverse events. Health service data including hospital length of stay, hospital readmissions, and emergency department presentations will be recorded. Semistructured interviews will be completed within an interpretive description framework to explore the patient experience. The primary outcome will be analyzed using linear mixed effects models. A cost-effectiveness analysis will also be performed.

Results: The trial commenced in April 2022. As of June 2022, we enrolled 14 participants.

Conclusions: This trial will inform the future implementation of cancer rehabilitation by providing important data about efficacy, safety, cost, and patient experience.

Trial Registration: Australian New Zealand Clinical Trials Registry ACTRN12621001417875; https://tinyurl.com/yc5crwtr

International Registered Report Identifier (IRRID): PRR1-10.2196/38553

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KEYWORDS

telehealth; exercise; telerehabilitation; physical activity; supportive care; cancer

Introduction

There are clear clinical practice recommendations to integrate exercise-based rehabilitation into cancer care [1,2]. However, access to exercise-based cancer rehabilitation is poor with just 1 in 200 cancer survivors able to access appropriate support [3]. This is a major concern given that exercise-based rehabilitation mitigates negative side effects of cancer treatment such as fatigue and depression and improves physical function and quality of life [4]. High levels of exercise after diagnosis can reduce the risk of developing comorbidities such as cardiovascular disease and is associated with a reduction in cancer-related death [5] and cancer recurrence [6]. Exercise-based cancer rehabilitation can facilitate the return to normalcy and establish positive lifestyle changes to prevent long-term morbidity [7].

In-person interventions are the standard for delivering exercise-based cancer rehabilitation. While effective at improving patient outcomes, in-person exercise-based cancer rehabilitation programs delivered in clinical settings often have poor adherence and attendance [8,9] owing to patient-related issues such as fatigue [10] and managing competing medical demands [11]. Other issues that can limit access and diminish the effectiveness of exercise-based cancer rehabilitation include logistical problems such as cost, parking, and location [3,11,12].

Telehealth may overcome barriers related to in-person care delivery. Telehealth uses technologies such as videoconferencing, telephone, and mobile apps for diagnosis, treatment, and prevention of disease [13]. An advantage of telehealth is convenience, and it has been described by cancer survivors as minimizing the treatment burden [14]. Rehabilitation delivered by telehealth (hereafter referred to as "telerehabilitation") can be used to implement the key elements of cancer rehabilitation including exercise demonstration, instruction, observation, and information provision. The feasibility of telerehabilitation has been established in a cancer context. Telerehabilitation interventions are safe, have good adherence, and provide a positive patient experience among cancer survivors [15,16]. Individual telerehabilitation improves physical activity levels and quality of life of cancer survivors when compared to usual care without exercise [17-19]. A phone-based telerehabilitation intervention compared with usual care focused on pain reduction, improved mobility, reduced pain, and hospital length of stay in people with advanced cancer [20]. However, despite the broad variety of telehealth technologies that are available, most trials investigating exercise telehealth interventions for people with cancer have used simple, individual telephone interventions [21-24].

Current telehealth approaches to exercise rehabilitation are limited in their ability to replicate traditional cancer rehabilitation. To date, no trials have evaluated the effectiveness of web-based group exercise for people with cancer [15,23]. Group exercise interventions may be superior to other exercise interventions [25] and are the most common way to deliver cancer rehabilitation in health services [3]. Groups provide a positive environment for exercise for cancer survivors [7] and allow opportunities for peer support, modeling, and feedback [26]. Groups are also an efficient way to deliver exercise that may facilitate access and be less resource-intensive on health services. There is potential for exercise groups to be delivered via telehealth as videoconferencing technology can enable the supervision of multiple participants. Since the COVID-19 pandemic, there has been a surge in the use of telehealth such as for the provision of group exercise [16,27]. Therefore, robust trials of group telerehabilitation including exercise for cancer survivors are required to determine their efficacy and effectiveness.

The primary aim of this pragmatic randomized controlled trial is to evaluate the efficacy of an exercise-based telerehabilitation program compared to usual care for improving the quality of life of cancer survivors. Secondary aims are to compare the effects of cancer telerehabilitation on walking capacity, physical activity levels, self-efficacy, and adverse events. We will also determine the costs associated with telerehabilitation and explore, in depth, the experience of cancer survivors completing cancer telerehabilitation.

Methods

Study Design

We will complete a prospective, parallel, assessor-blinded, pragmatic randomized controlled trial comparing the efficacy and cost-effectiveness of 8 weeks of group exercise–based cancer telerehabilitation to usual care (see Figure 1 for the study flowchart). Participants will be assessed at weeks 0 (baseline), 9 (post intervention), and 26 (follow-up) (Multimedia Appendix 1). Quantitative trial outcomes will be reported in accordance with the CONSORT (Consolidated Standards of Reporting Trials) statement [28], qualitative outcomes reported with consolidated criteria for reporting qualitative research [29] and health economic analysis reported with the Consolidated Health Economic Evaluation Reporting Standards [30]. The qualitative component of the study will be conducted using an interpretivist paradigm, which recognizes that multiple realities exist and this is affected by context [31].

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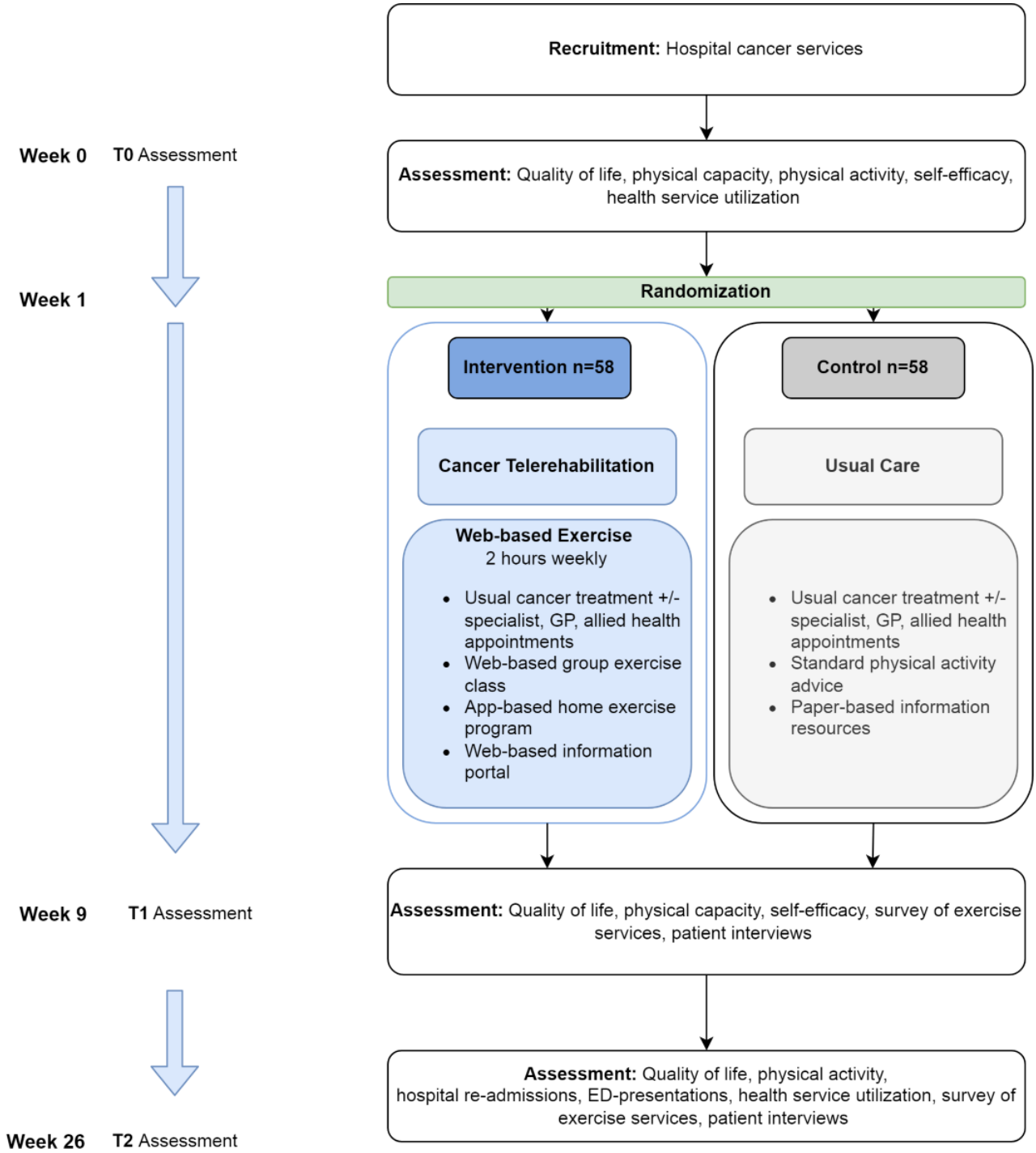
Figure 1. CONSORT (Consolidated Standards of Reporting Trials) diagram for the TeleCaRe trial. ED: emergency department; GP: general practitioner.



Randomization Procedures

Eligible participants who have completed baseline measurements will be randomly allocated to the telerehabilitation group or usual care control group using a concealed method in accordance with a web-based computer-generated randomization program using permuted blocks of 4, 6, and 8 participants. Allocations will be prepared prior to trial commencement by an independent researcher with no role in participant recruitment, trial administration of intervention delivery, or assessments. The trial coordinator will allocate participants after baseline assessment by contacting the independent researcher via email for random group allocation.

Setting

The trial will be conducted in a large public health network in Melbourne, Victoria, Australia, which services approximately 3000 cancer survivors annually. Participants will be recruited from cancer services at 3 metropolitan sites within this single health network.

Ethics Approval

The TeleCaRe trial has been approved by the Eastern Health and La Trobe University Human Research Ethics Committees (E21-012-74698) and is funded by the Victorian Cancer Agency.

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Patient Selection and Consent

Eligible participants will be identified by any member of the cancer services clinical team at the health network (eg, oncologists, nursing staff, and physiotherapists). Potential participants will be advised about the trial by clinic staff verbally or through flyers. If a patient consents, he/she will be contacted by a member of the research team who will provide details of the trial and arrange an outpatient appointment at home or at the clinical site to provide an opportunity for questions to be clarified and to provide written informed consent.

Inclusion and Exclusion Criteria

Participants will be eligible if they are aged 18 years and over, have a cancer diagnosis and are receiving cancer treatment (palliative or curative intent) or are within 12 months of completing adjuvant therapy (except for long term oral hormonal therapies), are functioning independently in the community (Australian Karnofsky Performance Status [AKPS] score≥60), are at a low risk of falls (Falls Risk for Older People in the Community score<4), are able to speak conversational English so participants can engage effectively in videoconferencing, have access to and be willing to use the internet, and be able to give written informed consent.

Participants will be excluded if they are medically unfit to participate in exercise as determined by a physiotherapist or medical practitioner on the basis of published recommendations [32], are residing in residential care or are an inpatient, or have cognitive impairment precluding the ability to provide written informed consent as assessed by their treating clinician.

Intervention

All participants will receive their usual medical care, which may include adjuvant, neoadjuvant, or palliative treatment, specialist, nursing and other health outpatient appointments (eg, to see a physiotherapist) and visits to their general practitioner.

As part of the trial, all participants will be provided with written educational materials relating to different aspects of cancer recovery (eg, exercise, nutrition, and fatigue) via standardized print or digital material readily available from the hospital.

Usual care in the community involves very little exercise support in relation to exercise. As part of the trial, usual care also includes standardized verbal and written advice to complete physical activity in line with current recommendations (aim for 3 times weekly exercise for 30 minutes, including twice weekly strength training) [4]. All participants will also have the opportunity to discuss their ongoing rehabilitation needs at the end of the 8-week intervention period. They will be provided written information for referral to appropriate local services for ongoing support if required in line with usual practice at the health service.

Experimental Group: Exercise-Based Cancer Telerehabilitation

In addition to usual care, participants randomized to the experimental group (telerehabilitation) will receive a 60-minute group exercise delivered by a physiotherapist via videoconferencing (Zoom) twice-weekly for 8 weeks. Exercise will comprise cardiovascular and resistance training guided by published recommendations [4]. Exercise sessions will be individually tailored and include the use of free weights, resistance bands, body weight, and functional activities. Supervised aerobics (eg, marching in place and side-stepping) will comprise the cardiovascular component. Participants will be provided with an exercise band, and the exercise program will be supplemented by participants' own exercise equipment or household items. The therapist will choose an exercise variation (eg, bicep curl using weights or with exercise band) based on the equipment available to the participant. Various upper- and lower-body stretches and balance exercises will be incorporated as required. Exercise intensity will be monitored during the exercise class using a Fitbit device (Fitbit Inspire) and modified Borg scale. The Fitbit will also be used for participants to self-monitor their physical activity levels throughout the 8-week intervention. A home exercise program will supplement exercise-based telerehabilitation sessions and be delivered via a web application (Physitrack). The home exercise program will encourage one additional 30-minute aerobic exercise session per week (eg, walking) during the intervention period and will be updated at the end of the rehabilitation program to encourage participants to conduct twice-weekly strength training and 3 times weekly aerobic training after the 8-week intervention period. Participants will also be provided education materials relating to different aspects of cancer recovery (eg, nutrition, emotions, and fatigue) via a web-based information portal (iLearn, Totara Learning Solutions, Wellington, New Zealand) (Table 1).

Physiotherapists conducting assessments and providing the exercise intervention will be trained in exercise rehabilitation for cancer survivors. They will participate in a 1-day web-based training session about cancer care and complete a self-directed web-based module about cancer-related fatigue management. They will also participate in 2 interactive 2-hour in-person workshops about exercise prescription for cancer survivors. They will also have access to a website [33] that provides education for clinicians providing exercise-based cancer rehabilitation. Physiotherapists will receive monthly clinical supervision in line with health service policy and regular mentoring with senior research staff. The fidelity of the intervention will be monitored by recording the content of exercise sessions using logbooks, including the number and duration of completed sessions. Participants in both groups will also be asked whether they received any exercise-based intervention outside of the trial at the 9-week assessment and 4-month follow-up.

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Table 1. Intervention and comparison group descriptions using the template for description and replication checklist (TIDier).

	Experimental group	Comparison group
Brief name	• Group exercise–based cancer telerehabilitation	• Usual care
Why	• Exercise interventions delivered via telehealth can be safe and effective for improving the quality of life of cancer survivors and offer convenience	• Cancer survivors are not routinely offered cancer rehabilitation
What: materials	• 2× weekly web-based supervised, group-based exercise (approximately 6 participants per group; Zoom) • Participants will be provided with an exercise band • Participants to receive a web-based (Physitrack), individualized home exercise program, and exercise band • Participants to receive access to a web-based information portal (iLearn) with webinars, web-based information handouts, and resources about cancer care and recovery including exercise • Participants will wear a physical activity device (Fitbit Inspire) continuously during waking hours for 8 weeks • Written information about local exercise services provided at 8 weeks	• Standard information booklets about cancer care and recovery including exercise • Written information about local exercise services provided at 8 weeks
What procedures		
Provider	• One physiotherapist with oncology experience provided by the hospital will provide exercise guidelines in verbal and written format and the web-based group intervention • One allied health assistant will support the web-based group intervention	• Usual care team (eg, specialist, general practitioner, and allied health professional) • One physiotherapist with oncology experience provided by the hospital will provide exercise guidelines in verbal and written format
How	• Supervised sessions via videoconference supplemented by web-based information above • Physical activity device for remote exercise and physical activity monitoring	• In person or via telehealth as available
Where	• Intervention clinicians are clinic-based • Participants receive an exercise program at home • Participants continue to receive usual cancer care in hospital or at home as indicated	• Participants receive usual care in hospital or at home as indicated
When and how much		
Intensity	• Cardiovascular: moderate (BORG 3-5, maximum heart rate=60%-85%) • Resistance: 2-3 sets with 10-12 repetitions • Participants progressed when completing 3 sets with 10-12 repetitions until fatigue	• Advised to undertake physical activity in accordance with current physical activity recommendations: advised to undertake physical activity in accordance with current physical activity recommendations • Moderate activity (cardiovascular: maximum heart rate=60%-85%, resistance=2-3 sets, 10-12 repetitions)
Frequency	• 2× weekly supervised • 1× weekly unsupervised	• Advised to participate in 3x weekly unsupervised physical activity
Session time	• 60-minute web-based exercise group • 30-minute unsupervised exercise session	• Advised to complete 30-minute unsupervised physical activity
Overall duration	• 8 weeks	• 8 weeks
Tailoring	• Individualized exercise program based on initial consultation and goals	• None

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	Experimental group	Comparison group
Trial fidelity	• Physiotherapists who are employed by the health service to provide the intervention will receive training and mentoring by a senior research physiotherapist with oncology experience • Electronic exercise log via the Physitrack app and Fitbit Inspire • Records of the content, number, and duration of completed web-based group sessions • Clinical supervision of therapists in accordance with standard health service policy • Exercise interventions that patients have participated in outside of the trial will be recorded	• Physiotherapists who are employed by the health service to provide assessment and advice will receive training and mentoring by a senior research physiotherapist with oncology experience • Clinical supervision of therapists in accordance with standard health service policy • Exercise interventions that patients have participated in outside of the trial will be recorded

Study Outcomes

Participants will complete an assessment of health-related quality of life at weeks 0, 9, and 26. Immediately post intervention (week 9) is the primary end point. Walking capacity and self-efficacy will also be assessed at weeks 0 and 9. Physical activity and health service usage utilization will be assessed at weeks 0 and 26. A clinician blind to group allocation will complete the assessments. Primary and secondary outcomes are outlined in Table 2.

Table 2. Primary and secondary outcomes.

Outcomes	Measures or sources	Definitions	Time points
Primary outcome			
Health-related quality of life	European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire	Score on the validated quality-of-life questionnaire before and after the intervention. Primary end point is postintervention.	• Week 0 • Week 9 • Week 26
Secondary outcomes			
Physical activity	activPAL accelerometer	Time spent in moderate to vigorous activity, walking, sitting, and step count before and after the intervention. Participants will wear the activity monitor continuously for 8 consecutive days. Only complete 24-hour recording days will be included for analysis. However, as monitors may need to be removed for the purpose of swimming or bathing, evidence of nonwear matching with an activity logbook will still be included.	• Week 0 • Week 26
Physical capacity	6-Minute walk test	Walk distance (in meters) before and after the intervention.	• Week 0 • Week 9
Self-efficacy for physical activity	Questionnaire developed using the Health Action Process Approach [34] (Multimedia Appendix 2)	Score on the self-efficacy questionnaire for physical activity before and after the intervention.	• Baseline • Week 9
Emergency department presentations	Hospital database and electronic medical record	Number of emergency department presentations during the trial period.	• Week 26
Hospital readmissions	Hospital database and electronic medical record	Number of hospital readmissions during the trial period, associated inpatient days, and duration between with each admission.	• Week 26
Health service utilization	Questionnaire (Multimedia Appendix 3)	Frequency of allied health and medical services, pharmaceutical use, and hospital admissions (external to the health network).	• Week 0 • Week 26
Audit of exercise interventions	Questionnaire	Frequency, type, and duration of any exercise interventions completed outside the trial.	• Week 9 • Week 26

Adverse events as defined by the World Health Organization [35] will be recorded from medical records, direct observation during classes, and by participant self-report to document the safety of the intervention. The event may or may not be related to the intervention but occurs while the person is participating in the intervention phase of the trial. Adverse events will be categorized as either minor or serious and as related or unrelated and expected or unexpected events. A minor adverse event is defined as an incident that occurs while a person is participating in the intervention that results in no injury or minor injury (eg, exacerbation of pre-existing musculoskeletal pain) that requires no or minor medical intervention. A serious adverse event is

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defined as an incident that occurs while a person is participating in the intervention that results in death, serious injury, or hospitalization (eg, injurious fall resulting in fracture). Serious adverse events will also be recorded for the usual care group. In addition, adverse events will be reported and graded using the Common Terminology Criteria for Adverse Events Version 4 [36]. The consequences of a serious adverse event in the control group (eg, hospitalization and emergency department admission) will be captured by our health service utilization questionnaire and medical record audit. Reasons for nonparticipation in an exercise session or noncompletion of the program will be recorded (eg, pain, fatigue, and unwell).

Consumer Perceptions

Semistructured interviews will be completed on 2 occasions (immediately after the intervention at week 9 and at week 26) with experimental group participants to explore in detail the experience of people participating in exercise-based cancer telerehabilitation and of behavior change. A purposive sample of participants in the telerehabilitation group will be asked questions relating to satisfaction, barriers, and facilitators to accessing cancer telerehabilitation and perceptions about sustaining physical activity on program completion. The same group will be interviewed at both time points. We will conduct interviews until we reach data saturation; that is, until no new ideas emerge from the data [37]. It is anticipated that this will be achieved by interviewing approximately 20 participants based on our previous qualitative studies of cancer rehabilitation [7,11]. Interviews of approximately 45-minute duration will be conducted in person, via the telephone, or through videoconference, if preferred, by a member of the research team. A different interview schedule at each time point (Multimedia Appendix 4) will be given to participants prior to the interview to allow them to prepare.

Other routinely collected data will be used to describe the sample, including age, gender, cancer type, cancer stage, treatment regimens, comorbidities, baseline functional performance status (AKPS), and baseline BMI.

Sample Size Estimation

It is estimated that 104 participants will be required to accomplish a power of 0.80 and a 2-tailed α level of .05 to detect a between-group difference of a 10-point change in the EORTC QLQ-C30 score [38] (the minimally important difference established for cancer survivors) assuming an SD of 18 points [39]. Based on our previous trial of cancer rehabilitation [39], we expect a dropout of 10%; therefore, 116 participants will be randomized.

Statistical Analysis

Analysis of Quantitative Data

The primary outcome (postintervention global health–related quality of life) will be analyzed using linear mixed effects models. Modeling will account for variation in baseline values. This method accounts for within-participant dependence of observations over time, and for missing data, allowing some participants to have missing observations at certain time points. If more than 5% of data are missing, a multiple imputation process will be used, providing the assumption that data are missing at random is met. A similar approach will be used for analysis of secondary continuous outcomes collected longitudinally. The time spent in moderate to vigorous physical activity will be estimated using a cut-off of 100 steps per minute for moderate-intensity physical activity [40]. The proportion of participants meeting physical activity guidelines will be described and compared using risk ratios. The number of emergency department and hospital admissions will be reported as an incidence rate ratio using a negative binomial regression model. To avoid bias and to maximize the randomization process, all available data will be analyzed in accordance with allocation (intention-to-treat analysis) regardless of adherence.

Total direct costs to the health service for each participant will be determined from the intervention costs and cost of health services utilized over 6 months as recorded from hospital administrative data and health service utilization questionnaire. Costs associated with delivering telerehabilitation will be attributed to the experimental group and cost associated with usual care will be attributed to the comparison group. These will be determined from a register of staff and the time engaged in telerehabilitation or usual care for each participant. Labor costs will be attributed to the staff member and the cost of the telerehabilitation intervention and usual care (based on time and location) to determine a total intervention cost for each participant as well as infrastructure costs. Total costs for each participant will be determined from the intervention costs, the cost of health services utilized over 6 months for experimental group participants, and the cost of health services utilized over 6 months for comparison group participants. The incremental cost-effectiveness ratio will be calculated as the difference in total program and health service costs per mean difference in the global quality-of-life score between the comparison and experimental groups over 6 months. A cost utility ratio will be calculated on the basis of the EORTC-QLQ C30 global quality-of-life score [41] as the change in total program and health service cost per change in quality-adjusted life years saved in the experimental and comparison groups over 6 months.

Analysis of Qualitative Data

Qualitative interview data will be analyzed inductively using interpretive description as a theoretical framework [42]. Interviews will be audio-recorded and transcribed verbatim. Transcripts will be provided to participants to check for accuracy and be given the opportunity to add additional content if they wish. Transcribed interviews will then be deidentified and imported into qualitative analysis software (NVivo [43]). Two researchers will read the interviews and assign codes to sections of the text using an inductive approach, independently. They will then look for connections between and within the data to identify and develop main themes and subthemes using reflective thematic analysis [44]. Once the main themes are decided upon, one researcher will go back and selectively search for text on those themes. Data will be documented using an audit trail including rich and thick descriptions to enhance credibility, trustworthiness, and dependability.

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Results

The trial was funded in April 2021 and registered on October 21, 2021. Participant recruitment commenced in April 2022. As of June 2022, a total of 14 participants were enrolled. Recruitment is expected to conclude in late 2023 and results are expected to be published in 2024.

Discussion

Principal Findings

It is hypothesized that patients receiving cancer telerehabilitation will demonstrate improvements in health-related outcomes when compared to usual care without rehabilitation. It is also hypothesized that a cancer telerehabilitation model will be cost-effective and demonstrate high patient satisfaction. These findings will inform future development of cancer rehabilitation programs in hospital-based settings, contributing to the global effort to integrate exercise-based rehabilitation into standard cancer care [1]. Telehealth may be a convenient and effective way to increase access to exercise. However, no previous randomized controlled trials have evaluated supervised, web-based group exercise via videoconferencing in a real-world health setting [15,24]. This trial will compare a comprehensive, exercise-based cancer telerehabilitation program, delivered in a supervised group and usual care on patient and health service outcomes within a pragmatic health service setting.

There are many possible advantages of exercise-based cancer telerehabilitation. Most notable is the possibility to reach a broader population of cancer survivors. Many existing cancer rehabilitation programs are centered in metropolitan areas [3,45]; hence, there is potential to improve access for those in regional and rural areas. Telerehabilitation also may provide an extra element of convenience for a population that usually has a high number of competing medical demands [11]. However, the convenience of telerehabilitation may be countered by the inability to provide exercise interventions with hands-on instruction and the use of specific equipment. There may also be additional challenges related to supervision and exercise monitoring, which may affect the fidelity of telerehabilitation. Despite this possible concern, telerehabilitation generally meets consumer needs [46], and patients have positive views of this type of service delivery [15,16].

Strengths and Limitations

A strength of this study is the inclusion of health service data. Few studies on cancer rehabilitation include end points meaningful to health services such as hospital length of stay, readmissions, health service utilization, and medication use [47]. This is an issue since costs are a key driver of decision-making in health care. Telerehabilitation has been demonstrated to reduce hospital readmissions compared to usual care in people with advanced-stage cancer and has shown cost savings in other chronic disease settings [48-50]. If shown to be cost-effective, results from this trial may encourage greater implementation of telerehabilitation in cancer settings to improve access to exercise for cancer survivors.

The pragmatic nature of this study implies that a possible limitation is the requirement of participants to have access to their own technology infrastructure to support telehealth. This may bias the population to include participants who have high levels of digital health literacy and access to technology. However, 86% of Australian households have access to the internet, with 91% of them using smartphones and 66% using tablets [51]. This approach is also consistent with the likelihood that future implementation of telerehabilitation programs would be targeted toward people who own suitable devices and have internet access. This trial also does not consider other models of rehabilitation such as 1:1 care. Given that high levels of supervision are important for effectively delivering exercise for cancer survivors [4], possible effects of the telerehabilitation intervention may be diluted owing to the inability to interact 1:1 in a web-based group setting. To account for this, the staff ratio has been kept high to support technology and practical difficulties that patients may encounter.

Conclusions

Telerehabilitation is a rapidly growing area that may have many positive impacts among cancer survivors. This trial has the potential to inform future models of cancer rehabilitation, which can be implemented in health services to improve access to exercise for cancer survivors.

Acknowledgments

AMD is funded by a Victorian Cancer Agency Fellowship.

Data Availability

Data sharing is not applicable to this article as no data sets were generated or analyzed in this study. Data will be made available at the conclusion of the trial in the published multimedia appendices.

Conflicts of Interest

None declared.

Multimedia Appendix 1
SPIRIT Table. Schedule of enrollment, interventions, and assessments.
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Multimedia Appendix 2
Self efficacy for physical activity questionnaire based on Health Action Process Approach.
[DOCX File , 70 KB - resprot_v11i7e38553_app2.docx]

Multimedia Appendix 3
Health Service Utilisation questionnaire.
[DOCX File , 19 KB - resprot_v11i7e38553_app3.docx]

Multimedia Appendix 4
Interview schedule.
[DOCX File , 18 KB - resprot_v11i7e38553_app4.docx]

References

1. Schmitz KH, Campbell AM, Stuiver MM, Pinto BM, Schwartz AL, Morris GS, et al. Exercise is medicine in oncology: Engaging clinicians to help patients move through cancer. CA Cancer J Clin 2019 Nov;69(6):468-484 [FREE Full text] [doi: 10.3322/caac.21579] [Medline: 31617590]
2. Cormie P, Atkinson M, Bucci L, Cust A, Eakin E, Hayes S, et al. Clinical Oncology Society of Australia position statement on exercise in cancer care. Med J Aust 2018 Aug 20;209(4):184-187. [doi: 10.5694/mja18.00199] [Medline: 29719196]
3. Dennett AM, Peiris CL, Shields N, Morgan D, Taylor NF. Exercise therapy in oncology rehabilitation in Australia: A mixed-methods study. Asia Pac J Clin Oncol 2017 Oct;13(5):e515-e527. [doi: 10.1111/ajco.12642] [Medline: 28004526]
4. Campbell KL, Winters-Stone KM, Wiskemann J, May AM, Schwartz AL, Courneya KS, et al. Exercise Guidelines for Cancer Survivors: Consensus Statement from International Multidisciplinary Roundtable. Med Sci Sports Exerc 2019 Nov;51(11):2375-2390 [FREE Full text] [doi: 10.1249/MSS.0000000000002116] [Medline: 31626055]
5. Patel AV, Friedenreich CM, Moore SC, Hayes SC, Silver JK, Campbell KL, et al. American College of Sports Medicine Roundtable Report on Physical Activity, Sedentary Behavior, and Cancer Prevention and Control. Med Sci Sports Exerc 2019 Nov;51(11):2391-2402 [FREE Full text] [doi: 10.1249/MSS.0000000000002117] [Medline: 31626056]
6. Cormie P, Zopf EM, Zhang X, Schmitz KH. The Impact of Exercise on Cancer Mortality, Recurrence, and Treatment-Related Adverse Effects. Epidemiol Rev 2017 Jan 01;39(1):71-92. [doi: 10.1093/epirev/mxx007] [Medline: 28453622]
7. Dennett AM, Peiris CL, Taylor NF, Reed MS, Shields N. 'A good stepping stone to normality': a qualitative study of cancer survivors' experiences of an exercise-based rehabilitation program. Support Care Cancer 2019 May;27(5):1729-1736. [doi: 10.1007/s00520-018-4429-1] [Medline: 30136023]
8. Tan G, Dennett A, Nagarajan D, Freeman J, Peiris C. Program for Oncology Wellness and Exercise Rehabilitation (POWER): A Feasibility Study of Oncology Rehabilitation in the Community. J Cancer Rehabil 2020;3:30-39 [FREE Full text] [doi: 10.48252/JCR1]
9. Dennett AM, Zappa B, Wong R, Ting SB, Williams K, Peiris CL. Bridging the gap: a pre-post feasibility study of embedding exercise therapy into a co-located cancer unit. Support Care Cancer 2021 Nov 08;29(11):6701-6711 [FREE Full text] [doi: 10.1007/s00520-021-06261-2] [Medline: 33963458]
10. Henriksson A, Arving C, Johansson B, Igelström H, Nordin K. Perceived barriers to and facilitators of being physically active during adjuvant cancer treatment. Patient Educ Couns 2016 Jul;99(7):1220-1226. [doi: 10.1016/j.pec.2016.01.019] [Medline: 26860549]
11. Dennett AM, Harding KE, Reed MS. The challenge of timing: a qualitative study on clinician and patient perspectives about implementing exercise-based rehabilitation in an acute cancer treatment setting. Support Care Cancer 2020 Dec;28(12):6035-6043. [doi: 10.1007/s00520-020-05436-7] [Medline: 32291598]
12. Granger CL, Denehy L, Remedios L, Retica S, Phongpagdi P, Hart N, et al. Barriers to Translation of Physical Activity into the Lung Cancer Model of Care. A Qualitative Study of Clinicians' Perspectives. Ann Am Thorac Soc 2016 Dec;13(12):2215-2222. [doi: 10.1513/AnnalsATS.201607-540OC] [Medline: 27689958]
13. Ryu S. Telemedicine: Opportunities and Developments in Member States: Report on the Second Global Survey on eHealth 2009 (Global Observatory for eHealth Series, Volume 2). Healthc Inform Res 2012;18(2):153. [doi: 10.4258/hir.2012.18.2.153]
14. Cox A, Lucas G, Marcu A, Piano M, Grosvenor W, Mold F, et al. Cancer Survivors' Experience With Telehealth: A Systematic Review and Thematic Synthesis. J Med Internet Res 2017 Jan 09;19(1):e11 [FREE Full text] [doi: 10.2196/jmir.6575] [Medline: 28069561]
15. Morrison KS, Paterson C, Toohey K. The Feasibility of Exercise Interventions Delivered via Telehealth for People Affected by Cancer: A Rapid Review of the Literature. Semin Oncol Nurs 2020 Dec;36(6):151092. [doi: 10.1016/j.soncn.2020.151092] [Medline: 33223409]
16. Dennett A, Harding K, Reimert J, Morris R, Parente P, Taylor N. Telerehabilitation's Safety, Feasibility, and Exercise Uptake in Cancer Survivors: Process Evaluation. JMIR Cancer 2021 Dec 21;7(4):e33130 [FREE Full text] [doi: 10.2196/33130] [Medline: 34854817]

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17. Bluethmann SM, Vernon SW, Gabriel KP, Murphy CC, Bartholomew LK. Taking the next step: a systematic review and meta-analysis of physical activity and behavior change interventions in recent post-treatment breast cancer survivors. Breast Cancer Res Treat 2015 Jan;149(2):331-342 [FREE Full text] [doi: 10.1007/s10549-014-3255-5] [Medline: 25555831]
18. Goode AD, Lawler SP, Brakenridge CL, Reeves MM, Eakin EG. Telephone, print, and Web-based interventions for physical activity, diet, and weight control among cancer survivors: a systematic review. J Cancer Surviv 2015 Dec;9(4):660-682. [doi: 10.1007/s11764-015-0442-2] [Medline: 25757733]
19. Larson JL, Rosen AB, Wilson FA. The effect of telehealth interventions on quality of life of cancer survivors: A systematic review and meta-analysis. Health Informatics J 2020 Jun;26(2):1060-1078 [FREE Full text] [doi: 10.1177/1460458219863604] [Medline: 31566455]
20. Cheville AL, Moynihan T, Herrin J, Loprinzi C, Kroenke K. Effect of Collaborative Telerehabilitation on Functional Impairment and Pain Among Patients With Advanced-Stage Cancer: A Randomized Clinical Trial. JAMA Oncol 2019 May 01;5(5):644-652 [FREE Full text] [doi: 10.1001/jamaoncol.2019.0011] [Medline: 30946436]
21. Brown L, Sabesan S, COSA Teleoncology Working Group. What models of care for teleoncology are available to nursing services? Cancer Council Australia. URL: https://wiki.cancer.org.au/australia/Clinical_question:What_models_of_care_for_teleoncology_are_available_to_nursing_services%3F [accessed 2022-06-22]
22. Furness K, Sarkies MN, Huggins CE, Croagh D, Haines TP. Impact of the Method of Delivering Electronic Health Behavior Change Interventions in Survivors of Cancer on Engagement, Health Behaviors, and Health Outcomes: Systematic Review and Meta-Analysis. J Med Internet Res 2020 Jun 23;22(6):e16112 [FREE Full text] [doi: 10.2196/16112] [Medline: 32574147]
23. Groen WG, van Harten WH, Vallance JK. Systematic review and meta-analysis of distance-based physical activity interventions for cancer survivors (2013-2018): We still haven't found what we're looking for. Cancer Treat Rev 2018 Sep;69:188-203. [doi: 10.1016/j.ctrv.2018.07.012] [Medline: 30077954]
24. Brick R, Padgett L, Jones J, Wood KC, Pergolotti M, Marshall TF, et al. The influence of telehealth-based cancer rehabilitation interventions on disability: a systematic review. J Cancer Surviv 2022 Feb 26 [FREE Full text] [doi: 10.1007/s11764-022-01181-4] [Medline: 35218521]
25. Burke SM, Carron AV, Eys MA, Ntoumanis N, Estabrooks PA. Group versus individual approach? A meta-analysis of the effectiveness of interventions to promote physical activity. Sport Exer Psych Rev 2006;2(1):19-35.
26. American College of Sports Medicine. ACSM's Guidelines for Exercise Testing and Prescription (10th edition). Philadelphia, PA: Wolters Kluwer; 2018.
27. Winters-Stone KM, Boisvert C, Li F, Lyons KS, Beer TM, Mitri Z, et al. Delivering exercise medicine to cancer survivors: has COVID-19 shifted the landscape for how and who can be reached with supervised group exercise? Support Care Cancer 2022 Mar;30(3):1903-1906 [FREE Full text] [doi: 10.1007/s00520-021-06669-w] [Medline: 34741653]
28. Schulz KF, Altman DG, Moher D, CONSORT Group. CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. BMJ 2010 Mar 23;340:c332 [FREE Full text] [doi: 10.1136/bmj.c332] [Medline: 20332509]
29. Tong A, Sainsbury P, Craig J. Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups. Int J Qual Health Care 2007 Dec;19(6):349-357. [doi: 10.1093/intqhc/mzm042] [Medline: 17872937]
30. Husereau D, Drummond M, Augustovski F, de Bekker-Grob E, Briggs AH, Carswell C, CHEERS 2022 ISPOR Good Research Practices Task Force. Consolidated Health Economic Evaluation Reporting Standards 2022 (CHEERS 2022) statement: updated reporting guidance for health economic evaluations. BMJ 2022 Jan 11;376:e067975 [FREE Full text] [doi: 10.1136/bmj-2021-067975] [Medline: 35017145]
31. Lincoln YS, Lynham SA, Guba EG. Paradigmatic controversies, contradictions, and emerging confluences, revisited. In: The SAGE Handbook of Qualitative Research. Thousand Oaks, CA: Sage Publications; 2011:97-128.
32. Mina DS, Langelier D, Adams SC, Alibhai SMH, Chasen M, Campbell KL, et al. Exercise as part of routine cancer care. Lancet Oncol 2018 Sep;19(9):e433-e436. [doi: 10.1016/S1470-2045(18)30599-0] [Medline: 30191843]
33. Cancer Exercise Toolkit. URL: https://cancerexercisetoolkit.trekeducation.org [accessed 2022-06-20]
34. Ungar N, Wiskemann J, Sieverding M. Physical Activity Enjoyment and Self-Efficacy As Predictors of Cancer Patients' Physical Activity Level. Front Psychol 2016 Jun 21;7:898 [FREE Full text] [doi: 10.3389/fpsyg.2016.00898] [Medline: 27445882]
35. World alliance for patient safety: WHO draft guidelines for adverse event reporting and learning systems: from information to action. World Health Organization. 2005. URL: https://apps.who.int/iris/handle/10665/69797 [accessed 2022-06-22]
36. Common Terminology Criteria for Adverse Events (CTCAE). Version 4.0. US Department of Health and Human Services. 2009. URL: https://evs.nci.nih.gov/ftp1/CTCAE/CTCAE_4.03/CTCAE_4.03_2010-06-14_QuickReference_8.5x11.pdf [accessed 2022-05-29]
37. Saunders B, Sim J, Kingstone T, Baker S, Waterfield J, Bartlam B, et al. Saturation in qualitative research: exploring its conceptualization and operationalization. Qual Quant 2018;52(4):1893-1907 [FREE Full text] [doi: 10.1007/s11135-017-0574-8] [Medline: 29937585]

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38. Cocks K, King MT, Velikova G, Martyn St-James M, Fayers PM, Brown JM. Evidence-based guidelines for determination of sample size and interpretation of the European Organisation for the Research and Treatment of Cancer Quality of Life Questionnaire Core 30. J Clin Oncol 2011 Jan 01;29(1):89-96. [doi: 10.1200/JCO.2010.28.0107] [Medline: 21098316]
39. Dennett AM, Shields N, Peiris CL, Prendergast LA, O'Halloran PD, Parente P, et al. Motivational interviewing added to oncology rehabilitation did not improve moderate-intensity physical activity in cancer survivors: a randomised trial. J Physiother 2018 Oct;64(4):255-263 [FREE Full text] [doi: 10.1016/j.jphys.2018.08.003] [Medline: 30217412]
40. Abel M, Hannon J, Mullineaux D, Beighle A. Determination of step rate thresholds corresponding to physical activity intensity classifications in adults. J Phys Act Health 2011 Jan;8(1):45-51. [doi: 10.1123/jpah.8.1.45] [Medline: 21297184]
41. King MT, Viney R, Simon Pickard A, Rowen D, Aaronson NK, Brazier JE, MAUCa Consortium. Australian Utility Weights for the EORTC QLU-C10D, a Multi-Attribute Utility Instrument Derived from the Cancer-Specific Quality of Life Questionnaire, EORTC QLQ-C30. Pharmacoeconomics 2018 Feb;36(2):225-238 [FREE Full text] [doi: 10.1007/s40273-017-0582-5] [Medline: 29270835]
42. Thompson Burdine J, Thorne S, Sandhu G. Interpretive description: A flexible qualitative methodology for medical education research. Med Educ 2021 Mar;55(3):336-343. [doi: 10.1111/medu.14380] [Medline: 32967042]
43. Unlock insights in your data with the best qualitative data analysis software. QSR International. URL: https://www.qsrinternational.com/nvivo-qualitative-data-analysis-software/home [accessed 2021-10-07]
44. Braun V, Clarke V. Using thematic analysis in psychology. Qual Res Psychol 2006 Jan;3(2):77-101. [doi: 10.1191/1478088706qp063oa]
45. Canestraro A, Nakhle A, Stack M, Strong K, Wright A, Beauchamp M, et al. Oncology Rehabilitation Provision and Practice Patterns across Canada. Physiother Can 2013 Jan;65(1):94-102 [FREE Full text] [doi: 10.3138/ptc.2011-53] [Medline: 24381389]
46. Dennett A, Taylor N, Williams K, Lewis A, Brann P, Hope J, et al. Consumer perspectives of telehealth in ambulatory care in an Australian health network. Health Soc Care Community 2021 Sep 23 [FREE Full text] [doi: 10.1111/hsc.13569] [Medline: 34558144]
47. Dennett AM, Sarkies M, Shields N, Peiris CL, Williams C, Taylor NF. Multidisciplinary, exercise-based oncology rehabilitation programs improve patient outcomes but their effects on healthcare service-level outcomes remain uncertain: a systematic review. J Physiother 2021 Jan;67(1):12-26 [FREE Full text] [doi: 10.1016/j.jphys.2020.12.008] [Medline: 33358544]
48. Udsen FW, Hejlesen O, Ehlers LH. A systematic review of the cost and cost-effectiveness of telehealth for patients suffering from chronic obstructive pulmonary disease. J Telemed Telecare 2014 Jun;20(4):212-220. [doi: 10.1177/1357633X14533896] [Medline: 24803277]
49. Tousignant M, Moffet H, Nadeau S, Mérette C, Boissy P, Corriveau H, et al. Cost analysis of in-home telerehabilitation for post-knee arthroplasty. J Med Internet Res 2015 Mar 31;17(3):e83 [FREE Full text] [doi: 10.2196/jmir.3844] [Medline: 25840501]
50. Sjöström M, Lindholm L, Samuelsson E. Mobile App for Treatment of Stress Urinary Incontinence: A Cost-Effectiveness Analysis. J Med Internet Res 2017 May 08;19(5):e154 [FREE Full text] [doi: 10.2196/jmir.7383] [Medline: 28483745]
51. Household use of information technology. Australian Bureau of Statistics. 2018. URL: https://www.abs.gov.au/statistics/industry/technology-and-innovation/household-use-information-technology/latest-release#data-download [accessed 2022-09-29]

Abbreviations

AKPS: Australian Karnofsky Performance Status
CONSORT: Consolidated Standards of Reporting Trials
EORTC-QLQ C30: European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire

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Protocol

Evaluating the Efficacy of a Guided and Unguided Internet-Based Self-help Intervention for Chronic Loneliness: Protocol for a 3-Arm Randomized Controlled Trial

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Abstract

Background: Loneliness, or perceived social isolation, is prevalent in both the general population and clinical practice. Although loneliness has repeatedly been associated with mental and physical health, research on interventions that reduce loneliness effectively is still rather scarce.

Objective: This study aims to evaluate the efficacy of a guided and an unguided version of the same internet-based cognitive behavioral self-help program for loneliness (SOLUS-D) for adults.

Methods: A total of 250 participants will be randomly assigned to 1 of 2 intervention groups (SOLUS-D with guidance or SOLUS-D without guidance) or a wait-list control group (2:2:1 allocation ratio). Adult participants experiencing high levels of loneliness will be recruited from the general population. Individuals currently experiencing at least moderately severe depressive symptoms, an ongoing severe substance use disorder, previous or current bipolar or psychotic disorder, or acute suicidality will be excluded from the trial. Assessments will take place at baseline, 5 weeks (midassessment), and 10 weeks (postassessment). The primary outcome is loneliness assessed using the 9-item University of California, Los Angeles Loneliness Scale at the posttreatment time point. Secondary outcomes include depressive symptoms, symptoms of social anxiety, satisfaction with life, social network size, and variables assessing cognitive bias and social behavior. The maintenance of potentially achieved gains will be assessed and compared at 6 and 12 months after randomization in the 2 active conditions. Potential moderators and mediators will be tested exploratorily. Data will be analyzed on an intention-to-treat basis.

Results: Recruitment and data collection started in May 2021 and are expected to be completed by 2022, with the 12-month follow-up to be completed by 2023. As of the time of submission of the manuscript, 134 participants were randomized.

Conclusions: This 3-arm randomized controlled trial will add to the existing research on the efficacy of loneliness interventions. Furthermore, it will shed light on the role of human guidance in internet-based treatments for individuals with increased levels of loneliness and the possible mechanisms of change. If SOLUS-D proves effective, it could provide a low-threshold, cost-efficient method of helping and supporting individuals with increased levels of loneliness.

Trial Registration: ClinicalTrials.gov NCT04655196; https://clinicaltrials.gov/ct2/show/NCT04655196

International Registered Report Identifier (IRRID): DERR1-10.2196/36358

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KEYWORDS

loneliness; subjective social isolation; internet-based intervention; self-help; guidance; online; mobile phone

Introduction

Background

Loneliness, or perceived social isolation, is a common phenomenon observed in clinical practice and in the general population. Some authors have even considered it an epidemic phenomenon [1]. Although an increase in the prevalence of loneliness has been observed after the onset of the COVID-19 pandemic and the accompanying social distancing measures [2,3], loneliness was a prevalent phenomenon even before. The prevalence of loneliness varies substantially among European countries [4]. In the general German population, 5% to 10% of individuals frequently experience feelings of loneliness [2,5], and a recent cross-temporal meta-analysis revealed an increase in loneliness in emerging adults over the past 40 years [6]. Within a representative German adult sample, loneliness was prevalent in all age groups, with peaks in young adults (aged approximately 30 years), in adults aged approximately 60 years, and in the oldest adults (≥80 years) [7]. Numerous studies have shown negative physical and mental health consequences associated with loneliness [8], and it is associated with all-cause mortality [9,10]. Consequently, loneliness has recently been increasingly recognized as a public health concern that needs to be addressed, leading to several national initiatives (eg, in the United Kingdom and Japan) to tackle loneliness and objective social isolation on a societal level. Furthermore, attempts have been made to develop and evaluate interventions to reduce loneliness at the individual level. However, evidence on what interventions work and for whom is still limited [11].

Conceptualizing Loneliness

Human connection is regarded as a basic psychological need [12]. Consequently, when this need cannot be met, feelings of loneliness may arise. Peplau and Perlman [13] defined loneliness as an aversive subjective experience resulting from a discrepancy between actual and desired social relationships. The quantity and quality of social contact seem to be relevant in this regard [14]. This means that a person can feel lonely despite having many social relationships, whereas another person with only a few meaningful connections may not feel lonely. Therefore, it is essential to distinguish between loneliness (ie, subjective social isolation) and objective social isolation. Although loneliness is often experienced as stressful, perceived control over the frequency with which individuals socialize, and the amount of time spent alone play an important role in whether social isolation, living alone, or being alone is perceived as distressing [7]. Researchers have argued that it is necessary to distinguish between different forms of loneliness in terms of the duration of the experience. For example, Young [15] suggested differentiating among transient, situational, and chronic loneliness. Transient feelings of loneliness are adaptive in motivating individuals to reconnect with others [16] and should not be considered pathological [17], whereas chronic loneliness is a more stable condition expressed as difficulties in engaging in satisfying social relationships. This experience is intrinsically aversive and is associated with a variety of severe consequences for physical and psychological health [18].

Maintaining Factors of Chronic Loneliness

According to the evolutionary theory of loneliness [16], transient feelings of loneliness are adaptive by functioning as a signal comparable with hunger or thirst, motivating individuals to reconnect with others to increase the likelihood of survival. However, some people get stuck in a vicious circle that maintains feelings of loneliness, leading to chronic loneliness. Cacioppo et al [16,19] outlined a cognitive model of loneliness. The model indicates that perceived social isolation causes initial social withdrawal, allowing one to observe and evaluate immediate social situations through physical distance [20]. When perceiving oneself as socially isolated, the motive for self-preservation may increase, leading to heightened hypervigilance for potential social threats and attacks [21,22]. Consequently, individuals perceive social stimuli as more threatening, especially when a situation is neutral or ambiguous. In line with this, individuals with increased levels of loneliness have shown a negative bias in several phases of social information processing (see the study by Spithoven et al [23] for an overview). According to Cacioppo and Hawkley [19], counterproductive social behavior, such as social avoidance or preventive rejection of others, is reinforced by biased information processing. Such behavior may help prevent further rejection or attacks but may also hinder behavior that could promote close satisfying social connections. In addition, the results of several studies show that individuals with chronic loneliness may lack social skills, such as authenticity [24] or self-disclosure [25,26], expressing emotions [27], or being compassionate toward others and the self [28], which are important in building close relationships [29-34]. Heightened rejection sensitivity [22] and negative evaluations of others can further foster negative experiences and expectations of social interactions [35]. Hence, a lack of perceived social efficacy, (ie, confidence in the ability to engage in social interactions or initiate and maintain interpersonal relationships) can be reduced in individuals with increased levels of loneliness [22,36,37]. The resulting social behavior hampers the forming of new relationships and the deepening of existing relationships, leading to more negativity and stronger feelings of loneliness. Consequently, negative biases in social situations are further increased, leading to a vicious circle and, therefore, to chronic loneliness.

Loneliness and Mental Disorders

Loneliness can be viewed as a transdiagnostic phenomenon [38], which is frequent in various psychological disorders and psychopathological symptoms. For example, it has been found to be associated with depression [39], psychosis [40], suicidal ideation [41,42], and generalized anxiety [5]. Impaired sleep quality and insomnia symptoms have also been repeatedly reported in individuals with increased levels of loneliness [43]. In line with these findings, loneliness is associated with reduced well-being [44]. Owing to the cross-sectional nature of most

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studies, the causality for the associations between loneliness and mental health problems is often unclear. However, reciprocal relationships have been found for a variety of psychopathological symptoms, such as depressive symptoms and symptoms of social anxiety [45-47]. Therefore, loneliness can be considered a risk and maintaining factor of mental disorders.

Interventions Against Loneliness

Loneliness, with its many detrimental effects on health, has led researchers to develop various interventions aiming to alleviate the condition. In general, psychological interventions have been found to reduce loneliness [48]. In an attempt to categorize different approaches, Masi et al [49] identified four groups of interventions that have been studied for loneliness: (1) developing social skills, (2) increasing social support, (3) augmenting opportunities for social interaction, and (4) changing maladaptive social cognitions. Interventions focusing on and changing social cognition were shown to be the most promising approaches compared with other intervention types [49]. A more recent systematic review [11] corroborated these findings by concluding that the most promising individual interventions had focused on cognitive interventions. These results are in line with the abovementioned cognitive model of loneliness, according to which interventions need to address hypervigilance to social threats and related cognitive biases that characterize individuals with increased levels of loneliness [16,19]. Recently, there have been several systematic review updates on interventions against loneliness in older adults in general [50], in individuals with mental health problems [51], and in randomized controlled trials (RCTs) [38], with all 3 reviews highlighting the largely unmet need for high-quality research on psychological interventions for loneliness.

Internet-Based Interventions for Loneliness

In recent years, cognitive behavioral therapy (CBT) has been applied as internet-delivered CBT (ICBT). Location- and time-independent use, high degree of anonymity and privacy, and low costs because of easy scalability are some of the advantages of ICBT [52]. Although most people are familiar with feelings of loneliness, it often has a negative connotation and is stigmatized [53]. Thus, low-threshold access to interventions may be especially helpful for individuals with increased levels of loneliness in need. In addition, it has been argued that ICBT might especially be accepted by individuals with increased levels of loneliness showing avoidant and withdrawing social behavior [54], as internet-based interventions are associated with diminished anxiety about social interactions with therapists [55].

Recently, there have been some promising studies on low-threshold internet-based self-help interventions against loneliness. In a pilot RCT, Käll et al [54] compared a guided ICBT with a wait-list control group. Significant reductions in loneliness were found with a between-group effect size (Cohen *d*) of 0.77 at the postintervention time point [54]. A further decrease in loneliness was observed at the 2-year follow-up [56].

More evidence for effectively alleviating loneliness by means of ICBT stems from a 3-armed trial comparing 2 active intervention groups (ICBT vs internet-based interpersonal therapy [IIPT]) with a wait-list control group [57]. Loneliness in individuals in the ICBT condition was significantly reduced after the intervention phase, with a moderate to large effect size (Cohen d=0.71) compared with the wait-list and a moderate effect size (Cohen d=0.53) compared with the IIPT group. No significant differences regarding loneliness were observed between the IIPT and wait-list groups [57].

An unguided, web-based, friendship enrichment program, including 3 coping strategies to tackle loneliness (ie, network development, adapting personal standards, and reducing the importance of the discrepancy between actual and desired relationships), was tested in 239 participants aged 50 to 86 years [58]. This study drew on the definition of loneliness from Peplau and Perlman [13] and suggested that not only increasing opportunities for social contact but also focusing on the discrepancy between actual and desired relationships and expectations for relationships are important in alleviating loneliness. On average, loneliness declined significantly over the course of the study [58]. However, the authors reported high dropout rates, with only 36% of the participants completing all modules of the program [59].

Although the first studies on ICBT for loneliness have shown promising results, more studies are needed for several reasons. First, the study designs applied in previous trials on ICBT for loneliness [54,57] do not allow controlling for nonspecific effects such as human contact on the outcome. However, guidance (ie, weekly human contact by email) might affect the decrease in loneliness other than through CBT by addressing principles relevant to building meaningful relationships (eg, validation) [54]. Moreover, guidance also yields larger effects when comparing guided and unguided interventions in other application fields of ICBT, such as depression [60]. Thus, it is important to investigate the effect of guidance on outcomes in internet interventions for loneliness. Second, there is a gap in the literature on who can profit from ICBT for loneliness and, for example, whether some people profit more from a guided than from an unguided version. Third, little is known about how interventions for loneliness work, and research is needed to identify mechanisms of change in these interventions and, thereby, improve the understanding of chronic loneliness.

Objectives

Given the need for more high-quality RCTs of interventions for alleviating loneliness, this study will be conducted to investigate the following objectives. First, we will test the efficacy of 2 web-based interventions (ICBT with or without guidance) compared with a wait-list control group regarding loneliness (primary outcome) and a range of secondary outcomes (eg, depression, anxiety, satisfaction with life, and factors of the cognitive model of loneliness). We expect individuals in both intervention groups to show a greater reduction in loneliness and more pronounced effects in the secondary outcomes than in the wait-list control group.

Second, we will compare the efficacy and long-term effects of the 2 active interventions regarding primary and secondary

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outcomes to specify the effects of added human contact through guidance. We expect greater changes in the primary and secondary outcomes in the intervention with guidance than in the intervention without guidance.

Third, we will test potential baseline predictors for the efficacy of the interventions and explore moderators between the 2 active conditions to better understand which intervention (with or without guidance) works best for whom. Considering the exploratory nature of this objective, we have no specified hypothesis for this objective.

Finally, we will explore potential mediators (mechanisms of change) of the interventions. We expect changes in cognitive bias and counterproductive social behavior, as described in the cognitive model of chronic loneliness [19], to explain reductions in loneliness.

Methods

Study Design

This study uses a 3-arm RCT design to compare 2 intervention groups (SOLUS-D with individualized guidance by a coach and SOLUS-D without guidance), with a wait-list control group. Participants in the 2 active conditions will have access to the 10-week internet-based self-help intervention immediately after randomization. Participants in the wait-list control group will receive access to the program after the intervention phase of 10 weeks and the completion of the postassessment measure. Assessments for all participants will be administered at baseline (time point 0), 5 weeks (time point 1, midtreatment), and 10 weeks (time point 2, after treatment) after randomization. In addition, participants in the 2 intervention groups will be followed up at 6 (time point 3) and 12 months (time point 4) after randomization. As participants in the control group will have access to the program after 10 weeks for ethical considerations, they will not be included in the follow-up measurements. The study design is illustrated in Figure 1.

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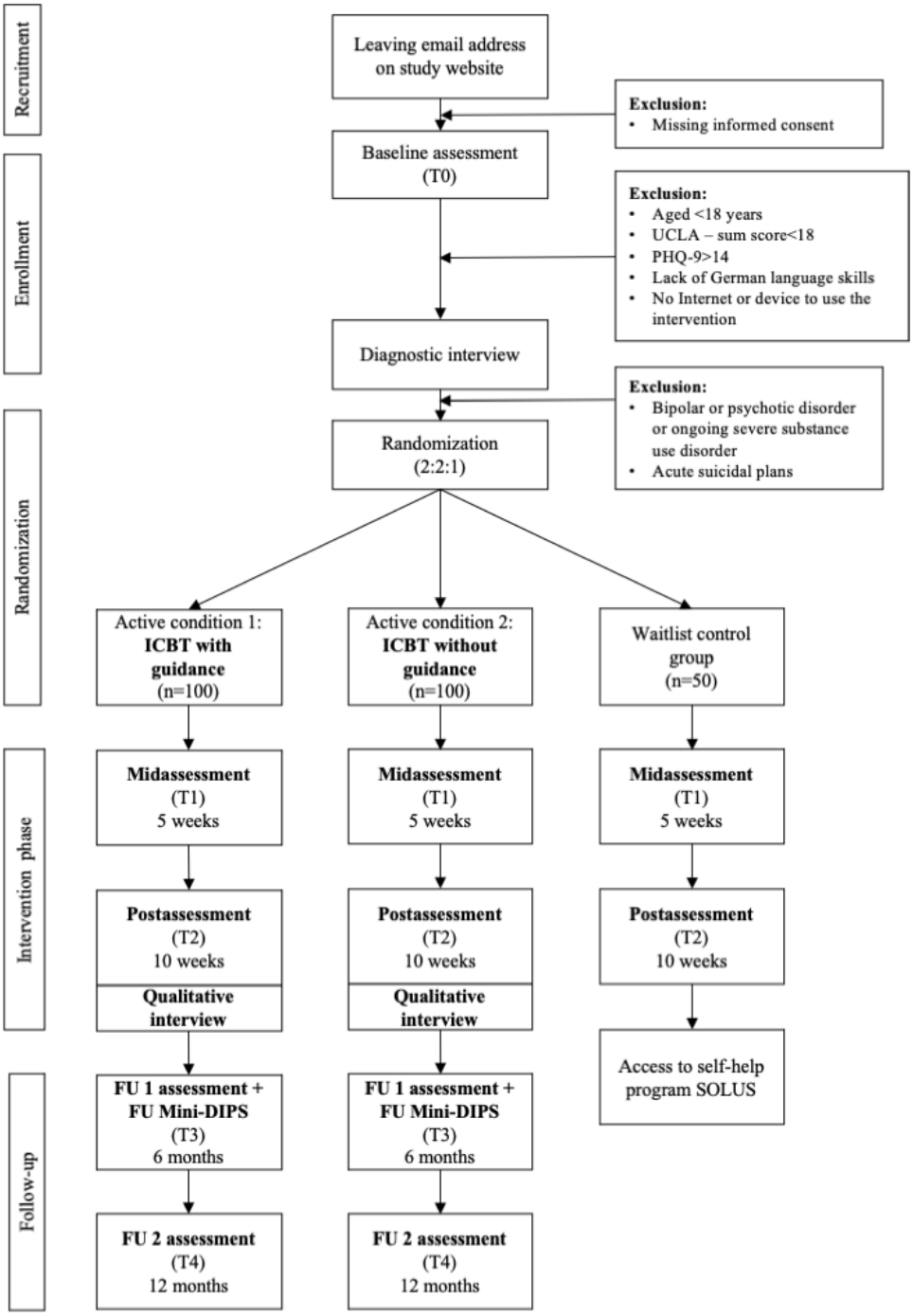
Figure 1. Participant flow. FU: follow-up; ICBT: internet-based cognitive behavioral therapy; Mini-DIPS: Mini Diagnostic Interview for Mental Disorders; PHQ-9: Patient Health Questionnaire-9; T0: time point 0; T1: time point 1; T2: time point 2; T3: time point 3; T4: time point 4; UCLA: University of California, Los Angeles.



Ethics Approval

This study is being conducted in compliance with the Declaration of Helsinki and has been approved by the Cantonal Ethics Committee, Bern (ID:202-01298). All participants will receive written information about the aim of the study, benefits, risks of participation, and procedure of the study. Participants will be informed that they can withdraw from the study at any time without disclosing their reasons. Written informed consent will be obtained from all participants before the baseline assessment. The trial was preregistered with ClinicalTrials.gov (NCT04655196).

Inclusion and Exclusion Criteria

The inclusion criteria for this study are as follows: (1) age of at least 18 years; (2) a score of at least 18 points on the

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University of California, Los Angeles (UCLA) Loneliness Scale-9; (3) sufficient German language skills; (4) access to an internet connection and a device to use the intervention; and (5) signed informed consent and the provision of a contact in case of emergency. The cutoff score of the UCLA Loneliness Scale-9 was derived from the cutoff score used in the aforementioned study by Käll et al [54] by transforming it to a mean score and adapting it to the short version used in this study. Individuals will be excluded from the study if they (1) currently have at least moderately severe depressive symptoms (as indicated by a Patient Health Questionnaire-9 [PHQ-9] score >14), (2) have a lifetime diagnosis of schizophrenia or bipolar disorder, (3) fulfill the criteria for a severe substance use disorder, or (4) have acute suicidal plans. The exclusion criterion for schizophrenia will be assessed by means of screening questions regarding a former formal diagnosis or by the diagnostic interview Mini Diagnostic Interview for Mental Disorders (Mini-DIPS). The exclusion criteria for substance use disorder and acute suicidal plans will be assessed during the diagnostic interview (Mini-DIPS). In this study, there will be no restrictions regarding the use of other treatments during the study.

Participants, Recruitment, and Randomization

Participants will be recruited in German-speaking countries through reports in newspapers and radio interviews, internet forums, social media, our study website [61], and the website for ongoing studies from our research hub [62]. After checking the inclusion and exclusion criteria by means of the baseline assessment and a diagnostic interview, eligible participants will be automatically randomly allocated in a blockwise manner (blocks of 10 participants) on the web-based platform Qualtrics (Qualtrics XM) to either of the 2 active conditions or the wait-list control group (randomization ratio 2:2:1).

Procedure

Interested individuals will leave their email addresses on the study website and receive the study information and consent form by email. Participants will be invited to ask questions about the study by phone. Once the signed consent form is returned, a link to the baseline assessment will be sent via email. After the baseline assessment is completed, the diagnostic interview will be conducted over the telephone by trained master's students and members of the study team. Subsequently, eligible participants will be randomly allocated to 1 of the 3 study groups. After randomization, individuals randomized to the 2 active conditions will receive immediate access to the internet-based self-help program SOLUS-D. Individuals in the wait-list control group will receive access to the program after a waiting period of 10 weeks after randomization. Participants in all 3 conditions will be asked to complete additional questionnaires 5 and 10 weeks after randomization. Furthermore, individuals in the 2 active conditions will be followed up for 6 and 12 months after randomization. Participants will receive a reminder via email each week for up to 3 weeks if they do not complete the questionnaires. After completing the postassessment measure, a random subsample of individuals in the active condition will be asked to participate in a qualitative interview. The aim is to gain more profound insight into their experience with the program and possible adverse effects during the intervention phase. At 6 months after randomization, participants in the 2 active conditions will be contacted once more by phone to conduct a second diagnostic interview. After the intervention phase, all participants will continue to have access to the self-help intervention in an unguided format. The participants will not be compensated for partaking in the trial.

Intervention: Internet-Based Self-help Program—SOLUS-D

Participants in both active conditions will have access to SOLUS-D, an internet-based self-help program. This intervention is a German adaptation and extension of the ICBT program developed by Käll et al [54]. The program is an internet-based and interactive self-help guide with text, audio, and video files and a diary function (Table 1). The program comprises 9 modules based on CBT principles. Expanding on the original program of Käll et al [54], the program used in this study has been enriched and extended with elements of mindfulness, self-compassion, acceptance and commitment, and social skills by our team. We will recommend completing 1 module per week and that participants work through the program sequentially. Each module builds on the previous module and takes approximately 50 minutes to complete. Theoretically, all modules can be completed at once; thus, they are not gradually made available weekly. Participants can navigate the content of the completed modules as they want and repeat the exercises and modules. Apart from working on the modules, the participants will be asked to complete exercises and web-based diaries as often as possible. The program is accessible on any computer, tablet, or smartphone. Secure Sockets Layer encryption will be used to secure internet-based communication with the program and guides, and participants will be identified with anonymous log-in names and passwords. The platform on which the program runs has been successfully used for several research projects in our research unit [63,64].

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Table 1. SOLUS-D content.

Module number	Module	Content	Exercises
1	Loneliness and personal values	Information about the program use, structure of the intervention, and psychoeducation on loneliness and personal values are provided in this module.	• Vicious circle of loneliness • Values in different life areas • Introduction to mood diary (continuous exercise)
2	Goal setting and mindfulness	Personal goals are set and a theoretical and practical introduction to mindfulness is provided.	• Setting goals • Mindful breathing • Body scan • 3-minute breathing space
3	Self-compassion	A theoretical and practical introduction to self-compassion is provided.	• Kindness meditation: self-compassion • LKM[a] • Introduction (self-) compassion diary (continuous exercise)
4	Acceptance of loneliness and solitude	The importance of emotions is highlighted and a strategy for accepting emotions is introduced. Furthermore, time spent alone is reflected.	• Accepting emotions • Exposition with time spent alone • Reframing time spent alone
5	Identifying and changing thoughts	The impact of negative automatic thoughts and the relationship among thoughts, experiences, and behavior are introduced. Dysfunctional thoughts are identified and revised.	• Identifying NAT[b] • Challenging NAT and formulating alternative thoughts
6	Rumination and behavioral experiments	Strategies for dealing with rumination and the idea of behavioral experiments are introduced.	• Disrupting rumination • Behavioral experiments
7	Social relationships and feeling connected	The current social relationship situation is evaluated more closely, values in social relationships are identified, and various social skills for relationship building are introduced.	• Social convoy • Values in close relationships • Boundaries
8	Building social activities	The relationship between behavior and loneliness is further highlighted, avoidance and passivity are addressed, and value-based social activities are introduced.	• Avoidance and passivity • Value-based behavioral activation
9	More social activities and further goals	Obstacles with behavioral activation are addressed, and new activities can be planned. Finally, the content of all modules is reviewed, and future goals can be set.	• Value-based behavioral activation • Formulating further goals • Strategy toolbox

[a]LKM: Loving Kindness Meditation.

[b]NAT: negative automatic thought.

Conditions

ICBT With Guidance

Individuals in this condition will use the SOLUS-D program while being guided by trained and supervised coaches. The coaches will regularly monitor the use of the program, provide weekly written feedback via chat within the self-help platform on exercises, and motivate participants to work with the program continuously. Each message will comprise personalized feedback on the participants' work during the previous week and answers to their questions. The content of these messages will be semistructured and manualized according to the theoretical model of Supportive Accountability [65]. This model argues that adherence increases with human support through accountability to a coach. The coaches will be 2 psychologists with a master's degree in clinical psychology in their first year of a postgraduate CBT program and several master's students in their last term of a graduate program in clinical psychology. All coaches will be trained in the specific approach and supervised by NS and TK.

ICBT Without Guidance

In this condition, participants will also have access to SOLUS-D. However, they will not be guided and will use it on their own; yet, the participants will receive weekly automated and fully standardized emails during the 10 weeks. The content of these emails aims to remind and motivate participants to continue engaging with the program. Within the information about group allocation, it is explicitly stated that the automated email is automatically sent from a computer and not by a human being. During the intervention period, questions concerning technical issues with the program will be answered upon request by the study team.

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Wait-list Control Group

Participants in this condition will receive access to the unguided intervention 10 weeks after randomization (ie, after the postassessment time point).

Measures

Overview

Demographic information such as gender, marital status, and education level will be self-reported by participants at baseline. In addition, we will assess participants' medication status at baseline and their use of psychotherapy at every measurement time point. Table 2 summarizes the instruments and schedule of the assessments in this study. In case there was no German version of a scale available, the original scale was translated from English to German by our research group and back translated by a native English-speaking person. Differences between this back-translation and the original scale were discussed until a consensus was reached regarding the necessary changes in the German version.

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Table 2. Assessment timeline.

Type of variable and variable	Measurement	Baseline (time point 0)	5 weeks (time point 1)	10 weeks (time point 2)	6 months[a] (time point 3)	12 months[a] (time point 4)
Primary outcome						
Loneliness	UCLA[b] Loneliness Scale 9-item version	✓	✓	✓	✓	✓
Secondary outcomes						
Depression	Patient Health Questionnaire-9	✓	✓	✓	✓	✓
Social anxiety	Social Interaction Anxiety Scale and Social Phobia Scale	✓	✓	✓	✓	✓
Satisfaction with life	Satisfaction with Life Scale	✓	✓	✓	✓	✓
Social isolation	Social Network Index	✓		✓	✓	✓
Self-compassion	Sussex Oxford Compassion Scale for the Self	✓		✓		
Maladaptive personality traits	PID-5-BF+[c]	✓		✓		
Misantropy	Bern Embitterment Inventory[d]	✓		✓		
Motivation for solitude	Motivation for Solitude Scale–Short Form[d]	✓		✓		
Negative effects	Inventory for the Assessment of Negative Effects of Psychotherapy[a]			✓		
Patient satisfaction	Client Satisfaction Questionnaire[a]			✓	✓	
System usability	System Usability Scale[a]			✓		
Mental disorders	Mini Diagnostic Interview for Mental Disorders	✓			✓[a]	
Mechanisms of change						
Interpretation bias	Interpretation and Judgmental Bias Questionnaire[e]	✓	✓	✓		
Rejection sensitivity	Adult Rejection Sensitivity Questionnaire	✓	✓	✓		
Social avoidance	Cognitive-Behavioral Avoidance Scale[d]	✓	✓	✓		
Self-Disclosure	Distress Disclosure Index	✓	✓	✓		
Authenticity	Kernis and Goldman Authenticity Inventory–Short Form	✓	✓	✓		
Self-esteem	Rosenberg Self-Esteem Scale	✓	✓	✓		
Therapeutic alliance	Working Alliance Inventory for internet interventions[a,f]		✓			
Moderators						
Mobility	Patient Questionnaire for Medical Rehabilitation[d]	✓				
Attachment style	Adult Attachment Scale	✓				
Childhood trauma	Childhood Trauma Questionnaire	✓				
Demographic variables	N/A[g]	✓				

[a]Intervention groups only.

[b]UCLA: University of California, Los Angeles.

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[c]PID-5-BF+: Personality Inventory for the Diagnostic and Statistical Manual of Mental Disorders-5 Brief Form Plus.

[d]Only subscales.

[e]Interpretation bias only.

[f]A total of 4 items will not be presented to participants in the SOLUS-D+automated feedback group as they are not plausible (eg, "The coach really cares about my well-being").

[g]N/A: not applicable.

Primary Outcome Measure

Loneliness, assessed with the 9-item short version [66] of the Revised UCLA Loneliness Scale [67,68] at the postassessment time point, is the primary outcome. The original scale, comprising 20 items, assesses 3 different facets of loneliness: intimate loneliness, relational loneliness, and collective loneliness [69]. The short version comprises the 3 items with the highest loading on each factor [70]. The reliability and validity of this short version are comparable with those of the full 20-item version [70]. The response options are *never* (1), *rarely* (2), *sometimes* (3), and *always* (4). Ratings are summed, and scores range from 9 to 36, with higher scores indicating greater loneliness levels.

Previous studies revealed a discrepancy, for example, in the prevalence of loneliness, when assessing loneliness directly or indirectly [71]. Therefore, loneliness will be further assessed with a single direct question ("Do you feel lonely"; rated on a 4-point scale with the response options 0=*no, never;* 1=*yes, sometimes*; 2=*yes, quite often*; 3=*yes, very often*) and a 3-item very short version [72] of the UCLA Loneliness Scale for which German population norms exist [73].

Secondary Outcome Measures

Depressive symptoms will be assessed using the 9-item depression module of the PHQ-9 [74,75]. All 9 items correspond to the 9 Diagnostic and Statistical Manual of Mental Disorders (DSM)–IV criteria for depression. The items are rated on a 4-point scale from 0 (not at all) to 3 (nearly every day). Ratings are summed up, and scores range from 0 to 27. The PHQ-9 shows good validity [74] and sensitivity to change [75].

Symptoms of social anxiety will be assessed with the short forms of the Social Interaction Anxiety Scale and Social Phobia Scale [76]. These 2 scales complement each other and are mostly administered together. The 12 items are rated on a 5-point scale from 0 (not at all) to 4 (extremely). The Social Interaction Anxiety Scale and Social Phobia Scale showed good validity and sensitivity to change over time [76].

Satisfaction with life will be measured with the Satisfaction With Life Scale [77,78]. A total of 5 items, such as "In most ways my life is close to my ideal," are rated on a 7-point scale from 1 (strongly disagree) to 7 (strongly agree). This scale shows good psychometric properties and norm values based on a large German sample [79].

Self-esteem will be assessed using the 10-item revised German version [80] of the Rosenberg Self-Esteem Scale [81]. This scale measures positive and negative aspects of self-esteem. Items are rated on a 4-point Likert scale ranging from 0 (strongly agree) to 3 (strongly disagree). The internal consistency of the 1 factorial solution is good (Cronbach α=.84) [80].

Objective social isolation will be measured using the Social Network Index [82]. This scale comprises 12 items assessing 12 different types of social relationships (eg, partner, parents, children, other close family members, close neighbors, friends, and fellow volunteers). Participants will be asked how many relationships of each type they have and how many of them they are in contact with at least once every 2 weeks. The network size, network diversity, and number of embedded subnetworks can be calculated using the Social Network Index [83].

Maladaptive personality traits will be assessed using the 34-item Personality Inventory for the DSM-5 Brief Form Plus [84], a 34-item short version of the Personality Inventory for DSM-5 [85]. The Personality Inventory for DSM-5 Brief Form Plus assesses 5 domains and 15 facets according to criterion B of the Alternative Model of Personality Disorders included in DSM-5, which are Negative Affectivity, Detachment, Antagonism, Disinhibition, and Psychoticism, plus the International Classification of Diseases (ICD)-11 domain Anankastia comprising 2 facets. Items are rated on a 4-point response scale ranging from 0 (very false or often false) to 3 (very true or often true). Scores can be calculated for the 17 facets and the 6 domains. Good internal consistency has been shown for the domain trait scores (McDonald ω=0.81) [84]. The average score of these 6 maladaptive trait domains can be used as an indicator of the severity of personality dysfunction according to the DSM-5 section III and the ICD-11 classification of Personality Disorders [86].

The negative effects of the intervention will be assessed with the Inventory for the Assessment of Negative Effects of Psychotherapy (INEP) [87]. The INEP assesses any adverse effects on social, intrapersonal, or work-related situations and whether they are attributed to the intervention. As in other studies on internet-based interventions, the INEP was slightly adapted for its use with internet-based interventions.

Client satisfaction with the treatment will be assessed with the Client Satisfaction Questionnaire-8 [88]. The 8 items are rated on a 4-point scale from 1 (low satisfaction) to 4 (high satisfaction). We adapted this measure to explore participants' satisfaction with the internet intervention applied in this study. The Client Satisfaction Questionnaire-8 is a valid measure for assessing client satisfaction [88] and shows good internal consistency (Cronbach α=.90) [89].

The usability of the web-based program will be assessed using the System Usability Scale [90]. For this study, we adapted the measure to explore the experienced usability of the web-based program used in this trial. A total of 10 items are rated on a 5-point scale ranging from 0 (*strongly disagree*) to 4 (strongly agree). The usability score is obtained by multiplying the sum of all item scores by 2.5 and ranges from 0 to 100.

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Diagnoses of mental disorders will be assessed using the short version of the Mini-DIPS–Open Access [91]. This structured interview is openly accessible and allows the reliable assessment of diagnoses according to the DSM-5 and ICD-10.

Adherence to the web-based program will be assessed using different indicators, such as (1) the number of modules completed and (2) time spent in the program. A module is completed when each page per module has been clicked at least once.

Assessment of Potential Mechanisms of Change

Interpretation bias will be assessed using the corresponding subscale of the Interpretation and Judgmental Bias Questionnaire [92,93]. The Interpretation and Judgmental Bias Questionnaire is a 24-item scale comprising brief scripts of 20 social events and 4 nonsocial control events. The social events can be divided into ambiguous, mildly negative, profoundly negative, and positive social events. For this study, we only assessed interpretation and not judgmental bias. For this purpose, each script will be followed with 4 alternative answers. The answers reflect positive, neutral, mildly negative, or profoundly negative interpretations of the event. The participants will be asked to rank the probability of these 4 interpretations. The score is the mean rank given to the profoundly negative interpretation of the scenarios and ranges between 1 and 4. A lower score indicates more negatively biased processing [94].

Rejection sensitivity will be assessed using the adapted adult version (Adult Rejection Sensitivity Questionnaire) [95] of the Rejection Sensitivity Questionnaire [96]. In the Adult Rejection Sensitivity Questionnaire, 9 hypothetical interpersonal situations are presented, and respondents indicate how they would feel or think in the stated situations. Respondents indicate on a 6-point scale how concerned they would be in that situation (very unconcerned to very concerned) and how likely they would expect to be accepted (very unlikely to very likely). One study shows high internal consistency (Cronbach α=.87) for the total score in a sample of adults with borderline personality disorder and acceptable consistency (Cronbach α=.75) for a healthy sample of adults [97].

Social avoidance behavior will be assessed with the subscale Behavior-social avoidance of the Cognitive-Behavioral Avoidance Scale [98,99]. Participants are asked to rate their social behavior on a 5-point Likert scale ranging from 1 (not at all true for me) to 5 (extremely true for me; eg, “I make excuses to get out of social activities.”). The subscale has shown good internal consistency (Cronbach α=.86) [99].

Comfort with self-disclosure will be assessed using the Distress Disclosure Index [100]. It is a 12-item scale designed to measure the degree to which a person is comfortable talking with others about personally distressing information (eg, “I am willing to tell others my distressing thoughts”). Items are rated on a 5-point Likert-type scale, with responses ranging from 1 (strongly disagree) to 5 (strongly agree). The Distress Disclosure Index has shown good psychometric properties [101].

Authenticity will be assessed using the 20-item short form (Kernis-Goldman Authenticity Inventory [KGAI]–Short Form [102]) of the KGAI version 3 [103]. It assesses 4 underlying dimensions of authenticity (awareness, unbiased processing, behavior, and relational orientation), and items are rated on a 5-point Likert scale ranging from 1 (*strongly disagree*) to 5 (*strongly agree*). The KGAI–Short Form shows good internal consistency (Cronbach α=.87) and good convergent and discriminant validity [102].

Self-compassion will be assessed using the Sussex Oxford Compassion Scale for the Self [104]. This scale measures five dimensions of compassion: (1) recognizing suffering, (2) understanding the universality of suffering, (3) feeling for the person in suffering, (4) tolerating uncomfortable feelings, and (5) motivation to act to alleviate the suffering. The 20 items will be rated on a 5-point scale ranging from 1 (not at all true) to 5 (always true). This scale shows adequate internal consistency and convergent and discriminant validity [104].

Misanthropy will be assessed using the respective subscale of the Bern Embitterment Inventory [105]. This subscale measures a general contempt of human beings (eg, “Sometimes I feel hatred towards mankind or a part of it”). The 4 items are rated on a scale from 0 (I do not agree) to 4 (I agree). The Cronbach α for this scale is .65 [105].

Self-determined motivation for solitude will be assessed with the corresponding 8-item subscale from the Motivation for Solitude Scale–Short Form [106]. This subscale measures the degree of the desire to spend time alone. Items are introduced with “When I spend time alone, I do so because...” and rated on a 4-point Likert scale from 1 (not at all important) to 4 (very important). The answers are summed, and higher scores indicate a higher self-determined motivation for solitude. The Motivation for Solitude Scale–Short Form is a reliable and valid measure of the motivation for solitude [106].

Working alliance will be assessed with the Working Alliance Inventory (Working Alliance Inventory-Short Revised) [107] adapted for guided internet interventions (WAI-I) [108]. The WAI-I comprises two subscales: (1) task and goal agreement dimension and (2) bond with the guide dimension (bond). The full scale comprises 12 items (eg, “With the online program, it has become clearer to me how I can change”) that are answered on a 5-point Likert scale ranging from 1 (never) to 5 (always). Participants in the ICBT condition without guidance will only respond to the 8 items of the task and goal dimension as the items of the bond dimension are not plausibly answerable. The WAI-I is a valid instrument for measuring working alliance in the context of guided interventions and shows good internal consistency for both the total score and the 2 subscales [108].

Assessment of Moderators

Mobility will be assessed using the corresponding subscale of the Patient Questionnaire for Medical Rehabilitation (Indicators of Rehabilitation Status-3) [109]. Respondents rate 4 items on a 5-point scale about how many difficulties they experienced during the past 4 weeks (eg, climbing a staircase over 3 floors). Items are rated on a 5-point scale from 1 (*impossible*) to 5 (*no difficulties*). The mobility subscale shows good internal consistency (Cronbach α=.85) [109].

Attachment style will be measured using the Adult Attachment Scale (AAS) [110,111]. The AAS comprises 16 items forming

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three subscales: (1) comfortability with closeness and intimacy, (2) the degree to which one can depend on others when they are needed, and (3) the degree to which one is worried about being rejected or unloved. The items are rated on a 5-point scale ranging from 1 (not at all characteristic of me) to 5 (very characteristic of me). The AAS shows satisfactory internal consistency (Cronbach α=.72-.79) [110].

Childhood trauma will be assessed using the 28-item Childhood Trauma Questionnaire [112,113]. Respondents are asked about their experiences of sexual, physical, and emotional maltreatment and physical and emotional neglect in childhood and adolescence. Items are rated on a 5-point Likert scale ranging from 1 (never true) to 5 (very often true). Higher values indicate a higher degree of childhood maltreatment. All scales (except physical neglect) show high internal consistency (Cronbach α ≥.89) [112].

Sample Size

A power analysis was conducted using G*Power 3 [114]. We aim to detect small effect sizes [115] of =0.10 (equivalent to Cohen *d*=0.20) regarding the time×group interaction for the 2 active conditions at an α error level of .05. A power analysis revealed that a sample size of 80 participants in each of the active study arms is required to detect a statistically significant difference with a power (1 – β) of 0.80, assuming correlations of *r*=0.60 between before and posttreatment measures, as previously found in another trial on ICBT for loneliness [57]. Sample size was further estimated based on a dropout rate of approximately 25%. We finally decided to randomize 100 participants to each of the active conditions. For the comparisons between the active conditions and the wait-list, 50 participants were considered sufficient for the wait-list control group condition as between-group effect sizes were assumed to be large based on the results of the aforementioned Swedish trials [54,57]. Consequently, we aim to randomize 250 participants with a randomization ratio of 2:2:1.

Statistical Analyses

Analyses will be conducted using an intention-to-treat sample. In addition, we will conduct analyses in the per-protocol sample (ie, comprising participants who complete both baseline and postassessment measures and log into ≥4 modules of the program, defined as minimal therapeutic exposure). To assess if randomization was successful, we will compare baseline characteristics between the 3 conditions using chi-square tests (categorical) and *F* tests (continuous). Continuous outcomes will be analyzed using mixed-effects models. These analyses will model random slopes and intercepts for participants and test the fixed effects of the condition, as well as repeated assessments over time, using data from all participants. Differential intervention efficacy shows in significant interactions between the condition and time. An advantage of mixed-effects models is their ability to account for missing values through maximum likelihood estimation [116]. Significant overall effects will be followed up with contrasts comparing the 2 active conditions pooled together (ie, ICBT with and without guidance) against the control group, followed by a comparison of the 2 active conditions against each other. Significance levels will be set at P=.05. Effect sizes will be computed based on the work by Cohen [117], dividing the treatment effect by the pooled SD. In addition, we will calculate reliable changes according to the Reliable Change Index [118].

To test the mediation hypotheses, we will determine the extent of mediation of the change scores from baseline to week 5 (midassessment) and baseline to week 10 (postassessment) on the potential mechanism of change in week 10 and follow-up loneliness scores, respectively. Indirect effects will be tested by calculating bootstrapped CIs [119].

To test the moderation hypotheses, we will exploratorily include the scores of the various measures as the moderation variable to build 3-way interaction terms (condition×time×moderator) in separate mixed models. To facilitate the post hoc interpretation of interaction effects, continuous moderator variables will be grand mean centered [120]. Significant interaction effects will be followed up by applying the Johnson-Neyman technique [121].

Results

Recruitment started in May 2021 and is expected to be completed in 2022, with the 12-month follow-ups to be completed in 2023. We intend to submit the first results for open access publication in 2023. In addition, the findings of this trial will be presented at national and international conferences. Only aggregated group data will be reported, and no individuals will be identifiable.

Discussion

General Discussion

Chronic loneliness is a prevalent clinical phenomenon in the population, with a variety of adverse effects on mental and physical health [8], leading to increased mortality [9]. Psychological interventions have generally been shown to be effective in reducing loneliness [48]. Such interventions at an individual level may play a crucial role in reducing the burden of loneliness and complementing social and societal-based interventions [122-124]. Although various treatments for alleviating loneliness have been developed and tested, more well-controlled clinical trials are needed to inform about efficacious interventions for loneliness.

This study aims to test the efficacy of an internet-based self-help intervention (*SOLUS-D*) in reducing loneliness. We expect participants in both intervention groups to show greater decreases in loneliness compared with a wait-list control group at the posttreatment time point. Furthermore, reductions in loneliness will be expected to be more pronounced in participants receiving guidance than in the group without guidance. By comparing the 2 intervention groups with and without guidance, we will be able to inform about the incremental effect of guidance beyond that of the ICBT intervention. We will also look at acceptability aspects such as intervention satisfaction, adherence, and potential negative effects to further refine the intervention. In addition, we will investigate potential moderating variables on an exploratory level to gain insights into how and for whom exactly the intervention works. Furthermore, knowledge on mechanisms

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of change in treating chronic loneliness will be expanded. This will provide further insight into the maintaining factors of chronic loneliness that interventions should focus on and, at the same time, test the proposed model of chronic loneliness [19]. Finally, the results of this study will inform which individuals can profit (most) from an internet-based ICBT intervention for loneliness.

Limitations

The limitations of our study must be considered. First, the sample in our study is self-selective and excludes individuals with no access to the internet or a device to use the intervention. Second, people with heightened degrees of symptom severity of mental disorders, such as at least moderately severe depressive symptoms, will be excluded from this study. Consequently, results will not be generalizable to all people experiencing loneliness. Third, within our study design, we will not be able to compare the long-term effects of the intervention with the wait-list, as we did not want the wait-list control group to wait too long to have access to the intervention. Fourth, we did not want to restrict access to care as usual in this study. This reduces the internal validity of this study to some extent while simultaneously increasing its external validity.

Conclusions

In this study protocol, we describe the design of an RCT evaluating an internet-based self-help intervention with and without guidance based on CBT principles for loneliness compared with a wait-list control group in adults. To the best of our knowledge, this is the first RCT to evaluate an internet-based self-help intervention based on CBT principles for loneliness in German-speaking countries. The results of this study will enrich previous findings on the efficacy of internet-based self-help interventions for loneliness and inform on what treatments work for whom in alleviating loneliness. On the basis of our findings, policy makers could be informed about the efficacy of interventions with low-threshold access for alleviating loneliness.

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Authors' Contributions

TK designed and received funding for this study. AK and GA provided the original Swedish version of the self-help program and provided helpful insights gained from their clinical trials on loneliness. NS, AS, and TK designed and extended the German version of the program. NS, AS, and TK conducted this study. NS and TK wrote the first draft of the manuscript. TB, ML, AK, and GA critically proofread the manuscript and provided valuable inputs for adjustments. All authors contributed to the final version of this manuscript.

Conflicts of Interest

None declared.

References

1. Jeste DV, Lee EE, Cacioppo S. Battling the modern behavioral epidemic of loneliness: suggestions for research and interventions. JAMA Psychiatry 2020 Jun 01;77(6):553-554 [FREE Full text] [doi: 10.1001/jamapsychiatry.2020.0027] [Medline: 32129811]
2. Lippke S, Keller F, Derksen C, Kötting L, Ratz T, Fleig L. Einsam(er) seit der Coronapandemie: Wer ist besonders betroffen? – psychologische Befunde aus Deutschland. Präv Gesundheitsf 2021 Mar 11;17(1):84-95. [doi: 10.1007/s11553-021-00837-w]
3. van der Velden PG, Hyland P, Contino C, von Gaudecker HM, Muffels R, Das M. Anxiety and depression symptoms, the recovery from symptoms, and loneliness before and after the COVID-19 outbreak among the general population: Findings from a Dutch population-based longitudinal study. PLoS One 2021;16(1):e0245057 [FREE Full text] [doi: 10.1371/journal.pone.0245057] [Medline: 33411843]
4. d'Hombres B, Schnepf S, Barjakovà M, Teixeira Mendonça F. Loneliness - an unequally shared burden in Europe*. European Commission. 2018. URL: https://knowledge4policy.ec.europa.eu/sites/default/files/fairness_pb2018_loneliness_jrc_i1.pdf [accessed 2022-06-16]
5. Beutel ME, Klein EM, Brähler E, Reiner I, Jünger C, Michal M, et al. Loneliness in the general population: prevalence, determinants and relations to mental health. BMC Psychiatry 2017 Mar 20;17(1):97 [FREE Full text] [doi: 10.1186/s12888-017-1262-x] [Medline: 28320380]

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6. Buecker S, Mund M, Chwastek S, Sostmann M, Luhmann M. Is loneliness in emerging adults increasing over time? A preregistered cross-temporal meta-analysis and systematic review. Psychol Bull 2021 Aug;147(8):787-805. [doi: 10.1037/bul0000332] [Medline: 34898234]
7. Luhmann M, Hawkley LC. Age differences in loneliness from late adolescence to oldest old age. Dev Psychol 2016 Jun;52(6):943-959 [FREE Full text] [doi: 10.1037/dev0000117] [Medline: 27148782]
8. Hawkley LC, Capitanio JP. Perceived social isolation, evolutionary fitness and health outcomes: a lifespan approach. Philos Trans R Soc Lond B Biol Sci 2015 May 26;370(1669):20140114 [FREE Full text] [doi: 10.1098/rstb.2014.0114] [Medline: 25870400]
9. Holt-Lunstad J, Smith TB, Baker M, Harris T, Stephenson D. Loneliness and social isolation as risk factors for mortality: a meta-analytic review. Perspect Psychol Sci 2015 Mar;10(2):227-237. [doi: 10.1177/1745691614568352] [Medline: 25910392]
10. Rico-Uribe LA, Caballero FF, Martín-María N, Cabello M, Ayuso-Mateos JL, Miret M. Association of loneliness with all-cause mortality: a meta-analysis. PLoS One 2018;13(1):e0190033 [FREE Full text] [doi: 10.1371/journal.pone.0190033] [Medline: 29300743]
11. Mann F, Bone JK, Lloyd-Evans B, Frerichs J, Pinfold V, Ma R, et al. A life less lonely: the state of the art in interventions to reduce loneliness in people with mental health problems. Soc Psychiatry Psychiatr Epidemiol 2017 Jun;52(6):627-638 [FREE Full text] [doi: 10.1007/s00127-017-1392-y] [Medline: 28528389]
12. Baumeister RF, Leary MR. The need to belong: desire for interpersonal attachments as a fundamental human motivation. Psychol Bull 1995 May;117(3):497-529. [Medline: 7777651]
13. Peplau L, Perlman D. Perspective on loneliness. In: Peplau LA, Perlman D, editors. Lonelinss: A Sourcebook of Current Theory, Research and Therapy. New York, NY, USA: John Wiley and Sons; 1982:1-18.
14. Hyland P, Shevlin M, Cloitre M, Karatzias T, Vallières F, McGinty G, et al. Quality not quantity: loneliness subtypes, psychological trauma, and mental health in the US adult population. Soc Psychiatry Psychiatr Epidemiol 2019 Sep;54(9):1089-1099. [doi: 10.1007/s00127-018-1597-8] [Medline: 30293176]
15. Young JE. Loneliness, depression and cognitive therapy: theory and application. In: Peplau LA, Perlman D, editors. Lonelinss: A Sourcebook of Current Theory, Research and Therapy. New York, NY, USA: John Wiley & Sons; 1982:379-405.
16. Cacioppo JT, Hawkley LC, Ernst JM, Burleson M, Berntson GG, Nouriani B, et al. Loneliness within a nomological net: an evolutionary perspective. J Res Pers 2006 Dec;40(6):1054-1085. [doi: 10.1016/j.jrp.2005.11.007]
17. Asher SR, Paquette JA. Loneliness and peer relations in childhood. Curr Dir Psychol Sci 2016 Jun 23;12(3):75-78 [FREE Full text] [doi: 10.1111/1467-8721.01233]
18. Shiovitz-Ezra S, Ayalon L. Situational versus chronic loneliness as risk factors for all-cause mortality. Int Psychogeriatr 2010 May;22(3):455-462. [doi: 10.1017/S1041610209991426] [Medline: 20003631]
19. Cacioppo JT, Hawkley LC. Perceived social isolation and cognition. Trends Cogn Sci 2009 Oct;13(10):447-454 [FREE Full text] [doi: 10.1016/j.tics.2009.06.005] [Medline: 19726219]
20. Qualter P, Vanhalst J, Harris R, Van Roekel E, Lodder G, Bangee M, et al. Loneliness across the life span. Perspect Psychol Sci 2015 Mar;10(2):250-264. [doi: 10.1177/1745691615568999] [Medline: 25910393]
21. Gardner WL, Pickett CL, Jefferis V, Knowles M. On the outside looking in: loneliness and social monitoring. Pers Soc Psychol Bull 2005 Nov;31(11):1549-1560. [doi: 10.1177/0146167205277208] [Medline: 16207773]
22. Watson J, Nesdale D. Rejection sensitivity, social withdrawal, and loneliness in young adults. J Appl Soc Psychol 2012 Jun 14;42(8):1984-2005 [FREE Full text] [doi: 10.1111/j.1559-1816.2012.00927.x]
23. Spithoven AW, Bijttebier P, Goossens L. It is all in their mind: a review on information processing bias in lonely individuals. Clin Psychol Rev 2017 Dec;58:97-114. [doi: 10.1016/j.cpr.2017.10.003] [Medline: 29102150]
24. Bryan JL, Baker ZG, Tou RY. Prevent the blue, be true to you: authenticity buffers the negative impact of loneliness on alcohol-related problems, physical symptoms, and depressive and anxiety symptoms. J Health Psychol 2017 Apr;22(5):605-616. [doi: 10.1177/1359105315609090] [Medline: 26490626]
25. Burke TJ, Woszidlo A, Segrin C. Social skills, family conflict, and loneliness in families. Commun Rep 2012 Jul 8;25(2):75-87. [doi: 10.1080/08934215.2012.719461]
26. Leung L. Loneliness, self-disclosure, and ICQ ("I seek you") use. Cyberpsychol Behav 2002 Jun;5(3):241-251. [doi: 10.1089/109493102760147240] [Medline: 12123247]
27. Preece DA, Goldenberg A, Becerra R, Boyes M, Hasking P, Gross JJ. Loneliness and emotion regulation. Pers Individ Dif 2021 Oct;180:110974. [doi: 10.1016/j.paid.2021.110974]
28. Best T, Herring L, Clarke C, Kirby J, Gilbert P. The experience of loneliness: the role of fears of compassion and social safeness. Pers Individ Dif 2021 Dec;183:111161. [doi: 10.1016/j.paid.2021.111161]
29. Collins NL, Miller LC. Self-disclosure and liking: a meta-analytic review. Psychol Bull 1994 Nov;116(3):457-475. [doi: 10.1037/0033-2909.116.3.457] [Medline: 7809308]
30. Laurenceau JP, Barrett LF, Pietromonaco PR. Intimacy as an interpersonal process: the importance of self-disclosure, partner disclosure, and perceived partner responsiveness in interpersonal exchanges. J Pers Soc Psychol 1998 May;74(5):1238-1251. [doi: 10.1037//0022-3514.74.5.1238] [Medline: 9599440]

XSL•FO
RenderX

31. Butler EA, Egloff B, Wilhelm FH, Smith NC, Erickson EA, Gross JJ. The social consequences of expressive suppression. Emotion 2003 Mar;3(1):48-67. [doi: 10.1037/1528-3542.3.1.48] [Medline: 12899316]
32. Plasencia ML, Taylor CT, Alden LE. Unmasking one's true self facilitates positive relational outcomes. Clin Psychol Sci 2016 Jun 23;4(6):1002-1014. [doi: 10.1177/2167702615622204]
33. Neff KD, Beretvas SN. The role of self-compassion in romantic relationships. Self Identity 2013 Jan;12(1):78-98. [doi: 10.1080/15298868.2011.639548]
34. Lathren CR, Rao SS, Park J, Bluth K. Self-compassion and current close interpersonal relationships: a scoping literature review. Mindfulness 2021 May;12(5):1078-1093 [FREE Full text] [doi: 10.1007/s12671-020-01566-5] [Medline: 35309268]
35. Bellucci G. Positive attitudes and negative expectations in lonely individuals. Sci Rep 2020 Oct 29;10(1):18595 [FREE Full text] [doi: 10.1038/s41598-020-75712-3] [Medline: 33122843]
36. Tsai FF, Reis HT. Perceptions by and of lonely people in social networks. Pers Relatsh 2009 Jun;16(2):221-238 [FREE Full text] [doi: 10.1111/j.1475-6811.2009.01220.x]
37. Wei M, Russell DW, Zakalik RA. Adult attachment, social self-efficacy, self-disclosure, loneliness, and subsequent depression for freshman college students: a longitudinal study. J Couns Psychol 2005 Oct;52(4):602-614. [doi: 10.1037/0022-0167.52.4.602]
38. Käll A, Shafran R, Lindegaard T, Bennett S, Cooper Z, Coughtrey A, et al. A common elements approach to the development of a modular cognitive behavioral theory for chronic loneliness. J Consult Clin Psychol 2020 Mar;88(3):269-282. [doi: 10.1037/ccp0000454] [Medline: 32068427]
39. Santini ZI, Jose PE, York Cornwell E, Koyanagi A, Nielsen L, Hinrichsen C, et al. Social disconnectedness, perceived isolation, and symptoms of depression and anxiety among older Americans (NSHAP): a longitudinal mediation analysis. Lancet Public Health 2020 Jan;5(1):e62-e70 [FREE Full text] [doi: 10.1016/S2468-2667(19)30230-0] [Medline: 31910981]
40. Michalska da Rocha B, Rhodes S, Vasilopoulou E, Hutton P. Loneliness in psychosis: a meta-analytical review. Schizophr Bull 2018 Jan 13;44(1):114-125 [FREE Full text] [doi: 10.1093/schbul/sbx036] [Medline: 28369646]
41. Ernst M, Klein EM, Beutel ME, Brähler E. Gender-specific associations of loneliness and suicidal ideation in a representative population sample: young, lonely men are particularly at risk. J Affect Disord 2021 Nov 01;294:63-70. [doi: 10.1016/j.jad.2021.06.085] [Medline: 34274789]
42. Gomboc V, Krohne N, Lavrič M, Podlogar T, Poštuvan V, Zadravec Šedivy N, et al. Emotional and social loneliness as predictors of suicidal ideation in different age groups. Community Ment Health J 2022 Feb;58(2):311-320. [doi: 10.1007/s10597-021-00823-8] [Medline: 33847847]
43. Griffin SC, Williams AB, Ravyts SG, Mladen SN, Rybarczyk BD. Loneliness and sleep: a systematic review and meta-analysis. Health Psychol Open 2020;7(1):2055102920913235 [FREE Full text] [doi: 10.1177/2055102920913235] [Medline: 32284871]
44. VanderWeele TJ, Hawkley LC, Cacioppo JT. On the reciprocal association between loneliness and subjective well-being. Am J Epidemiol 2012 Nov 01;176(9):777-784 [FREE Full text] [doi: 10.1093/aje/kws173] [Medline: 23077285]
45. Cacioppo JT, Hawkley LC, Thisted RA. Perceived social isolation makes me sad: 5-year cross-lagged analyses of loneliness and depressive symptomatology in the Chicago Health, Aging, and Social Relations Study. Psychol Aging 2010 Jun;25(2):453-463 [FREE Full text] [doi: 10.1037/a0017216] [Medline: 20545429]
46. Cacioppo JT, Hughes ME, Waite LJ, Hawkley LC, Thisted RA. Loneliness as a specific risk factor for depressive symptoms: cross-sectional and longitudinal analyses. Psychol Aging 2006 Mar;21(1):140-151. [doi: 10.1037/0882-7974.21.1.140] [Medline: 16594799]
47. Lim MH, Rodebaugh TL, Zyphur MJ, Gleeson JF. Loneliness over time: the crucial role of social anxiety. J Abnorm Psychol 2016 Jul;125(5):620-630. [doi: 10.1037/abn0000162] [Medline: 27124713]
48. Hickin N, Käll A, Shafran R, Sutcliffe S, Manzotti G, Langan D. The effectiveness of psychological interventions for loneliness: a systematic review and meta-analysis. Clin Psychol Rev 2021 Aug;88:102066. [doi: 10.1016/j.cpr.2021.102066] [Medline: 34339939]
49. Masi CM, Chen HY, Hawkley LC, Cacioppo JT. A meta-analysis of interventions to reduce loneliness. Pers Soc Psychol Rev 2011 Aug;15(3):219-266 [FREE Full text] [doi: 10.1177/1088868310377394] [Medline: 20716644]
50. Poscia A, Stojanovic J, La Milia DI, Duplaga M, Grysztar M, Moscato U, et al. Interventions targeting loneliness and social isolation among the older people: an update systematic review. Exp Gerontol 2018 Feb;102:133-144. [doi: 10.1016/j.exger.2017.11.017] [Medline: 29199121]
51. Ma R, Mann F, Wang J, Lloyd-Evans B, Terhune J, Al-Shihabi A, et al. The effectiveness of interventions for reducing subjective and objective social isolation among people with mental health problems: a systematic review. Soc Psychiatry Psychiatr Epidemiol 2020 Jul;55(7):839-876 [FREE Full text] [doi: 10.1007/s00127-019-01800-z] [Medline: 31741017]
52. Andersson G. Internet-delivered psychological treatments. Annu Rev Clin Psychol 2016;12:157-179. [doi: 10.1146/annurev-clinpsy-021815-093006] [Medline: 26652054]
53. Lau S, Gruen GE. The social stigma of loneliness: effect of target person's and perceiver's sex. Pers Soc Psychol Bull 1992 Apr;18(2):182-189. [doi: 10.1177/0146167292182009]

XSL•FO
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54. Käll A, Jägholm S, Hesser H, Andersson F, Mathaldi A, Norkvist BT, et al. Internet-based cognitive behavior therapy for loneliness: a pilot randomized controlled trial. Behav Ther 2020 Jan;51(1):54-68. [doi: 10.1016/j.beth.2019.05.001] [Medline: 32005340]
55. Soucy JN, Hadjistavropoulos HD. Treatment acceptability and preferences for managing severe health anxiety: perceptions of Internet-delivered cognitive behaviour therapy among primary care patients. J Behav Ther Exp Psychiatry 2017 Dec;57:14-24. [doi: 10.1016/j.jbtep.2017.02.002] [Medline: 28242411]
56. Käll A, Backlund U, Shafran R, Andersson A. Lonesome no more? A two-year follow-up of internet-administered cognitive behavioral therapy for loneliness. Internet Interv 2020 Mar;19:100301 [FREE Full text] [doi: 10.1016/j.invent.2019.100301] [Medline: 32071885]
57. Käll A, Bäck M, Welin C, Åman H, Bjerkander R, Wänman M, et al. Therapist-guided internet-based treatments for loneliness: a randomized controlled three-arm trial comparing cognitive behavioral therapy and interpersonal psychotherapy. Psychother Psychosom 2021;90(5):351-358 [FREE Full text] [doi: 10.1159/000516989] [Medline: 34182552]
58. Bouwman TE, Aartsen MJ, van Tilburg TG, Stevens NL. Does stimulating various coping strategies alleviate loneliness? Results from an online friendship enrichment program. J Soc Pers Relat 2017 Sep;34(6):793-811 [FREE Full text] [doi: 10.1177/0265407516659158] [Medline: 28867863]
59. Bouwman T, van Tilburg T, Aartsen M. Attrition in an online loneliness intervention for adults aged 50 years and older: survival analysis. JMIR Aging 2019 Jul 24;2(2):e13638 [FREE Full text] [doi: 10.2196/13638] [Medline: 31518268]
60. Moshe I, Terhorst Y, Philippi P, Domhardt M, Cuijpers P, Cristea I, et al. Digital interventions for the treatment of depression: a meta-analytic review. Psychol Bull 2021 Aug;147(8):749-786. [doi: 10.1037/bul0000334] [Medline: 34898233]
61. Study Website SOLUS. SOLUS. URL: https://selfhelp.psy.unibe.ch/solus/Homepage [accessed 2022-06-16]
62. Online self-help and psychotherapy at the University of Bern. Department of Clinical Psychology and Psychotherapy, University of Bern. 2021. URL: http://www.online-therapy.ch/ [accessed 2022-06-16]
63. Bur OT, Krieger T, Moritz S, Klein JP, Berger T. Optimizing the context of support of Web-based self-help in individuals with mild to moderate depressive symptoms: a randomized full factorial trial. Behav Res Ther 2022 May;152:104070 [FREE Full text] [doi: 10.1016/j.brat.2022.104070] [Medline: 35306266]
64. Brog NA, Hegy JK, Berger T, Znoj H. Effects of an Internet-based self-help intervention for psychological distress due to COVID-19: results of a randomized controlled trial. Internet Interv 2022 Mar;27:100492 [FREE Full text] [doi: 10.1016/j.invent.2021.100492] [Medline: 34956841]
65. Mohr DC, Cuijpers P, Lehman K. Supportive accountability: a model for providing human support to enhance adherence to eHealth interventions. J Med Internet Res 2011 Mar 10;13(1):e30 [FREE Full text] [doi: 10.2196/jmir.1602] [Medline: 21393123]
66. Luhmann M, Bohn J, Holtmann J, Koch T, Eid M. I'm lonely, can't you tell? Convergent validity of self- and informant ratings of loneliness. J Res Pers 2016 Apr;61:50-60. [doi: 10.1016/j.jrp.2016.02.002]
67. Döring N, Bortz J. Psychometrische Einsamkeitsforschung: Deutsche Neukonstruktion der UCLA Loneliness Scale. Diagnostica 1993;39(3):224-239.
68. Russell DW. UCLA Loneliness Scale (Version 3): reliability, validity, and factor structure. J Pers Assess 1996 Feb;66(1):20-40. [doi: 10.1207/s15327752jpa6601_2] [Medline: 8576833]
69. Hawkley LC, Browne MW, Cacioppo JT. How can I connect with thee? Let me count the ways. Psychol Sci 2005 Oct;16(10):798-804. [doi: 10.1111/j.1467-9280.2005.01617.x] [Medline: 16181443]
70. Cacioppo JT, Adler AB, Lester PB, McGurk D, Thomas JL, Chen HY, et al. Building social resilience in soldiers: a double dissociative randomized controlled study. J Pers Soc Psychol 2015 Jul;109(1):90-105. [doi: 10.1037/pspi0000022] [Medline: 26098588]
71. Shiovitz-Ezra S, Ayalon L. Use of direct versus indirect approaches to measure loneliness in later life. Res Aging 2011 Dec 14;34(5):572-591. [doi: 10.1177/0164027511423258]
72. Hughes ME, Waite LJ, Hawkley LC, Cacioppo JT. A short scale for measuring loneliness in large surveys: results from two population-based studies. Res Aging 2004;26(6):655-672 [FREE Full text] [doi: 10.1177/0164027504268574] [Medline: 18504506]
73. Klein E, Zenger M, Tibubos AN, Ernst M, Reiner I, Schmalbach B, et al. Loneliness and its relation to mental health in the general population: validation and norm values of a brief measure. J Affect Disord Rep 2021 Apr;4:100120. [doi: 10.1016/j.jadr.2021.100120]
74. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. J Gen Intern Med 2001 Sep;16(9):606-613 [FREE Full text] [doi: 10.1046/j.1525-1497.2001.016009606.x] [Medline: 11556941]
75. Löwe B, Kroenke K, Herzog B, Gräfe K. Measuring depression outcome with a brief self-report instrument: sensitivity to change of the Patient Health Questionnaire (PHQ-9). J Affect Disord 2004 Jul;81(1):61-66. [doi: 10.1016/S0165-0327(03)00198-8] [Medline: 15183601]
76. Peters L, Sunderland M, Andrews G, Rapee RM, Mattick RP. Development of a short form Social Interaction Anxiety (SIAS) and Social Phobia Scale (SPS) using nonparametric item response theory: the SIAS-6 and the SPS-6. Psychol Assess 2012 Mar;24(1):66-76. [doi: 10.1037/a0024544] [Medline: 21744971]

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77. Diener E, Emmons RA, Larsen RJ, Griffin S. The satisfaction with life scale. J Pers Assess 1985 Feb;49(1):71-75. [doi: 10.1207/s15327752jpa4901_13] [Medline: 16367493]
78. Schumacher J. Satisfaction with life scale. In: Schumacher J, Klaiberg A, Brähler E, editors. Diagnostische Verfahren zu Lebensqualität und Wohlbefinden. Göttingen, Germany: Hogrefe Publishing; 2003:305-309.
79. Hinz A, Conrad I, Schroeter ML, Glaesmer H, Brähler E, Zenger M, et al. Psychometric properties of the Satisfaction with Life Scale (SWLS), derived from a large German community sample. Qual Life Res 2018 Jun;27(6):1661-1670. [doi: 10.1007/s11136-018-1844-1] [Medline: 29589212]
80. von Collani G, Herzberg PY. Eine revidierte Fassung der deutschsprachigen Skala zum Selbstwertgefühl von Rosenberg. Zeitschrift für Differentielle und Diagnostische Psychologie 2003 Mar;24(1):3-7. [doi: 10.1024//0170-1789.24.1.3]
81. Rosenberg M. Society and the Adolescent Self-Image. Princeton, NJ, USA: Princeton University Press; 1965.
82. Cohen S, Doyle WJ, Skoner DP, Rabin BS, Gwaltney JM. Social ties and susceptibility to the common cold. JAMA 1997 Jun 25;277(24):1940-1944. [Medline: 9200634]
83. Liebke L, Bungert M, Thome J, Hauschild S, Gescher DM, Schmahl C, et al. Loneliness, social networks, and social functioning in borderline personality disorder. Personal Disord 2017 Oct;8(4):349-356. [doi: 10.1037/per0000208] [Medline: 27505189]
84. Kerber A, Schultze M, Müller S, Rühling RM, Wright AG, Spitzer C, et al. Development of a short and ICD-11 compatible measure for maladaptive personality traits using ant colony optimization algorithms. Assessment 2022 Apr;29(3):467-487 [FREE Full text] [doi: 10.1177/1073191120971848] [Medline: 33371717]
85. Krueger RF, Derringer J, Markon KE, Watson D, Skodol AE. Initial construction of a maladaptive personality trait model and inventory for DSM-5. Psychol Med 2012 Sep;42(9):1879-1890 [FREE Full text] [doi: 10.1017/S0033291711002674] [Medline: 22153017]
86. Zimmermann J, Müller S, Bach B, Hutsebaut J, Hummelen B, Fischer F. A common metric for self-reported severity of personality disorder. Psychopathology 2020 May 19;53(3-4):168-178. [doi: 10.1159/000507377]
87. Ladwig I, Rief W, Nestoriuc Y. Welche Risiken und Nebenwirkungen hat Psychotherapie? - Entwicklung des Inventars zur Erfassung Negativer Effekte von Psychotherapie (INEP). Verhaltenstherapie 2014 Oct 30;24(4):252-263 [FREE Full text] [doi: 10.1159/000367928]
88. Schmidt J, Lamprecht F, Wittmann WW. Zufriedenheit mit der stationären Versorgung. Entwicklung eines Fragebogens und erste Validitätsuntersuchungen. Psychother Psychosom Med Psychol 1989 Jul;39(7):248-255. [Medline: 2762479]
89. Kriz D, Nübling R, Steffanowski A, Wittmann WW, Schmidt J. Patientenzufriedenheit in der stationären rehabilitation: psychometrische Reanalyse des ZUF-8 auf der Basis multizentrischer Stichproben verschiedener Indikation. Z Med Psychol 2008;17(2-3):67-79 [FREE Full text]
90. Brooke J. SUS: a 'quick and dirty' usability scale. In: Jordan PW, Thomas B, McClelland IL, Weerdmeester B, editors. Usability Evaluation in Industry. London, UK: Taylor & Francis; 1996:189-194.
91. Margraf J, Cwik JC, Pflug V, Schneider S. Strukturierte klinische Interviews zur Erfassung psychischer Störungen über die Lebensspanne. Z Klin Psychol Psychother 2017 Jul;46(3):176-186. [doi: 10.1026/1616-3443/a000430]
92. Brettschneider M, Neumann P, Berger T, Renneberg B, Boettcher J. Internet-based interpretation bias modification for social anxiety: a pilot study. J Behav Ther Exp Psychiatry 2015 Dec;49(Pt A):21-29. [doi: 10.1016/j.jbtep.2015.04.008] [Medline: 26005201]
93. Voncken MJ, Bögels SM, de Vries K. Interpretation and judgmental biases in social phobia. Behav Res Ther 2003 Dec;41(12):1481-1488. [doi: 10.1016/s0005-7967(03)00143-8] [Medline: 14583415]
94. Badra M, Schulze L, Becker ES, Vrijsen JN, Renneberg B, Zetsche U. The association between ruminative thinking and negative interpretation bias in social anxiety. Cogn Emot 2017 Sep;31(6):1234-1242. [doi: 10.1080/02699931.2016.1193477] [Medline: 27279528]
95. Berenson KR, Gyurak A, Ayduk O, Downey G, Garner MJ, Mogg K, et al. Rejection sensitivity and disruption of attention by social threat cues. J Res Pers 2009 Dec 01;43(6):1064-1072 [FREE Full text] [doi: 10.1016/j.jrp.2009.07.007] [Medline: 20160869]
96. Downey G, Feldman SI. Implications of rejection sensitivity for intimate relationships. J Pers Soc Psychol 1996 Jun;70(6):1327-1343. [doi: 10.1037//0022-3514.70.6.1327] [Medline: 8667172]
97. Bungert M, Liebke L, Thome J, Haeussler K, Bohus M, Lis S. Rejection sensitivity and symptom severity in patients with borderline personality disorder: effects of childhood maltreatment and self-esteem. Borderline Personal Disord Emot Dysregul 2015;2:4 [FREE Full text] [doi: 10.1186/s40479-015-0025-x] [Medline: 26401307]
98. Ottenbreit ND, Dobson KS. Avoidance and depression: the construction of the cognitive-behavioral avoidance scale. Behav Res Ther 2004 Mar;42(3):293-313. [doi: 10.1016/S0005-7967(03)00140-2] [Medline: 14975771]
99. Röthlin P, Grosse Holtforth M, Bergomi C, Berking M, Ottenbreit ND, Caspar F. Vermeidung und depression. Diagnostica 2010 Jan 22;56(1):46-55. [doi: 10.1026/0012-1924/a000008]
100. Kahn JH, Hessling RM. Measuring the tendency to conceal versus disclose psychological distress. J Soc Clin Psychol 2001 Mar;20(1):41-65. [doi: 10.1521/jscp.20.1.41.22254]
101. Kahn JH, Hucke BE, Bradley AM, Glinski AJ, Malak BL. The Distress Disclosure Index: a research review and multitrait-multimethod examination. J Couns Psychol 2012 Jan;59(1):134-149. [doi: 10.1037/a0025716] [Medline: 22023329]

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102. Bond MJ, Strauss NE, Wickham RE. Development and validation of the Kernis-Goldman authenticity inventory-short form (KGAI-SF). Pers Individ Dif 2018 Nov;134:1-6. [doi: 10.1016/j.paid.2018.05.033]
103. Kernis MH, Goldman BM. A multicomponent conceptualization of authenticity: theory and research. Adv Exp Soc Psychol 2006;38:283-357 [FREE Full text] [doi: 10.1016/s0065-2601(06)38006-9]
104. Gu J, Baer R, Cavanagh K, Kuyken W, Strauss C. Development and psychometric properties of the Sussex-Oxford Compassion Scales (SOCS). Assessment 2020 Jan;27(1):3-20 [FREE Full text] [doi: 10.1177/1073191119860911] [Medline: 31353931]
105. Znoj H. Berner Verbitterungs-Inventar. Göttingen, Germany: Hogrefe Publishing; 2008.
106. Thomas V, Azmitia M. Motivation matters: development and validation of the Motivation for Solitude Scale - Short Form (MSS-SF). J Adolesc 2019 Jan;70:33-42. [doi: 10.1016/j.adolescence.2018.11.004] [Medline: 30472399]
107. Munder T, Wilmers F, Leonhart R, Linster HW, Barth J. Working Alliance Inventory-Short Revised (WAI-SR): psychometric properties in outpatients and inpatients. Clin Psychol Psychother 2010;17(3):231-239. [doi: 10.1002/cpp.658] [Medline: 20013760]
108. Gómez Penedo JM, Berger T, Grosse Holtforth M, Krieger T, Schröder J, Hohagen F, et al. The Working Alliance Inventory for guided Internet interventions (WAI-I). J Clin Psychol 2020 Jun;76(6):973-986. [doi: 10.1002/jclp.22823] [Medline: 31240727]
109. Bührlen B, Gerdes N, Jäckel WH. [Development and psychometric testing of a patient questionnaire for medical rehabilitation (IRES-3)]. Rehabilitation (Stuttg) 2005 Apr;44(2):63-74. [doi: 10.1055/s-2004-834687] [Medline: 15789288]
110. Schmidt S, Strauss B, Höger D, Brähler E. Die Adult Attachment Scale (AAS) - Teststatistische Prüfung und Normierung der deutschen Version. Psychother Psychosom Med Psychol 2004;54(9-10):375-382. [doi: 10.1055/s-2003-815000] [Medline: 15343479]
111. Collins NL, Read SJ. Adult attachment, working models, and relationship quality in dating couples. J Pers Soc Psychol 1990 Apr;58(4):644-663. [doi: 10.1037//0022-3514.58.4.644] [Medline: 14570079]
112. Wingenfeld K, Spitzer C, Mensebach C, Grabe HJ, Hill A, Gast U, et al. Die deutsche Version des Childhood Trauma Questionnaire (CTQ): Erste Befunde zu den psychometrischen Kennwerten. Psychother Psychosom Med Psychol 2010 Nov;60(11):442-450. [doi: 10.1055/s-0030-1247564] [Medline: 20200804]
113. Bernstein DP, Stein JA, Newcomb MD, Walker E, Pogge D, Ahluvalia T, et al. Development and validation of a brief screening version of the Childhood Trauma Questionnaire. Child Abuse Negl 2003 Feb;27(2):169-190. [doi: 10.1016/s0145-2134(02)00541-0] [Medline: 12615092]
114. Faul F, Erdfelder E, Lang A, Buchner A. G*Power 3: a flexible statistical power analysis program for the social, behavioral, and biomedical sciences. Behav Res Methods 2007 May;39(2):175-191. [doi: 10.3758/bf03193146] [Medline: 17695343]
115. Baumeister H, Reichler L, Munzinger M, Lin J. The impact of guidance on Internet-based mental health interventions — a systematic review. Internet Interv 2014 Oct;1(4):205-215. [doi: 10.1016/j.invent.2014.08.003]
116. Graham JW. Missing data analysis: making it work in the real world. Annu Rev Psychol 2009;60:549-576. [doi: 10.1146/annurev.psych.58.110405.085530] [Medline: 18652544]
117. Cohen J. A power primer. Psychol Bull 1992 Jul;112(1):155-159. [doi: 10.1037//0033-2909.112.1.155] [Medline: 19565683]
118. Jacobson NS, Truax P. Clinical significance: a statistical approach to defining meaningful change in psychotherapy research. J Consult Clin Psychol 1991 Feb;59(1):12-19. [doi: 10.1037//0022-006x.59.1.12] [Medline: 2002127]
119. Preacher KJ, Hayes AF. SPSS and SAS procedures for estimating indirect effects in simple mediation models. Behav Res Methods Instrum Comput 2004 Nov;36(4):717-731. [doi: 10.3758/bf03206553] [Medline: 15641418]
120. Aiken LS, West SG. Multiple Regression: Testing and Interpreting Interactions. Thousand Oaks, CA, USA: Sage Publications; 1991.
121. Hayes AF. Introduction to Mediation, Moderation, and Conditional Process Analysis: A Regression-based Approach. 2nd edition. New York, NY, USA: The Guilford Press; 2018.
122. Wang J, Mann F, Lloyd-Evans B, Ma R, Johnson S. Associations between loneliness and perceived social support and outcomes of mental health problems: a systematic review. BMC Psychiatry 2018 May 29;18(1):156 [FREE Full text] [doi: 10.1186/s12888-018-1736-5] [Medline: 29843662]
123. Holt-Lunstad J. Why social relationships are important for physical health: a systems approach to understanding and modifying risk and protection. Annu Rev Psychol 2018 Jan 04;69:437-458. [doi: 10.1146/annurev-psych-122216-011902] [Medline: 29035688]
124. Holt-Lunstad J. Social connection as a public health issue: the evidence and a systemic framework for prioritizing the "social" in social determinants of health. Annu Rev Public Health 2022 Apr 05;43:193-213. [doi: 10.1146/annurev-publhealth-052020-110732] [Medline: 35021021]

Abbreviations

AAS: Adult Attachment Scale
CBT: cognitive behavioral therapy
DSM: Diagnostic and Statistical Manual of Mental Disorders

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ICBT: internet-based cognitive behavioral therapy
ICD: International Classification of Diseases
IIPT: internet-based interpersonal therapy
INEP: Inventory for the Assessment of Negative Effects of Psychotherapy
KGAI: Kernis-Goldman Authenticity Inventory
Mini-DIPS: Mini Diagnostic Interview for Mental Disorders
PHQ-9: Patient Health Questionnaire-9
RCT: randomized controlled trial
UCLA: University of California, Los Angeles
WAI-I: Working Alliance Inventory for Internet interventions

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Protocol

Smartphone App Delivery of a Just-In-Time Adaptive Intervention for Adult Gamblers (Gambling Habit Hacker): Protocol for a Microrandomized Trial

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Abstract

Background: People with gambling problems frequently report repeated unsuccessful attempts to change their behavior. Although many behavior change techniques are available to individuals to reduce gambling harm, they can be challenging to implement or maintain. The provision of implementation support tailored for immediate, real-time, individualized circumstances may improve attempts at behavior change.

Objective: We aimed to develop and evaluate a Just-In-Time Adaptive Intervention (JITAI) for individuals who require support to adhere to their gambling limits. JITAI development is based on the principles of the Health Action Process Approach with delivery, in alignment with the principles of self-determination theory. The primary objective was to determine the effect of action- and coping planning compared with no intervention on the goal of subsequently adhering to gambling expenditure limits.

Methods: *Gambling Habit Hacker* is delivered as a JITAI providing in-the-moment support for adhering to gambling expenditure limits (primary proximal outcome). Delivered via a smartphone app, this JITAI delivers tailored behavior change techniques related to goal setting, action planning, coping planning, and self-monitoring. The *Gambling Habit Hacker* app will be evaluated using a 28-day microrandomized trial. Up to 200 individuals seeking support for their own gambling from Australia and New Zealand will set a gambling expenditure limit (ie, goal). They will then be asked to complete 3 time-based ecological momentary assessments (EMAs) per day over a 28-day period. EMAs will assess real-time adherence to gambling limits, strength of intention to adhere to goals, goal self-efficacy, urge self-efficacy, and being in high-risk situations. On the basis of the responses to each EMA, participants will be randomized to the control (a set of 25 self-enactable strategies containing names only and no implementation information) or intervention (self-enactable strategy implementation information with facilitated action- and coping planning) conditions. This microrandomized trial will be supplemented with a 6-month within-group follow-up that explores the long-term impact of the app on gambling expenditure (primary distal outcome) and a range of secondary outcomes, as well as an evaluation of the acceptability of the JITAI via postintervention surveys, app use and engagement indices, and semistructured interviews. This trial has been approved by the Deakin University Human Research Ethics Committee (2020-304).

Results: The intervention has been subject to expert user testing, with high acceptability scores. The results will inform a more nuanced version of the *Gambling Habit Hacker* app for wider use.

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Conclusions: *Gambling Habit Hacker* is part of a suite of interventions for addictive behaviors that deliver implementation support grounded in lived experience. This study may inform the usefulness of delivering implementation intentions in real time and in real-world settings. It potentially offers people with gambling problems new support to set their gambling intentions and adhere to their limits.

Trial Registration: Australian New Zealand Clinical Trials Registry ACTRN12622000497707; www.anzctr.org.au/Trial/Registration/TrialReview.aspx?id=383568

International Registered Report Identifier (IRRID): DERR1-10.2196/38919

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KEYWORDS

Just-In-Time Adaptive Intervention; JITAI; ecological momentary assessment; EMA; ecological momentary intervention; EMI; gambling; behavior change technique; implementation intentions; action planning; coping planning; microrandomized trial; mobile phone

Introduction

Background

Gambling disorder is classified as an addiction and related disorder in The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition. It is characterized by repeated unsuccessful attempts to change behavior, loss of control, and the development of tolerance and withdrawal symptoms [1]. Problem gambling is a commonly used term in many jurisdictions, such as Australia and New Zealand, to denote gambling that negatively impacts the gambler as well as their family, friends, and the community [2]. Worldwide, prevalence estimates of past-year problem gambling in adults have ranged from 0.1% to 5.8% over the last decade [3]. In Australia and New Zealand, approximately 0.4% to 0.7% of adults report past-year problem gambling, with an additional 2% to 11% reporting moderate-risk gambling and 3% to 7.7% reporting moderate-risk gambling [4-6]. Although a relatively low prevalence disorder, recent estimates have indicated that the burden of harm associated with gambling problems in the population is relatively high [7] and can include a range of financial, relationship, and psychological harms [8]. Moreover, although people with problem gambling experience more individual harm than people at lower risk for problem gambling, it has been estimated that 85% of the total burden of harm can be attributed to people with low- and moderate-risk gambling because of their greater prevalence in the population [7]. Gambling problems are also highly comorbid with other addictive behaviors such as nicotine and alcohol use and mental health disorders, including anxiety, depression, and personality disorders [9,10]. Global estimates of help seeking indicate 1 in 25 moderate-risk gamblers and 1 in 5 people with problem gambling have sought help for problems related to their gambling [11].

There is evidence that problem gambling can be responsive to treatment, with the most efficacious interventions being cognitive behavioral therapy and, to a lesser extent, motivational interviewing [12,13]. These interventions include a range of professionally derived behavior change techniques (BCTs) [14]. These techniques are the theorized active ingredients of behavior change interventions that can be observed and replicated [14]. Research examining the components of gambling interventions identified 18 categories of techniques, including cognitive restructuring, behavior substitution, stimulus control, social support, and self-monitoring [15]. In addition to these professionally derived techniques, studies indicate that people with gambling problems select and implement similar techniques without professional oversight [15-20]. Many gamblers attempt to reduce their gambling behavior by setting expenditure, frequency, and time limits [21]. Research on gamblers has identified 15 different categories of self-enacted strategies used to adhere to gambling limits [22]. Gamblers also use strategies before gambling (eg, setting a limit), while gambling (eg, placing low-value bets), and after gambling (eg, having a plan on when to walk away) [20,23,24].

Gamblers may implement strategies to limit or reduce gambling behaviors, but high rates of relapse suggest that these are not always successful in the long term [25]. Variable success may be due to a failure to select a specific strategy fit for a purpose, shifting priorities, an inability to maintain the approach, or implementing conflicting strategies [26]. Advice to individuals on how to adhere to gambling limits is available, but this is limited to brief information such as “Set a money limit in advance” and “Exercise control over your gambling” [20]. Gamblers find it challenging to adhere to limits, and knowing how to implement these strategies may be difficult. For example, in-venue messaging may suggest taking a break, but details as to when, where, and for how long to take a break are not broken down or personalized. Messages such as *gamble responsibly* may be too broad to be easily applied, especially when an individual is already in a venue gambling or when gambling urges are intense. When these strategies have previously been delivered as part of an intervention, gamblers have recommended individual tailoring by matching strategy and motivation or situation [27]. These findings are consistent with self-determination theory, which posits that behavior change occurs when an individual is intrinsically motivated and able to drive their own change through self-selection and enactment of self-management strategies, as well as the enhancement of competence and self-efficacy [28,29]. The value of interventions specifically designed to support gamblers in implementing strategies to reduce gambling-related harm has also been previously identified [23,30].

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Planning Techniques for Gambling Reduction

People with gambling problems experience repeated failed attempts to change their behavior [1]. Research indicates that this may be owing to implementation failure, whereby good intentions have not consistently led to intended actions [24,26]. Social cognitive theories such as the theory of planned behavior focus on factors that predict intention, including attitudes, perceived behavioral control, and subjective norms, on the basis that intention predicts subsequent behavior [31]. Although meta-analyses indicate a strong relationship between intention and behavior, accounting for more than one-fourth (27%) of the variance in health behavior change [31], there appears to be a gap between intention to perform a behavior and successful implementation of that behavior. To address this gap, researchers have developed social cognitive models such as the Health Action Process Approach (HAPA) [32]. HAPA proposes that behavior change follows a continuous 2-phase process that involves motivation and volition. In this model, motivation refers to forming an intention by realizing that a particular behavior needs to change, that such change would be worthwhile and should be prioritized over and above other competing demands, and that the individual can implement the selected action (task self-efficacy) [33]. The volitional phase facilitates forward movement toward implementing intentions with techniques such as action planning, coping planning, and self-monitoring [34-36]. Factors that can help or hinder the implementation of intentions in the volitional phase include maintenance self-efficacy (belief in the ability to maintain plans and cope with barriers that arise) and recovery self-efficacy (belief in the ability to regain control after failure to cope with implementation barriers) [36].

Overall, 2 implementation planning techniques for addressing this gap have been subject to extensive evaluation across a range of health behaviors: action planning and coping planning. Action- and coping planning are BCTs [14] that can be delivered independently or combined with other BCTs, such as rewards, social support, or environmental restructuring, to form a multicomponent intervention. Action planning outlines how, when, and where a specific behavior will be implemented [36], whereas coping planning pre-empts barriers to implementing the desired behavior, developing an if-then plan. The if-then plan links specific situations or events with a detailed plan that can be implemented when a situation or barrier to implementing the behavior is present [34]. Action- and coping planning require little effort and can be easily personalized for each individual.

Recent meta-analyses have shown that action- or coping planning successfully improves addiction-related behaviors such as smoking and alcohol use [37,38]. For example, a review of 12 randomized controlled trials revealed that the use of action- or coping planning (pen-and-paper or web-based delivery) significantly improved smoking cessation rates [37]. Overall, the attrition rates were high, and there were few follow-up periods beyond 2 months. Another meta-analytic review, including 15 randomized controlled trials, reported that planning displayed a small to medium effect size in reducing alcohol use after treatment compared with active and passive control conditions [38]. Although the results from studies with low methodological quality were retained in the analysis, these findings support the need to establish the effectiveness of these interventions.

Preliminary work has examined the use of action- and coping planning by gamblers to support the successful implementation of goals in a real-world setting [39]. A brief intervention by Rodda et al [39] comprised individually set expenditure goals (intended expenditure set before gambling); tailored action plans that detail how, when, and where strategy is implemented; and coping plans that detail what to do if a barrier to implementing a strategy occurs. This gambling venue-based study reported substantial reductions in actual venue expenditure compared with intended expenditure for people with moderate risk and problem gambling but not for people with nonproblem or low-risk gambling. Notably, 50% of the total sample (intervention and assessment-only control) reported a plan to be implemented before coming to the venue. However, more than two-thirds (69%) of the intervention group were unable to complete a coping plan despite being prompted by the researcher. During the development of plans, gamblers indicated that they could not envisage specific barriers to implementation. Planning techniques, by design, are intended to be completed in advance to link internal states such as urge and situational cues such as being near a venue with a prespecified and semiautomatic action [36,40]. Planning for internal and situational cues is problematic when barriers cannot be identified.

Taken together, these findings indicate that addictive behaviors may be difficult to change owing to their complexity and multiple internal or situational cues for the behavior. As such, single plans may be insufficient because they cannot cover an array of relevant or unidentified cues that can affect motivation and volition [41]. However, having multiple action or coping plans may not effectively address behavior, because the advanced development of action plans for all possible internal or situational cues is not feasible. Furthermore, the likelihood of multiple plans being effective is reduced because of the cognitive burden of retaining and activating the details of multiple plans [41,42]. Just-In-Time Adaptive Intervention (JITAI) approaches may be effective for delivering the range of plans needed to address varying internal or situational cues that render self-regulation challenges.

JITAI Approach

JITAIs, which use computer algorithms to decide when and how support is provided, address dynamically changing individual needs by providing the type and amount of support required at the right time and only when needed [43]. Nahum-Shani et al [43] describe several key components to guide the design of JITAIs: *decision points*, which refer to the points in time at which decisions about intervention delivery are made; *intervention options*, which include the type, timing, dose, and delivery mode of support that can be delivered at each decision point; *tailoring variables*, which are defined as those that collect internal state or ecological context to decide when or how interventions are delivered; and *decision rules*, which determine which intervention options to offer, for whom, and when at different levels of each tailoring variable. Ecological momentary assessments (EMAs) [44] can be used to provide a

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real-time evaluation of a person's current internal and situational cues through mini-assessments delivered via smartphones multiple times per day. The JITAI design is guided by a distal outcome, which is a long-term goal achieved via changes to proximal outcomes, which are short-term goals [43].

JITAIs are effective for a range of health and mental health outcomes, with a recent meta-analysis reporting moderate to large effects for improvements in a range of outcomes, including mental health, diet or weight loss, and physical activity, when compared with wait-list controls and non-JITAI treatments [45]. JITAIs for the treatment and recovery of addictions such as tobacco, alcohol, and drug use show promise [46], while others are underway [47]. In the gambling field, 2 smartphone JITAIs have proposed using geolocation sensors to notify gamblers of situational cues [48,49]. One of these apps, which notified users when in proximity to gambling venues, has been partially evaluated. Humphrey et al [48] conducted a focus group of potential users who reported an interest in the app but low uptake or retention due to high battery use. In addition, 2 smartphone apps that use EMA to identify internal or situational cues for gambling have been developed [50-52]. Compared with geolocation sensors, smartphone JITAIs using EMAs are unlikely to have an impact on battery use. However, of these smartphone JITAIs, only one has been evaluated, with Merkouris et al [50] developing and evaluating a JITAI targeting gambling cravings and reporting high ratings for app helpfulness, usability, and improvements in time-related craving intensity [52]. They also reported medium to large effects for improved gambling symptom severity, cravings, frequency, and gambling expenditure. To date, JITAIs have delivered planning interventions for alcohol reduction [53,54], but no JITAI has delivered tailored action- and coping planning interventions for gambling, despite research testing planning interventions for gamblers recommending the use of in-the-moment support in delivering such interventions [39].

Research Aims and Hypotheses

This protocol presents the development and evaluation of a theoretically derived JITAI for people who want support in adhering to their gambling expenditure limits. *Gambling Habit Hacker* is a smartphone-delivered JITAI informed by HAPA and the implementation intention literature and delivered in accordance with self-determination theory. This JITAI uses decision rules specifying that participants who are receptive to treatment and report low strength of goal intention, low goal self-efficacy, low urge self-efficacy, or a high-risk situation (tailoring variables) in time-based EMAs sent during 3 semirandom times a day are delivered action- and coping planning activities to implement selected behavior change strategies. Implementation support includes providing a tailored set of self-enactable cognitive and behavioral strategies derived from data synthesis of lived experience [17,22,23,26]. These components are guided primarily by the long-term goal of reducing gambling expenditure (distal outcome), which is posited to be achieved through the short-term goal of adhering to gambling expenditure limits (primary proximal outcome) through increased strength of intention, goal self-efficacy, and urge self-efficacy (secondary proximal outcomes).

This protocol describes the theoretical basis of the intervention and research design of a 28-day microrandomized trial (MRT). An MRT design is a form of sequential factorial design in which each individual is randomized to intervention options at each decision point across a period of weeks or months [55]. In this MRT, each participant will be randomized to an action- and coping planning intervention that responds immediately to real-time implementation barriers (and therefore helps individuals adhere to gambling expenditure limits) and a control condition involving the presentation of a set of 25 self-enactable strategy groups alone (strategy group names only without any implementation guidance). The results will inform the optimization of future versions of the intervention [55].

The primary aim of the 28-day MRT was to determine the efficacy of action- and coping planning versus control on goal adherence. Goal adherence is the primary proximal outcome and refers to adhering to gambling expenditure limits, which is operationalized as a binary outcome, with success defined as actual expenditure being no greater than 10% higher than the planned expenditure limit. Secondary proximal outcomes are strength of intention, goal self-efficacy, and urge self-efficacy. It is hypothesized that action- and coping planning interventions will be associated with higher rates of adherence to gambling expenditure limits compared with the control condition, as well as higher levels of strength of intention, goal self-efficacy, and urge self-efficacy. Should data allow, the secondary aims of this trial are to (1) determine how each of the following influences the intervention effect on adherence to gambling expenditure limits: time-variant (EMA) strength of intention, goal self-efficacy, urge self-efficacy or being in a positive or negative high-risk situation, alcohol or drug consumption, and gambling proximity and time-invariant factors measured before intervention, including age, gender, volitional phase, gambling symptom severity, gambling expenditure, and planning propensity and (2) explore whether the effect of the intervention on adhering to gambling expenditure limits changes over time as the treatment progresses over the course of the 28-day MRT.

Methods

Trial Design

A 28-day MRT will be used to facilitate the optimization of *Gambling Habit Hacker*. In this trial, *decision points* comprise notifications that participants will receive via their smartphones to complete a time-based EMA 3 times a day. In each EMA, *tailoring variables*, including strength of intention, goal self-efficacy, urge self-efficacy, and high-risk situations, are used to determine intervention eligibility according to *decision rules* based on EMA cutoff points. At each decision point, participants will be randomly allocated to either the intervention or a control condition (*intervention options*). This MRT will evaluate the JITAI entirely as a *push* intervention.

This MRT will be supplemented with (1) a 6-month within-group follow-up that explores the long-term impact of the app on gambling expenditure (primary distal outcome) and a range of secondary outcomes (gambling frequency, gambling symptom severity, psychological distress, well-being, situational confidence, and planning propensity) as well as the predictors

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of longer-term treatment outcomes and (2) an evaluation of the acceptability of the JITAI via postintervention surveys, app use and engagement indices, and semistructured interviews.

Participant Eligibility and Recruitment

Participants will be recruited using a range of strategies, such as web-based advertising, social media, gambling-related websites, and advertisements in public places such as mental health and addiction services, general practices, and universities. Gambling counseling services and gaming venues across Australia and New Zealand may also assist in participant recruitment. The eligibility criteria are (1) current Australian or New Zealand residence, (2) aged ≥18 years, (3) able to install an app on their own smartphone with internet access, (4) willing to have app notifications activated, (5) English fluency, and (6) seeking assistance for their own gambling. The target population is those with less severe gambling problems who want to adhere to their gambling expenditure limits through the promotion of the app. Consistent with a pragmatic design, there is no requirement to meet any problem gambling diagnostic criteria, and participants are able to engage in other help-seeking activities [56]. However, we will measure the severity of gambling problems using the Gambling Symptom Assessment Scale (G-SAS) [57] to determine the gambling symptom severity of gamblers using the app and explore the degree to which gambling symptom severity influences the efficacy of the intervention.

Participant Time and Reimbursement

The total time required to complete the intervention is approximately 6 hours. This includes registration and follow-up evaluation surveys (1 hour), 3 time-based EMAs per day for 28 days (3 hours), and 2 hours of engagement with the action- and coping planning intervention (5 minutes for the intervention flow at an estimated 24 times over the 28 days). Participants could receive a maximum of Aus $230 (US $160) in e-gift vouchers for participating in this study. Participants will receive Aus $1 (US $0.70) for each completed EMA, a Aus $20 (US $13) bonus if >75% of EMAs are completed (to a maximum of Aus $100 [US $69]), $50 for the posttreatment evaluation, and Aus $50 (US $34) for the 6-month follow-up evaluation. If selected for a semistructured interview (optional participation), interviewees will receive an Aus $30 (US $20) e-gift voucher.

Onboarding Procedure

Recruitment materials will direct participants to Apple or Android app stores. Once the app is downloaded, potential participants will be directed to review the plain language statement, as well as the terms of use and privacy policy. During this process, potential participants will also be asked to provide informed consent by confirming that they meet the eligibility criteria and are willing to participate in the trial activities (completion of brief surveys, EMAs, and ecological momentary interventions). Participants are advised during the consent process that, during the trial period, the app will present strategies specifically aligned with EMA responses with varying levels of detail. Those who provide consent will create an account for the *Cogniss* platform, including setting a username and password and providing an email address. Following account creation, participants will be required to read a brief app description and information about how the app works. Participants will then be directed to the preintervention survey (including their mobile number, interest in being contacted for further research, and interest in participating in the optional semistructured interview), after which they will be encouraged to complete an EMA.

Distal and Proximal Outcomes

The *distal outcome* for *Gambling Habit Hacker* is gambling expenditure. The *primary proximal outcome* is goal adherence (operationalized as a binary outcome, with success defined as actual gambling expenditure being no greater than 10% higher than planned gambling expenditure). In exploratory analyses, the impact of altering the flexibility percentage (eg, 20% flexibility) and continuously scaled measures of adherence may also be explored. To specify expenditure goals over the 28-day MRT, participants are required to indicate their intended gambling episodes and associated expenditure during preintervention measurement using a TimeLine Follow-Forward [58]. Actual expenditure will be collated via the event record in each EMA: S*ince the last time you checked in, how much have you spent in $ gambling? Record 0 if you have not gambled*. *Secondary proximal outcomes* are drawn from EMA data, which allows us to examine changes across the course of the intervention. Outcomes include the strength of intention to adhere to gambling goals, goal self-efficacy, and urge self-efficacy, all of which are measured in the subsequent EMA (see the *Tailoring Variables* section for information on the source and description of each variable).

Decision Points

Participants will take part in a 28-day MRT in which *Gambling Habit Hacker* will administer an EMA protocol that uses time-based sampling that incorporates event-based sampling. Each EMA comprises 18 items that assess influential internal or situational cues and an item that assesses an event record of any gambling expenditure since the previous EMA. The EMA is an active assessment that is undertaken in-app and by self-report, with completion prompted by push notifications delivered to participants at random times during 3 prespecified times during a day: morning (8:30 AM-11:00 AM), afternoon (1:00 PM-3:30 PM), and evening (5:30 PM-8:00 PM). EMA can be auto-launched via notification or through the app. Each EMA takes approximately 2 minutes to complete and is most often measured on a 5-point Likert-type scale with varying response options. In the case where participants are not able to complete the EMA when the push notification is delivered, they will be able to complete the EMA up to two hours after receiving the push notification to accommodate possible unavailability such as driving or working [55,59]. If the EMA is not completed within 2 hours of receiving the push notification, it is no longer accessible and is considered *not completed*.

To enhance EMA compliance at the outset and during the delivery of the intervention, the following contact protocol will be adopted: (1) an automated welcome email when registering, (2) a reminder email to participants who fail to complete onboarding or fail to complete an EMA for >48 hours following onboarding, and (3) a reminder telephone call by qualitatively

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or clinically trained research fellows who still fail to complete onboarding or an EMA in the subsequent 48-hour period (with a follow-up SMS text message, if no answer or second follow-up email, if they provided no valid phone number). Participants who fail to complete an EMA following this protocol will receive no further contact but will be eligible to receive follow-up evaluations, as long as they complete onboarding, at least one EMA, and have some engagement with the app interventions.

Tailoring Variables

The eligibility for EMI content is guided by a set of tailoring variables and decision rules [43,45,60-62]. In this study, all 18 EMA items serve as tailoring variables to ensure *Gambling Habit Hacker* delivers the right amount of support at the right time. The choice of tailoring variables is aligned with the HAPA model in terms of strengthening goal intention and addressing internal or situational variables that could weaken intention and the ability to implement and maintain behavioral attention. Gamblers report that motivation is a major barrier to adhering to gambling expenditure limits and that internal and situational factors make it challenging to maintain change [63]. Tailoring variables targeting both the motivation (strength of intention for goal adherence) and volition (being able to implement and maintain actions to limit gambling) phases were selected.

Tailoring variables are presented in Multimedia Appendix 1 [64-66]. The first set of tailoring variables was the strength of intention (*Right now, I intend to meet my goal*) and goal self-efficacy. (*Right now, I am confident that I can stick to my goal*). These variables relate to the proximal outcome of adhering to gambling expenditure limits and were adapted from the study by Schwarzer et al [64]. The second tailoring variable was designed to support urge self-efficacy and focused on the confidence to adhere to gambling limits despite an urge to gamble (*Right now, it would be difficult to turn down a bet*). This variable is measured using a single item from the Gambling Urge Scale [65]. The third set of tailoring variables supports maintenance of self-efficacy (confidence in implementing an action). To do this, the focus is on high-risk situations, which are internal and situational variables that are well-established barriers to adhering to gambling expenditure limits [63]. Participants are asked to indicate whether they were currently experiencing negative reinforcement high-risk situations (*difficulties and conflict or arguments with other people*), positive reinforcement high-risk situations (*thinking that my skill or system could help me to win at gambling*), consuming alcohol or drugs, and gambling proximity (*gambling right now as planned*). Positive and negative reinforcement high-risk situations were drawn from the study by Smith et al [66], with the addition of a single item assessing current physical discomfort (*physically uncomfortable or trouble sleeping*). Alcohol and drug consumption and gambling proximity were single items developed for this study. High-risk situations are assessed on a 5-point Likert scale from 1=*not at all* to 5=*completely*.

Decision Rules

Gambling Habit Hacker determines eligibility for an intervention based on responses to the 18 tailoring variables. A threshold was set for each tailoring variable, which was used to determine whether the person was eligible for an EMI. As shown in Multimedia Appendix 1, the thresholds varied across each tailoring variable. A score of 1 to 3 (strongly disagree to neutral) was the threshold for the strength of intention (to adhere to gambling expenditure limits) and goal self-efficacy. A score of 3 to 5 (neutral to strongly agree) was the threshold for urge self-efficacy. A score of 2 to 5 was the threshold for being in a high-risk situation.

Each strategy group is linked to at least one tailoring variable, whereby 14 strategy groups were identified for strengthening intention to adhere to gambling limits, 12 strategy groups for goal self-efficacy, 16 strategies for urge self-efficacy, and all 25 strategy groups for high-risk situations. As shown in Table 1, each high-risk situation was allocated between 2 and 9 different strategies that could be used to directly address potential risk to adhering to gambling expenditure limits. Some strategies were specific to only 1 or 2 tailoring variables; for example, the strategy *slow down the bets* is only relevant to gambling on an intended gambling day. Other strategy groups, such as *talk to someone*, *seek professional support*, and *improve motivation*, are offered across almost all situations.

If participants reach EMI eligibility on several tailoring variables, a predetermined hierarchy (achieved through researcher consensus) is implemented, in which the app will deliver the EMI relevant for the highest ranked EMA item. The following hierarchy was determined, ranging from the most to least immediate threat to adhering to gambling expenditure limits: gambling proximity (whether the person is currently engaged in planned or unplanned gambling or whether it is a planned gambling day), weakened urge self-efficacy, being in a high-risk situation, weakened strength of intention to adhere to limits, and weakened goal self-efficacy. We consider current gambling to be the most serious high-risk situation for adhering to gambling expenditure limits, whether planned or unplanned.

Importantly, a *provide nothing* option is provided for situations in which the participant ignores the push notification prompting EMA completion or presses the *snooze* function to indicate that they are currently unable to complete the EMA (which suggests that they are not in a state of receptivity).

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Table 1. Just-In-Time Adaptive Intervention decision rules linking tailoring variable (time-based ecological momentary assessment) with ecological momentary intervention response[a].

Strength of intention	Goal self-efficacy	Urge self-efficacy	High-risk situations[b]	EMI strategy group activated[c]
✓	✓	✓	Q1, Q4, Q5, Q6, Q7, Q11, and Q14	Build commitment
✓	✓		Q3 and Q8	Build momentum
✓			Q6, Q9, Q10, Q13, and Q14	Control cash in venue
✓	✓	✓	Q1, Q4, Q6, Q8, Q9, Q10, Q12, Q13, and Q14	Control gambling urges
✓	✓	✓	Q1, Q2, Q3, Q4, Q5, Q6, Q7, Q9, Q11, and Q14	Do something else
✓		✓	Q1, Q3, Q4, Q5, Q6, Q11, and Q14	Deal with emotions
		✓	Q2, Q3, Q5, Q7, Q8, Q11, and Q13	Grab a treat
✓		✓	Q3 and Q12	Impose rewards and consequences
	✓		Q8 and Q12	Keep to budget
✓		✓	Q1, Q3, Q6, Q8, Q12, and Q14	Know reasons for change
✓	✓		Q4, Q9, Q12, Q13, Q14, and Q15	Know tricks pokies play
			Q4, Q13, Q14, and Q15	Know when to walk away
	✓	✓	Q1, Q4, Q7, Q8, Q10, Q13, Q14, and Q15	Limit cash
	✓	✓	Q6, Q7, Q8, Q10, Q13, and Q15	Prepokies prep
		✓	Q1, Q4, Q5, Q8, Q9, Q10, Q12, Q13, and Q14	Reduce cash in hand
✓	✓	✓	Q1, Q4, Q5, Q6, Q7, Q9, and Q10	Reduce gambling thoughts
			Q2, Q8, Q10, and Q11	Reduce stress
✓	✓	✓	Q1, Q2, Q4, Q6, Q8, Q13, Q14, and Q15	Strengthen goal
✓			Q3, Q10, Q11, and Q12	Support good health
✓	✓	✓	Q1, Q2, Q3, Q8, Q9, Q10, Q11, Q13, and Q14	Seek professional support
			Q4, Q9, Q13, Q14, and Q15	Self-control in the venue
			Q9 and Q13	Slow down the bets
		✓	Q1, Q4, Q5, Q6, Q7, Q9, Q10, and Q12	Stay away from venues
		✓	Q5, Q6, Q7, and Q11	Swap gambling
✓	✓	✓	Q1, Q2, Q3, Q5, Q6, Q7, and Q14	Talk to someone

[a]On the basis of whether the participant has the current availability to complete the ecological momentary assessment.

[b]Q1: temptations to gamble, such as having money or being reminded of gambling; Q2: difficulties, conflict, or arguments with other people; Q3: unpleasant feelings such as depression, loneliness, or frustration; Q4: wanting to win back money or thinking about winning more; Q5: feeling good and want to gamble today, but today is a no gamble day; Q6: people are encouraging, pressuring, or creating a desire to gamble; Q7: wanting to pass some time; Q8: worry about debt or how you will pay the bills; Q9: thinking that your skill or system could help you to win at gambling; Q10: you are drinking or taking drugs; Q11: physically uncomfortable or having trouble sleeping; Q12: beginning to think that you no longer have a gambling problem; Q13: gambling right now as planned; Q14: gambling right now but not planned; Q15: not gambling right now but a planned gambling day.

[c]Refer to Table 2 for strategies within each group.

Microrandomization Procedure

Each time a participant completes an EMA, responses will be assessed for intervention eligibility (Figure 1). If a participant is eligible for an EMI at that point in time, they will be randomized to one of the following two conditions: (1) specific strategies with facilitated action- and coping planning or (2) control group (strategy groups—strategy group level names only). Randomization to the 2 conditions occurs in real time within the app algorithm; at the time, the participant becomes eligible for the EMI and occurs on a 50:50 split between control and intervention. The microrandomization procedure used by *Gambling Habit Hacker* uses a fully automated randomization process, whereby a random number generator is embedded in the app. This guarantees that the administration of treatments and assessment of outcomes are fully blinded.

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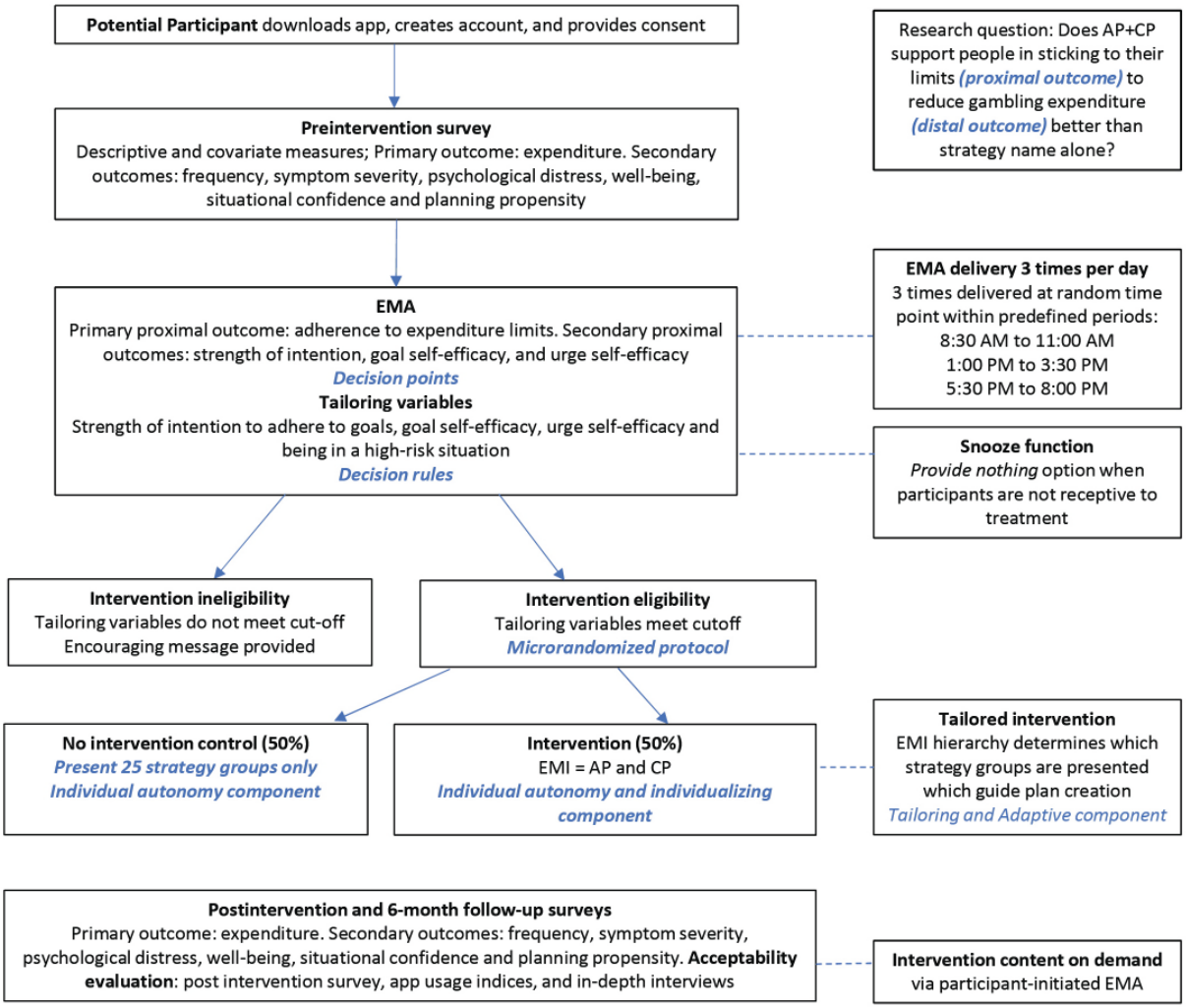
Figure 1. Microrandomized trial design of *Gambling Habit Hacker*. AP: action planning; CP: coping planning; EMA: ecological momentary assessment; EMI: ecological momentary intervention.



Intervention Options

Overview

The *Gambling Habit Hacker* app is part of a suite of interventions for addictive behaviors that delivers implementation support based on lived experience, along with goal setting, action planning, and coping planning [39,58,67]. In this study, *Gambling Habit Hacker* is delivered as a JITAI that delivers in-the-moment support for adhering to the gambling expenditure limits. The overarching set of principles guiding the *Gambling Habit Hacker* app is the HAPA [32] and self-determination theory [29]. HAPA guided the selection of BCTs: goal setting, action planning, coping planning, and self-monitoring as the mechanism for bridging the gap between intention and behavior. Self-determination theory guided the delivery of BCTs, whereby goal setting and planning were personalized to support individual autonomy and the development of competence [29,35]. In-app communication was nonjudgmental and respectful and aimed to support relatedness through the inclusion of lived experience information and quotes. In accordance with self-determination theory, participants can select any gambling expenditure limit, including reduction or abstinence [29].

Intervention Condition—Strategy Groups, Action Planning, and Coping Planning

Gamblers use a wide range of cognitive and behavioral strategies to limit or reduce their gambling behavior [15,17,18,20,23,26,30,68]. To support participants in selecting and implementing the right strategy at the right time, we developed a comprehensive list of strategy options. Each option contains a strategy name such as *social support* and implementation guidance such as *talking to someone about gambling*. Each strategy was categorized into a higher order group, which is referred to as a strategy group (n=25). Each strategy group contains between 4 and 6 strategies, each with detailed implementation guidance (120 strategies in total). For reporting and comparison with the broader literature, strategy groups were organized into 10 higher order BCT categories [14]. As indicated in Table 2, these were avoidance, rewards, substitution activities and social support, and categories of BCTs identified in the gambling literature [15], including maintaining momentum, staying in control while gambling, urge management, financial management, and managing emotions.

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Table 2. Individual strategies for adhering to gambling expenditure limits organized by behavior change technique (BCT) category and strategy group.

BCT category (n=10) and strategy group (n=25)	Individual strategies (n=120)
Avoidance	
Stay away from venues	Ban yourself; go away now; block online venue; deal with social pressure.
Financial management	
Keep to budget	Calculate cash allowance; get a debit card without cash access; block access to online banking; cancel or destroy credit cards; ensure you cannot draw money from assets; keep wages safe.
Reduce cash in hand	Pay bills; buy essentials; set up savings account.
Limit cash	Set a cash limit today; leave cards at home; change personal identification numbers; give cards to a family member; use prepaid cards; reduce automated teller machine limits.
Maintaining momentum	
Build momentum	Know reasons for change; take it a day at a time; take it slow and steady; pause and celebrate.
Strengthen goal	Keep your plan number 1; slow down the emotional roller coaster; let go of guilt and shame; get inspiration.
Know reason for change	Identify gambling cons; change pros; know your rock bottom; identify harm; stop chasing losses; accept loss of control.
Build commitment	Build confidence; build willpower; increase accountability; focus on today.
Managing emotions	
Deal with emotions	Deal with boredom; deal with frustration; deal with pain; deal with anger; deal with loneliness; deal with happiness.
Rewards	
Impose rewards and consequences	Accept a reward; give yourself a reward; create a future reward; set up a penalty system; give yourself a red card.
Grab a treat	Feel good treat; get creative; connect with someone; achieve something; do something fun.
Substitution activities	
Do something else	Get busy; get moving; connection; get a positive addiction; feel good.
Swap gambling	Play low-cost games; play no cost pokies; play no cost casino games; get adrenaline in a different way; play other games.
Social support	
Talk to someone	Talk it over; admit or confess; be accountable; get advice; find someone to support your goals.
Seek professional support	Talk to a gambling counselor; talk to a counselor about mental health; talk to a financial counselor; go to a support group; go to a 12-step group; access online support.
Staying in control while gambling	
Prepokies prep	Set your loss limit; set your time limit; leave cash and cards at home; leave cash and cards in the car; give cash and cards to a friend.
Control cash in venue	Avoid automated teller machines; do not borrow money; keep winnings.
Slow down the bets	Change machines often; take breaks; keep the same bet size; take time between spins; avoid chasing losses.
Know when to walk away	Walk away when limits are reached; walk away when you hit your time limit even if it is fun; walk away when it is no longer fun; walk away from social pressure.
Increase self-control in venue	Do not get comfortable; view gambling as entertainment; address thoughts of abandoning limits; avoid stimulants.
Stress management	
Reduce stress	Sleep; take a walk; cut stimulants; relax; self-massage.
Support good health	Eat healthy; cut alcohol; check your mental health; practice mindfulness; exercise.
Urge management	
Control gambling urges	Stay away from a venue; reduce mental tension; walk out of a venue; remove access to cash; deal with payday; do something else; learn to say no.

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BCT category (n=10) and strategy group (n=25)	Individual strategies (n=120)
Reduce gambling thoughts	Deal with advertising; address thoughts of wining; address thoughts of gambling; deal with permission giving.
Know tricks pokies play	Let go of lucky charms; remember pokies are based completely on chance; notice losses disguised as wins; remember no skill is needed.

Even though gamblers use a wide range of strategies, studies indicate that up to 80% of gamblers fail to adhere to their gambling limits [25]. Forming specific plans about how, when, and where to act has been shown to increase adherence to gambling limits in gambling venues [39]. The action planning component prompts participants to develop personally tailored action plans that respond to immediate threats to adhering to gambling limits. Participants allocated to the intervention condition received a list of tailored strategy groups (6-16 groups) based on the results of their EMA. Participants can select a strategy group, and the app then provides a list of all relevant individual strategies from which they can select. Upon selection, the app provides a detailed description of methods for implementation (drawn from lived experience research; see the *Consumer Participation* section [15]) and offers strategy-specific prompts for the personalization of the strategy. As an illustration of this process, if the participant were to select *Talk to someone* from the list of strategy groups, they would then be presented with a list of five individual strategies: Talk it over, Admit or confess, Be accountable, Get advice, and Someone to support your goals. If the participant then selected the strategy *Be accountable*, the app will provide the following information: *how to identify someone that will hold you accountable for your plan, different ways to involve others for accountability, how having someone for accountability can make you feel, and what can get in the way of your plans.* The app further prompts the participant to think of specific details, such as the name of the person they will be accountable to; why this person is a good option; and whether they will text, call, chat, or email that person. Once participants are provided with all the information and prompted to consider specific details, they are asked to record their action plan. The app produces the following prompt: *If this strategy sounds good to you, then take action. Write your plan here on how you will* (name of the strategy). *Include in your plan something you can do right now. Be specific about what you will do and how you will do it.* The prompt is followed by an open text field for the participant to detail their personalized, detailed action plan.

Action planning can bridge intention and behavior, but it does not directly address barriers that can get in the way of even the most robust plans. The coping planning component involves the development of a personally tailored coping plan in response to a proximal implementation barrier [69]. Action planning and coping planning are developed simultaneously, based on a series of prompts in the app. Participants are prompted to identify the main barriers to their action plan implementation by selecting 1 of 7 categories: thoughts, emotions, motivation, situation, self-belief, financial, and social. Participants are prompted to describe the selected barrier in an open text field and to detail how that barrier can get in the way of their action plan. The app then prompts participants to identify what they can do right now to overcome the barrier and get back on track with the plan (open text field).

Once the plan is saved, commitment and self-efficacy activities facilitate the strategy's engagement and throughput. This activity involves focusing on character strength and mental rehearsal [70,71]. Consideration of character strengths is prompted by *Name your strength that can help you stick to your plan and overcome the barrier you have identified. Write down exactly how this strength will be useful* (open text field). To undertake mental rehearsal, the person is prompted to imagine implementing their plans. A prompt for mental imagery is provided as follows:

> *You have decided what to do, so take a moment to visualize yourself doing it. Close your eyes and imagine yourself doing what you need to do. Imagine it going well. Imagine feeling happy that you take this action. You feel proud of yourself and feel good because you have control. You are ready to do this action right now.*

Once completed, the app provides an encouraging message:

> *Great work in putting together your plan and identifying your strengths. This is really going to help you stick to your gambling goals. We will check in again in a few hours to see how you are going.*

Control Condition—Strategy Group Names Only

Participants allocated to the control condition will receive a list of all 25 strategy groups (names only), with no specific strategies or implementation guidance provided. Once participants select a strategy group name, such as *Talk to someone*, the app provides an encouraging message: *It is a great idea to* (insert strategy group name). *We will get in touch with you soon to check how you are doing*. Providing information at the strategy group level is similar to responsible gambling messaging and reflects a real-world experience of these messages.

Consumer Participation

People with lived experience of gambling problems are represented in all aspects of *Gambling Habit Hacker*, including identification of intervention content, testing of app functionality, and recommendations for future improvements via postintervention survey items and semistructured interviews. The app includes detailed implementation support, delivering >70,000 words of content. This content was sourced from consumer accounts representing >2000 individuals from various sources, including counseling transcripts [26], in-venue surveys [23], online forums [17], and community-based quantitative and qualitative surveys [15,30]. Within the app, quotes are taken directly from this lived experience research, selected to align with each strategy group.

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Within-Group Evaluation

In addition to MRT, this study will include a within-group follow-up evaluation over a 6-month period to (1) examine within-group change over the 6 months following the end of the MRT and (2) identify predictors of these longer-term treatment outcomes (including usage of the app over the follow-up period). Surveys taking 10 to 15 minutes will be administered before intervention (via the app), as well as after intervention and at the 6-month follow-up (via Qualtrics). Descriptive and covariate measures will include sociodemographic characteristics (age, sex, current residence, primary ethnicity, and personal annual gross income), problem gambling activities (6 types of gambling), and intended gambling behavior as measured by the TimeLine Follow-Forward [58], volitional phase [72], and help seeking [73]. To assess the volitional phase, participants will be presented with 4 statements: I am deciding whether I need to change my gambling (predecisional); I am getting ready to change my gambling (postdecisional); I have already started to change my gambling (actional); and I have successfully changed my gambling and want to maintain this change (postactional). Posttrial and 6-month follow-up participants will be asked to report on their previous help-seeking behavior using 9 items from the Help-Seeking Questionnaire [73]. This includes 5 items related to high-intensity help seeking and 3 items related to low-intensity help seeking. An item related to self-directed help seeking will also be administered to assess engagement with self-exclusion.

The primary outcome for the within-group evaluation will be gambling expenditure (measured using a TimeLine Follow-Back at the preintervention evaluation, the EMA data collected during the intervention period and amalgamated for the posttreatment evaluation, and single items at the 6-month evaluation). Secondary outcomes will include gambling symptom severity measured using the G-SAS [57], gambling frequency with the TimeLine Follow-Back at the preintervention evaluation (EMA data at the posttreatment evaluation and single items at the 6-month evaluation) [74], psychological distress measured using the Kessler 6 Psychological Distress Scale [75], personal well-being measured using the Personal Wellbeing Index [76], the Brief Situational Confidence Questionnaire [77], and planning propensity measured using an adapted action control questionnaire that assesses action planning, coping planning, and action control [78]. A summary of the measures and the measurement time points (before intervention, after intervention, and follow-up) for the within-group evaluation are presented in Multimedia Appendix 2.

To enhance engagement with the posttreatment and 6-month follow-up evaluations, the following protocols will be implemented. An email will be sent to all participants to prompt survey completion, with a second reminder email for those who fail to complete within a week. An advance notice email will also be sent a week before the 6-month surveys are administered. For those who have not completed the survey after a further week, up to two reminder telephone calls will be made by a clinical or qualitatively trained researcher. At each time point, the option to complete the survey over the phone with a trained research fellow will be offered. Participants who do not complete posttreatment evaluation will be contacted at the 6-month evaluation unless they have withdrawn from the study.

During the 6-month evaluation period, *Gambling Habit Hacker* will be available to participants for continued use. The tailored intervention content will be available on demand, meaning that participants can complete EMAs at any time of the day or night. The intervention content will still be tailored, but participants will not receive the 3 times daily prompts for EMA completion. This approach is designed to encourage participants to incorporate action- and coping planning skills in everyday situations and settings when there is a shift in motivation, self-efficacy, or the presence of high-risk situations.

Acceptability Outcomes

Acceptability is operationalized as a multifaceted construct reflecting the degree to which participants consider *Gambling Habit Hacker* to be appropriate, based on their emotional and cognitive responses to the app [79]. Specifically, *intervention fidelity* will be assessed by the proportional response to EMA notifications, strategy selection, and completion of the written text for EMI action and coping plans. The content of each personalized action and coping plan will also be reviewed and rated: 0=not completed, 1=partially completed (ie, plan is created but is missing key detail on how or what the person will do right now), and 2=completed (ie, plan is created and includes all details as prompted). Subscales of the *Mobile App Rating Scale* [80] will be used to measure the subjective quality (4 items: willingness to recommend the app, future use, willingness to pay, and overall perception of quality) and perceived impact (6 items: awareness, knowledge, attitudes, intention to change, help seeking, and behavior change) of the app. *App use and engagement* will be assessed across the 28-day MRT and 6-month follow-up period by download information, onboarding information, app use information (eg, EMA compliance, intervention eligibility, participant retention, and intervention activities completed), and other evaluation information. A series of *semistructured interviews* will be conducted 28 days after trial with a subsample of 10 participants from the MRT. Participants will be selected based on gender and app use (high or low), with participants prioritizing the state of New South Wales in alignment with the funding source. Participants will be individually interviewed via videoconferencing and asked about their experiences with the *Gambling Habit Hacker* app as well as its perceived helpfulness and areas for improvement.

Sample Size

A sample size of 200 will be recruited based on a conservative anticipated 40% attrition rate [52], providing a final sample of 120 at 6 months after evaluation. This sample size provides >85% power to detect a small binary outcome intervention effect of relative risk=1.20 (α=.05; availability parameter=0.3; randomization probability=.50; probability of outcome without intervention=.25) [81].

Statistical Analyses

To assess the research questions, the method of generalized estimating equations will be used, with an appropriate link function for the outcome of interest (eg, logit or identity). Although an exchangeable working correlational structure is

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intended to be used for the analyses, considerations will be given to alternative correlational structures based on the observed within-person correlation pattern over the course of the study (eg, independent or auto-regressive). For all MRT analyses, the (lagged) outcome of interest (eg, adherence to expenditure limit at $Time_{t+1}$) will be regressed on a variable denoting the treatment received (ie, intervention vs control) at $Time_t$, as well as covariates (including unbalanced time). The primary analyses will explore the effect of intervention versus control on the probability of adherence to expenditure limits in the subsequent episode. The identification of the conditions under which the interventions are most beneficial and how the effect of the interventions changes over the course of the MRT will be examined by specifying interaction terms between the intervention variable and interaction variables of interest (eg, strength of intention and time).

The long-term outcomes of the intervention (within-group follow-up evaluation) will be explored, whereby distal outcomes will be assessed using generalized estimating equations by regressing the outcome of interest (eg, gambling expenditure) on a variable denoting time (ie, before intervention, after intervention, and 6-month follow-up) and covariates. The identification of factors predicting longer-term outcomes will also be assessed by regressing the outcome of interest (eg, clinically significant changes in gambling expenditure) with selected preintervention, postintervention, and app usage variables. Where appropriate, missingness will be addressed using multiple imputations with appropriate accounting for the multilevel nature of the data (eg, multilevel multiple imputation).

In addition to the effect sizes for all primary and secondary outcomes, the metrics of individual-level change will be calculated for all primary and secondary outcomes. Changes beyond that attributable to chance or measurement error will be evaluated using Reliable Change Indices [82], and clinically significant changes [83] will subsequently be calculated at postintervention and 6-month evaluation using functional score ranges where possible (G-SAS score of ≤20 and K6 score of ≤13) or at least a 25% improvement in scores [84]. Participants will be identified as *recovered* (final score falls into the functional range and corresponds to a reliable change), *improved* (final score corresponds to a reliable change but falls into the dysfunctional range), *unchanged* (final score does not correspond to a reliable change), or *deteriorated* (final score corresponds to a relative change in the negative direction).

Ethics Approval

This trial has been approved by the Deakin University Human Research Ethics Committee (2020-304) and prospectively registered with the Australian New Zealand Clinical Trials Registry (ACTRN12622000497707).

Results

The development and evaluation of *Gambling Habit Hacker* was a collaboration between Deakin University, University of Auckland, Turning Point, and 2and2 (app developers) and funded in June 2019 by the New South Wales Government's Responsible Gambling Fund. In line with JITAI development recommendations [43], a multidisciplinary team was created to draw on behavior change expertise from clinical and social psychology, implementation science, biostatistics, and research design, in conjunction with smartphone app developers. The development of the treatment content was led by the first author (SNR) and is part of a broader program investigating implementation planning for addictive behaviors. The app is hosted on the Cogniss behavior change platform created by 2and2, a custom technology solution developer. Illustrative screenshots of this JITAI are displayed in Figure 2.

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Figure 2. Illustrative screenshots of the *Gambling Habit Hacker* app.

Following an extensive development period, *Gambling Habit Hacker* was subjected to user testing of app functionality between June 2021 and July 2021 with 14 gambling experts. The testers included gambling counselors (n=5), gambling researchers (n=5), and people with lived experience (n=4). Consumers were 3 men and 1 woman, with an average score on the Problem Gambling Severity Index in the problem range (mean 13.0, SD 9.1). Testers used the app on Android and IOS devices for a 3-day period and provided quantitative and qualitative feedback on acceptability, usability, and quality. Quantitative evaluation was performed using the Mobile App Rating Scale [80], which comprises 23 items across 4 subscales measuring perceived engagement, look and feel, functionality, and quality. Experts were reimbursed with an Aus $50 (US $34) e-gift voucher for their time.

Quantitative evaluation indicated that all scores were higher than the minimum acceptability score of 3, which suggests that the app may be helpful [85] (Multimedia Appendix 3). Intervention content was rated highly in terms of strategy relevance to plan creation (>7 out of 10), helpfulness of strategy description (almost 8 out of 10), and quotes on lived experience were perceived as helpful (>7 out of 10). Experts rated planning functionality highly (>7 out of 10) and indicated slightly lower scores for helpfulness of information in coping planning (>6 out of 10). The lowest rated items were TimeLine Follow-Back (calendar to assess past-month gambling behavior) and TimeLine Follow-Forward (calendar to assess planned gambling behavior over the next month), where ease of completion was rated as just over 3 out of 10. Qualitative data were generally positive in terms of comprehensiveness and quality of information, credibility, graphics, and interactivity. The main issues raised were related to functionality in terms of loading times, errors in the notification schedule, and difficulty in entering and saving data in the timeline calendars. The evaluation also indicated that the participant burden needed to be reduced in terms of the length of pretrial measures and the time required to complete the EMA items. Technical issues, including user acceptability concerns, were addressed through extensive redevelopment of the calendars, reducing the number of items in the baseline and EMAs, and correcting the schedule of notifications. A total of 3 testers subsequently used the app again and confirmed that the issues had been satisfactorily resolved.

The user testing phase of the app-administered action planning and coping planning as separate interventions, where coping planning was delivered 30 minutes after action planning and only where participants indicated that they had not implemented their action plan. User testing revealed that this was confusing and was an added burden, which meant most participants did not complete coping plans even if they were assessed as eligible (ie, they had not implemented the action plan). In response to this finding, we merged action- and coping planning as a single intervention delivered concurrently (without a time delay).

The empirical data gathered as part of this trial will be used to optimize the JITAI and to make it more efficient, effective, and scalable. The app is available for download in Australia and New Zealand for Apple (App Store) and Android (Google Play Store) devices. Following its release on the app stores, a total of 7 pilot participants were recruited to check all protocols, and the functionality was operated as intended. Advertising commenced on April 11, 2022, and as of May 26, 2022, a total of 36 participants were recruited for the trial. The trial is expected to conclude in early 2023 with results published mid-2024.

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Discussion

Overview

Preliminary findings suggest that *Gambling Habit Hacker* is acceptable and feasible for adhering to gambling expenditure limits. To the best of our knowledge, this study is the first to examine the effectiveness of real-time support for implementation planning activities to adhere to gambling expenditure limits. Using an MRT design, this trial will determine if real-time action- and coping planning are more effective than no intervention in adhering to gambling expenditure limits (primary proximal outcome), and using a within-group evaluation, it will determine whether there are reductions in gambling expenditure (distal primary outcome). Consistent with the HAPA model and implementation planning literature, participants are encouraged to specify their gambling intentions (using the TimeLine Follow-Foward) and then use tailored planning to identify opportunities to act. This information will be used to optimize the content of the next version of *Gambling Habit Hacker* in line with recommendations for digital behavior change methods and JITAI development [43,86,87].

Consistent with recommendations [43,87], *Gambling Habit Hacker* is based on well-established behavior change frameworks that delineate intentional and volitional phases, targeting the volitional phase. It is also based on the BCT of goal setting (TimeLine Follow-Forward) with BCTs for specific steps of planning and self-regulation incorporated within the intervention. EMA items are drawn from areas consistently associated with gambling lapses, such as urges and high-risk situations. The EMI content of the active components is designed from the planning literature, specifically examining action- and coping planning. The MRT design allows the evaluation of the intervention components within each subject, providing enhanced statistical power to explore the efficacy of the intervention on real-time variations in behavioral outcomes. All communications within the app are aligned with the self-determination theory, whereby the app offers real-world stories by way of developing relatedness, offers personalized goal setting and planning (autonomy), and provides repeated attempts to practice planning, as well as the identification of barriers that can improve the individual's chances of adhering to their limits (competence).

Similar to previous studies [36,40], it is proposed that the structure of this intervention could be relevant to any behavior change. We selected adhering to gambling expenditure limits as the proximal goal to be attained, and the strategies presented have come from gamblers' reports on how to adhere to gambling limits and the associated challenges. EMAs assess the presence of internal and situational cues for unplanned gambling; however, the app design could be adapted to other behaviors where threats to adhering to limits have been identified. The planning framework would remain the same across any health behavior.

Little is known about hourly, daily, or weekly fluctuations in the strength of individuals' gambling goals or the experience of internal or situational cues associated with unplanned gambling. Although this work will provide such knowledge, there is a risk that the timing and frequency of the EMAs (3 times per day) may be too few on some days and too many on others or that the timing is not aligned with high-risk situations. For example, evening EMAs conclude at 8 PM even though the risk of being in a gambling venue may be outside these hours. Following this, there is a chance that a limited number of EMI-eligible moments will be identified. Although designed for low burden, the repetitive nature of EMA items may lead to low engagement and automatic responses to questions or dropouts. While planning activities are undertaken within the app, implementing the plan is done *in the real world*. A subsequent limitation is that the completion of activity after planning cannot be monitored.

Dissemination of Findings

The results of this trial will be disseminated to peer-reviewed journals, conference presentations, and stakeholder forums. Plain language findings will be disseminated to participants who indicate an interest in the study findings. Participants can access the findings on project websites [88,89].

Conclusions

The aim of *Gambling Habit Hacker* is to provide evidence-based, real-time support for individuals wishing to adhere to their gambling expenditure limits. Through the use of the app, individuals' cognitive burden in identifying, evaluating, selecting, and operationalizing an appropriate option is reduced. The app and associated algorithms present appropriate strategies in line with personalized real-time EMA outcomes.

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Authors' Contributions

The development of the *Gambling Habit Hacker* app is led by SNR (Auckland University of Technology [88]) and is part of a broader program investigating implementation planning and behavior change for addictive behaviors. NAD, with support from SNR and SSM, conceived the project, developed the methodology, and acquired funding. KLB and SNR developed the specific design for this protocol manuscript with advice from NAD, SSM, and DIL and statistical advice from GY. The first draft of the manuscript was prepared by KLB, and all authors contributed to the final draft.

Conflicts of Interest

None declared.

Multimedia Appendix 1
Tailoring variables collected in the time-based ecological momentary assessment.
[DOCX File , 19 KB - resprot_v11i7e38919_app1.docx]

Multimedia Appendix 2
Summary of Gambling Habit Hacker time points for components and measures.
[DOCX File , 22 KB - resprot_v11i7e38919_app2.docx]

Multimedia Appendix 3
User testing: Gambling Habit Hacker expert evaluation scores (n=14).
[DOCX File , 19 KB - resprot_v11i7e38919_app3.docx]

References

1. Diagnostic And Statistical Manual Of Mental Disorders, Fifth Edition. Virginia, United States: American Psychiatric Association; 2013.
2. Neal P, Delfabbro P, O'Neil M. Problem Gambling and Harm: Towards a National Definition. Melbourne: Office of Gaming and Racing; 2005.
3. Calado F, Griffiths MD. Problem gambling worldwide: an update and systematic review of empirical research (2000-2015). J Behav Addict 2016 Dec;5(4):592-613 [FREE Full text] [doi: 10.1556/2006.5.2016.073] [Medline: 27784180]
4. New Zealand 2012 national gambling study: overview and gambling participation. Auckland University of Technology. 2012. URL: https://www.health.govt.nz/publication/new-zealand-2012-national-gambling-study-overview-and-gambling-participation [accessed 2020-06-10]
5. Dowling NA, Youssef GJ, Jackson AC, Pennay DW, Francis KL, Pennay A, et al. National estimates of Australian gambling prevalence: findings from a dual-frame omnibus survey. Addiction 2016 Mar 06;111(3):420-435 [FREE Full text] [doi: 10.1111/add.13176] [Medline: 26381314]
6. Gainsbury SM, Russell A, Hing N, Wood R, Lubman DI, Blaszczynski A. The prevalence and determinants of problem gambling in Australia: assessing the impact of interactive gambling and new technologies. Psychol Addict Behav 2014 Sep;28(3):769-779. [doi: 10.1037/a0036207] [Medline: 24865462]
7. Browne M, Greer N, Rawat V, Rockloff M. A population-level metric for gambling-related harm. Int Gambling Stud 2017 Mar 31;17(2):163-175. [doi: 10.1080/14459795.2017.1304973]
8. Langham E, Thorne H, Browne M, Donaldson P, Rose J, Rockloff M. Understanding gambling related harm: a proposed definition, conceptual framework, and taxonomy of harms. BMC Public Health 2016 Jan 27;16(1):80 [FREE Full text] [doi: 10.1186/s12889-016-2747-0] [Medline: 26818137]
9. Dowling NA, Cowlishaw S, Jackson AC, Merkouris SS, Francis KL, Christensen DR. Prevalence of psychiatric co-morbidity in treatment-seeking problem gamblers: a systematic review and meta-analysis. Aust N Z J Psychiatry 2015 Jun 03;49(6):519-539 [FREE Full text] [doi: 10.1177/0004867415575774] [Medline: 25735959]
10. Lorains F, Cowlishaw S, Thomas S. Prevalence of comorbid disorders in problem and pathological gambling: systematic review and meta-analysis of population surveys. Addiction 2011 Mar;106(3):490-498. [doi: 10.1111/j.1360-0443.2010.03300.x] [Medline: 21210880]
11. Bijker R, Booth N, Merkouris S, Dowling N, Rodda S. Global prevalence of help-seeking for problem gambling: a systematic review and meta-analysis. Addiction 2020. [doi: 10.1111/ADD.15952]

XSL•FO
RenderX

12. Cowlishaw S, Merkouris S, Dowling N, Anderson C, Jackson A, Thomas S. Psychological therapies for pathological and problem gambling. Cochrane Database Syst Rev 2012 Nov 14;11:CD008937. [doi: 10.1002/14651858.CD008937.pub2] [Medline: 23152266]
13. Thomas SA, Merkouris SS, Radermacher HL, Dowling NA, Misso ML, Anderson CJ, et al. Australian guideline for treatment of problem gambling: an abridged outline. Med J Aust 2011 Dec 19;195(11-12):664-665. [doi: 10.5694/mja11.11088] [Medline: 22171860]
14. Michie S, Richardson M, Johnston M, Abraham C, Francis J, Hardeman W, et al. The behavior change technique taxonomy (v1) of 93 hierarchically clustered techniques: building an international consensus for the reporting of behavior change interventions. Ann Behav Med 2013 Aug 20;46(1):81-95. [doi: 10.1007/s12160-013-9486-6] [Medline: 23512568]
15. Rodda S, Merkouris SS, Abraham C, Hodgins DC, Cowlishaw S, Dowling NA. Therapist-delivered and self-help interventions for gambling problems: a review of contents. J Behav Addict 2018 Jun 01;7(2):211-226 [FREE Full text] [doi: 10.1556/2006.7.2018.44] [Medline: 29895185]
16. Abbott M. Self-directed interventions for gambling disorder. Curr Opin Psychiatry 2019 Jul;32(4):307-312. [doi: 10.1097/YCO.0000000000000515] [Medline: 31008729]
17. Rodda SN, Hing N, Hodgins DC, Cheetham A, Dickins M, Lubman DI. Behaviour change strategies for problem gambling: an analysis of online posts. Int Gambling Stud 2018 Feb 08:1-19. [doi: 10.1080/14459795.2018.1432670]
18. Currie SR, Brunelle N, Dufour M, Flores-Pajot M, Hodgins D, Nadeau L, et al. Use of self-control strategies for managing gambling habits leads to less harm in regular gamblers. J Gambl Stud 2020 Jun 11;36(2):685-698. [doi: 10.1007/s10899-019-09918-0] [Medline: 31828695]
19. Matheson FI, Hamilton-Wright S, Kryszajtys DT, Wiese JL, Cadel L, Ziegler C, et al. The use of self-management strategies for problem gambling: a scoping review. BMC Public Health 2019 Apr 29;19(1):445 [FREE Full text] [doi: 10.1186/s12889-019-6755-8] [Medline: 31035978]
20. Hing N, Browne M, Russell AM, Rockloff M, Rawat V, Nicoll F, et al. Avoiding gambling harm: an evidence-based set of safe gambling practices for consumers. PLoS One 2019 Oct 17;14(10):e0224083 [FREE Full text] [doi: 10.1371/journal.pone.0224083] [Medline: 31622430]
21. Currie SR, Hodgins DC, Wang J, el-Guebaly N, Wynne H, Miller NV. Replication of low-risk gambling limits using canadian provincial gambling prevalence data. J Gambl Stud 2008 Sep 4;24(3):321-335. [doi: 10.1007/s10899-008-9091-y] [Medline: 18317888]
22. Rodda SN, Bagot KL, Cheetham A, Hodgins DC, Hing N, Lubman DI. Types of change strategies for limiting or reducing gambling behaviors and their perceived helpfulness: a factor analysis. Psychol Addict Behav 2018 Sep;32(6):679-688. [doi: 10.1037/adb0000393] [Medline: 30211588]
23. Rodda SN, Bagot KL, Manning V, Lubman DI. 'Only take the money you want to lose' strategies for sticking to limits in electronic gaming machine venues. Int Gambling Stud 2019 May 22;19(3):489-507. [doi: 10.1080/14459795.2019.1617330]
24. Rodda SN, Bagot KL, Manning V, Lubman DI. "It was terrible. I didn't set a limit": proximal and distal prevention strategies for reducing the risk of a bust in gambling venues. J Gambl Stud 2019 Dec 29;35(4):1407-1421. [doi: 10.1007/s10899-019-09829-0] [Medline: 30694401]
25. Ledgerwood DM, Petry NM. What do we know about relapse in pathological gambling? Clin Psychol Rev 2006 Mar;26(2):216-228. [doi: 10.1016/j.cpr.2005.11.008] [Medline: 16356614]
26. Rodda SN, Hing N, Hodgins DC, Cheetham A, Dickins M, Lubman DI. Change strategies and associated implementation challenges: an analysis of online counselling sessions. J Gambl Stud 2017 Sep 17;33(3):955-973. [doi: 10.1007/s10899-016-9661-3] [Medline: 27988863]
27. Rodda SN, Dowling NA, Knaebe B, Lubman DI. Does SMS improve gambling outcomes over and above access to other e-mental health supports? A feasibility study. Int Gambl Stud 2017 Nov 05;18(2):343-357. [doi: 10.1080/14459795.2017.1388831]
28. Sheeran P, Wright CE, Avishai A, Villegas ME, Lindemans JW, Klein WM, et al. Self-determination theory interventions for health behavior change: meta-analysis and meta-analytic structural equation modeling of randomized controlled trials. J Consult Clin Psychol 2020 Aug;88(8):726-737. [doi: 10.1037/ccp0000501] [Medline: 32437175]
29. Deci EL, Ryan RM. Self-determination theory: a macrotheory of human motivation, development, and health. Can Psychol/Psychologie canadienne 2008;49(3):182-185. [doi: 10.1037/a0012801]
30. Bagot K, Cheetham A, Lubman D, Rodda S. Predictors of strategy engagement for the prevention and reduction of gambling harm: a prospective application of the theory of planned behaviour. Int J Ment Health Addiction 2020 Apr 04;19(5):1812-1828 [FREE Full text] [doi: 10.1007/s11469-020-00265-5]
31. Armitage C, Conner M. Efficacy of the theory of planned behaviour: a meta-analytic review. Br J Soc Psychol 2001 Dec;40(Pt 4):471-499. [doi: 10.1348/014466601164939] [Medline: 11795063]
32. Schwarzer R, Luszczynska A. How to overcome health-compromising behaviors. Eur Psychol 2008 Jan;13(2):141-151. [doi: 10.1027/1016-9040.13.2.141]
33. Schwarzer R. Modeling health behavior change: how to predict and modify the adoption and maintenance of health behaviors. Applied Psychol 2008 Jan;57(1):1-29. [doi: 10.1111/j.1464-0597.2007.00325.x]

XSL•FO
RenderX

34. Gollwitzer PM. Implementation intentions: strong effects of simple plans. Am Psychol 1999;54(7):493-503. [doi: 10.1037/0003-066x.54.7.493]
35. Sheeran P. Intention—behavior relations: a conceptual and empirical review. Eur Rev Soc Psychol 2002 Jan;12(1):1-36. [doi: 10.1080/14792772143000003]
36. Sniehotta FF, Schwarzer R, Scholz U, Schüz B. Action planning and coping planning for long-term lifestyle change: theory and assessment. Eur J Soc Psychol 2005 Jul;35(4):565-576 [FREE Full text] [doi: 10.1002/ejsp.258]
37. McWilliams L, Bellhouse S, Yorke J, Lloyd K, Armitage CJ. Beyond "planning": a meta-analysis of implementation intentions to support smoking cessation. Health Psychol 2019 Dec;38(12):1059-1068. [doi: 10.1037/hea0000768] [Medline: 31414843]
38. Malaguti A, Ciocanel O, Sani F, Dillon JF, Eriksen A, Power K. Effectiveness of the use of implementation intentions on reduction of substance use: a meta-analysis. Drug Alcohol Depend 2020 Sep 01;214:108120. [doi: 10.1016/j.drugalcdep.2020.108120] [Medline: 32622228]
39. Rodda SN, Bagot KL, Manning V, Lubman DI. An exploratory RCT to support gamblers' intentions to stick to monetary limits: a brief intervention using action and coping planning. J Gambl Stud 2020 Mar 13;36(1):387-404. [doi: 10.1007/s10899-019-09873-w] [Medline: 31302802]
40. Sniehotta FF, Scholz U, Schwarzer R. Bridging the intention–behaviour gap: planning, self-efficacy, and action control in the adoption and maintenance of physical exercise. Psychol Health 2005 Apr;20(2):143-160. [doi: 10.1080/08870440512331317670]
41. Verhoeven AA, Adriaanse MA, de Ridder DT, de Vet E, Fennis BM. Less is more: the effect of multiple implementation intentions targeting unhealthy snacking habits. Eur J Soc Psychol 2013 Jul 02;43(5):344-354. [doi: 10.1002/ejsp.1963]
42. Vinkers CD, Adriaanse MA, Kroese FM, de Ridder DT. Better sorry than safe: making a plan B reduces effectiveness of implementation intentions in healthy eating goals. Psychol Health 2015 Jan 28;30(7):821-838. [doi: 10.1080/08870446.2014.997730] [Medline: 25563570]
43. Nahum-Shani I, Smith S, Spring B, Collins L, Witkiewitz K, Tewari A, et al. Just-in-time adaptive interventions (JITAIs) in mobile health: key components and design principles for ongoing health behavior support. Ann Behav Med 2018 May 18;52(6):446-462 [FREE Full text] [doi: 10.1007/s12160-016-9830-8] [Medline: 27663578]
44. Shiffman S. Ecological momentary assessment (EMA) in studies of substance use. Psychol Assess 2009 Dec;21(4):486-497 [FREE Full text] [doi: 10.1037/a0017074] [Medline: 19947783]
45. Wang L, Miller LC. Just-in-the-moment adaptive interventions (JITAI): a meta-analytical review. Health Commun 2020 Nov 05;35(12):1531-1544. [doi: 10.1080/10410236.2019.1652388] [Medline: 31488002]
46. Gustafson DH, McTavish FM, Chih M, Atwood AK, Johnson RA, Boyle MG, et al. A smartphone application to support recovery from alcoholism: a randomized clinical trial. JAMA Psychiatry 2014 May 01;71(5):566-572 [FREE Full text] [doi: 10.1001/jamapsychiatry.2013.4642] [Medline: 24671165]
47. Carpenter SM, Menictas M, Nahum-Shani I, Wetter DW, Murphy SA. Developments in mobile health just-in-time adaptive interventions for addiction science. Curr Addict Rep 2020 Sep 01;7(3):280-290 [FREE Full text] [doi: 10.1007/s40429-020-00322-y] [Medline: 33747711]
48. Humphrey G, Newcombe D, Whittaker R, Parag V, Bullen C. SPGeTTI: a smartphone-based problem gambling evaluation and technology testing initiative final report. The University of Auckland. 2019. URL: https://www.health.govt.nz/publication/spgetti-smartphone-based-problem-gambling-evaluation-and-technology-testing-initiative [accessed 2021-05-09]
49. Coral R, Esposito F, Weinstock J. Don't go there: a zero-permission geofencing app to alleviate gambling disorders. In: Proceedings of the 2020 IEEE 17th Annual Consumer Communications & Networking Conference (CCNC). 2020 Presented at: 2020 IEEE 17th Annual Consumer Communications & Networking Conference (CCNC); Jan 10-13, 2020; Las Vegas, NV, USA. [doi: 10.1109/ccnc46108.2020.9045251]
50. Merkouris SS, Hawker CO, Rodda SN, Youssef GJ, Dowling NA. Gamblingless: curb your urge: development and usability testing of a smartphone-delivered ecological momentary intervention for problem gambling. Int Gambl Stud 2020 Apr 10;20(3):515-538. [doi: 10.1080/14459795.2020.1749293]
51. Khazaal Y, Monney G, Richter F, Achab S. « Jeu-contrôle », rationnel d'une application de soutien aux limites de jeux. J de Thérapie Comportementale et Cognitive 2017 Sep;27(3):129-137. [doi: 10.1016/j.jtcc.2017.05.003]
52. Hawker CO, Merkouris SS, Youssef GJ, Dowling NA. A smartphone-delivered ecological momentary intervention for problem gambling (gamblingless: curb your urge): single-arm acceptability and feasibility trial. J Med Internet Res 2021 Mar 26;23(3):e25786 [FREE Full text] [doi: 10.2196/25786] [Medline: 33769294]
53. Wright C, Dietze PM, Agius PA, Kuntsche E, Livingston M, Black OC, et al. Mobile phone-based ecological momentary intervention to reduce young adults' alcohol use in the event: a three-armed randomized controlled trial. JMIR Mhealth Uhealth 2018 Jul 20;6(7):e149 [FREE Full text] [doi: 10.2196/mhealth.9324] [Medline: 30030211]
54. O'Donnell R, Richardson B, Fuller-Tyszkiewicz M, Staiger PK. Delivering personalized protective behavioral drinking strategies via a smartphone intervention: a pilot study. Int J Behav Med 2019 Aug 03;26(4):401-414. [doi: 10.1007/s12529-019-09789-0] [Medline: 31161592]

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55. Klasnja P, Hekler EB, Shiffman S, Boruvka A, Almirall D, Tewari A, et al. Microrandomized trials: an experimental design for developing just-in-time adaptive interventions. Health Psychol 2015 Dec;34S(Suppl):1220-1228 [FREE Full text] [doi: 10.1037/hea0000305] [Medline: 26651463]
56. Treweek S, Zwarenstein M. Making trials matter: pragmatic and explanatory trials and the problem of applicability. Trials 2009 Jun 03;10(1):37 [FREE Full text] [doi: 10.1186/1745-6215-10-37] [Medline: 19493350]
57. Kim SW, Grant JE, Potenza MN, Blanco C, Hollander E. The Gambling Symptom Assessment Scale (G-SAS): a reliability and validity study. Psychiatry Res 2009 Mar 31;166(1):76-84 [FREE Full text] [doi: 10.1016/j.psychres.2007.11.008] [Medline: 19200607]
58. Park JJ, Booth N, Bagot KL, Rodda SN. A brief internet-delivered intervention for the reduction of gaming-related harm: a feasibility study. Comput Human Behav Report 2020 Aug;2:100027. [doi: 10.1016/j.chbr.2020.100027]
59. Goldstein SP, Evans BC, Flack D, Juarascio A, Manasse S, Zhang F, et al. Return of the JITAI: applying a just-in-time adaptive intervention framework to the development of m-health solutions for addictive behaviors. Int J Behav Med 2017 Oct 12;24(5):673-682 [FREE Full text] [doi: 10.1007/s12529-016-9627-y] [Medline: 28083725]
60. Heron K, Smyth J. Ecological momentary interventions: incorporating mobile technology into psychosocial and health behaviour treatments. Br J Health Psychol 2010 Feb;15(Pt 1):1-39 [FREE Full text] [doi: 10.1348/135910709X466063] [Medline: 19646331]
61. Nahum-Shani I, Smith S, Spring BJ, Collins LM, Witkiewitz K, Tewari A, et al. Just-in-time adaptive interventions (JITAIs) in mobile health: key components and design principles for ongoing health behavior support. The Methodology Center, Penn State. URL: https://cmapspublic2.ihmc.us/rid=1P0PJNP7V-12LPKBQ-273F/Nahum-Shani%20et%20al.%20-%202014%20-%20Just%20in%20time%20adaptive%20interventions%20(jitais)%20An%20o.pdf [accessed 2022-06-16]
62. Nahum-Shani I, Hekler EB, Spruijt-Metz D. Building health behavior models to guide the development of just-in-time adaptive interventions: a pragmatic framework. Health Psychol 2015 Dec;34S(Suppl):1209-1219 [FREE Full text] [doi: 10.1037/hea0000306] [Medline: 26651462]
63. Marlatt G, Donovan D. Relapse Prevention: Maintenance Strategies in the Treatment of Addictive Behaviors, 2nd Ed. New York: Guilford press; 2005.
64. Schwarzer R, Lippke S, Luszczynska A. Mechanisms of health behavior change in persons with chronic illness or disability: the Health Action Process Approach (HAPA). Rehabil Psychol 2011 Aug;56(3):161-170. [doi: 10.1037/a0024509] [Medline: 21767036]
65. Raylu N, Oei TP. The gambling urge scale: development, confirmatory factor validation, and psychometric properties. Psychol Addictive Behav 2004 Jun;18(2):100-105. [doi: 10.1037/0893-164x.18.2.100]
66. Smith C, Stewart SH, O'Connor RM, Collins P, Katz J. Development and psychometric evaluation of a 10-item short form inventory of gambling situations. J Gambl Stud 2011 Mar 1;27(1):115-128. [doi: 10.1007/s10899-010-9192-2] [Medline: 20432058]
67. Brittain M, Consedine N, Bagot KL, Booth N, Rodda SN. Sugar Habit Hacker: initial evidence that a planning intervention reduces sugar intake. J Behav Addict 2021 Sep 22;10(3):471-481 [FREE Full text] [doi: 10.1556/2006.2021.00054] [Medline: 34550904]
68. Bischof A, Bischof G, Meyer C, John U, Hodgins DC, Rumpf H. Untreated pathological gamblers: who recovers and who does not? Int Gambl Stud 2019 Dec 19;20(2):200-213. [doi: 10.1080/14459795.2019.1703201]
69. Armitage CJ. Effectiveness of experimenter-provided and self-generated implementation intentions to reduce alcohol consumption in a sample of the general population: a randomized exploratory trial. Health Psychol 2009 Sep;28(5):545-553. [doi: 10.1037/a0015984] [Medline: 19751080]
70. Knäuper B, Roseman M, Johnson PJ, Krantz LH. Using mental imagery to enhance the effectiveness of implementation intentions. Curr Psychol 2009 May 5;28(3):181-186. [doi: 10.1007/s12144-009-9055-0]
71. Hamilton K, Keech JJ, Peden AE, Hagger MS. Protocol for developing a mental imagery intervention: a randomised controlled trial testing a novel implementation imagery e-health intervention to change driver behaviour during floods. BMJ Open 2019 Feb 19;9(2):e025565 [FREE Full text] [doi: 10.1136/bmjopen-2018-025565] [Medline: 30782937]
72. Heckhausen H, Gollwitzer PM. Thought contents and cognitive functioning in motivational versus volitional states of mind. Motiv Emot 1987 Jun;11(2):101-120. [doi: 10.1007/bf00992338]
73. Rodda SN, Dowling NA, Lubman DI. Gamblers seeking online help are active help-seekers: time to support autonomy and competence. Addict Behav 2018 Dec;87:272-275. [doi: 10.1016/j.addbeh.2018.06.001] [Medline: 29935737]
74. Weinstock J, Whelan JP, Meyers AW. Behavioral assessment of gambling: an application of the timeline followback method. Psychol Assess 2004 Mar;16(1):72-80. [doi: 10.1037/1040-3590.16.1.72] [Medline: 15023094]
75. Kessler RC, Andrews G, Colpe LJ, Hiripi E, Mroczek DK, Normand SL, et al. Short screening scales to monitor population prevalences and trends in non-specific psychological distress. Psychol Med 2002 Aug 26;32(6):959-976. [doi: 10.1017/s0033291702006074] [Medline: 12214795]
76. International Wellbeing Group. Personal Wellbeing Index: 5th Edition. Melbourne: Australian Centre on Quality of Life, Deakin University; 2013.
77. Breslin F, Sobell LC, Sobell MB, Agrawal S. A comparison of a brief and long version of the situational confidence questionnaire. Behav Res Ther 2000 Dec;38(12):1211-1220. [doi: 10.1016/s0005-7967(99)00152-7]

XSL•FO
RenderX

78. Reyes Fernández B, Knoll N, Hamilton K, Schwarzer R. Social-cognitive antecedents of hand washing: action control bridges the planning-behaviour gap. Psychol Health 2016 Aug 26;31(8):993-1004. [doi: 10.1080/08870446.2016.1174236] [Medline: 27049339]
79. Sekhon M, Cartwright M, Francis JJ. Acceptability of healthcare interventions: an overview of reviews and development of a theoretical framework. BMC Health Serv Res 2017 Jan 26;17(1):88 [FREE Full text] [doi: 10.1186/s12913-017-2031-8] [Medline: 28126032]
80. Stoyanov SR, Hides L, Kavanagh DJ, Zelenko O, Tjondronegoro D, Mani M. Mobile app rating scale: a new tool for assessing the quality of health mobile apps. JMIR Mhealth Uhealth 2015 Mar 11;3(1):e27 [FREE Full text] [doi: 10.2196/mhealth.3422] [Medline: 25760773]
81. Qian T, Walton AE, Collins LM, Klasnja P, Lanza ST, Nahum-Shani I, et al. The microrandomized trial for developing digital interventions: experimental design and data analysis considerations. Psychol Methods 2022 Jan 13. [doi: 10.1037/met0000283] [Medline: 35025583]
82. Christensen L, Mendoza JL. A method of assessing change in a single subject: an alteration of the RC index. Behav Ther 1986 Jun;17(3):305-308. [doi: 10.1016/s0005-7894(86)80060-0]
83. Jacobson NS, Truax P. Clinical significance: a statistical approach to defining meaningful change in psychotherapy research. J Consulting Clin Psychol 1991;59(1):12-19. [doi: 10.1037/0022-006x.59.1.12]
84. Maust D, Cristancho M, Gray L, Rushing S, Tjoa C, Thase M. Psychiatric rating scales. In: Handbook of Clinical Neurology. Amsterdam, Netherlands: Elsevier Science; 2012:227-237.
85. Masterson Creber RM, Maurer MS, Reading M, Hiraldo G, Hickey KT, Iribarren S. Review and analysis of existing mobile phone apps to support heart failure symptom monitoring and self-care management using the Mobile Application Rating Scale (MARS). JMIR Mhealth Uhealth 2016 Jun 14;4(2):e74 [FREE Full text] [doi: 10.2196/mhealth.5882] [Medline: 27302310]
86. Kok G, Gottlieb NH, Peters GY, Mullen PD, Parcel GS, Ruiter RA, et al. A taxonomy of behaviour change methods: an Intervention Mapping approach. Health Psychol Rev 2016 Sep 15;10(3):297-312 [FREE Full text] [doi: 10.1080/17437199.2015.1077155] [Medline: 26262912]
87. Michie S, Yardley L, West R, Patrick K, Greaves F. Developing and evaluating digital interventions to promote behavior change in health and health care: recommendations resulting from an international workshop. J Med Internet Res 2017 Jun 29;19(6):e232 [FREE Full text] [doi: 10.2196/jmir.7126] [Medline: 28663162]
88. Change strategies project. Change Strategies. URL: https://changestrategies.ac.nz/ [accessed 2022-06-27]
89. GamblingLess. Deakin University. URL: https://gamblingless.org/ [accessed 2022-06-28]

Abbreviations

BCT: behavior change technique
EMA: ecological momentary assessment
G-SAS: Gambling Symptom Assessment Scale
HAPA: Health Action Process Approach
JITAI: Just-In-Time Adaptive Intervention
MRT: microrandomized trial

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Protocol

Assessing an Internet-Delivered, Emotion-Focused Intervention Compared With a Healthy Lifestyle Active Control Intervention in Improving Mental Health in Cancer Survivors: Protocol for a Randomized Controlled Trial

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Abstract

Background: Cancer survivors are vulnerable to experiencing symptoms of anxiety and depression and may benefit from accessible interventions focused on improving emotion regulation. CanCope Mind (CM) was developed as an internet-delivered intervention adapted from the Unified Protocol for Transdiagnostic Treatment of Emotional Disorders to improve emotion regulation and support the mental health of cancer survivors.

Objective: This protocol aims to provide an outline of the CanCope Study, a trial comparing the efficacy of a Unified Protocol–adapted internet-delivered intervention (CM) designed for cancer survivors compared with an active control condition—an internet-delivered healthy lifestyle intervention, CanCope Lifestyle (CL). The primary aim is to assess and compare the efficacy of both interventions in improving emotion regulation, anxiety and depressive symptoms, and quality of life. The secondary aims involve assessing the mechanisms of the CM intervention.

Methods: This trial is a 2-arm randomized controlled trial that allocates cancer survivors to either CM or CL. Both interventions comprise 4 web-based modules and are expected to take participants at least 8 weeks to complete. Participants' mental and physical health will be assessed via self-reported surveys at baseline (T_0), between each module (T_1, T_2, and T_3), immediately after the intervention (T_4), and at 3-month follow-up (T_5). The study aims to recruit 110 participants who have completed T_4.

Results: The CanCope study began recruitment in September 2020. A total of 224 participants have been randomized to the CM (n=110, 49.1%) and CL (n=114, 50.9%) groups.

Conclusions: This is one of the first trials to develop and investigate the efficacy of a web-based intervention for cancer survivors that specifically targets emotion regulation.

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KEYWORDS

cancer survivor; depressive symptoms; anxiety symptoms; emotion regulation; Unified Protocol; transdiagnostic; internet-delivered intervention; quality of life; eHealth; randomized controlled trial; psycho-oncology; mobile phone

Introduction

Background

The end of cancer treatment is a challenging transition for many cancer survivors. Individuals can continue to experience cancer-related distress long after primary treatment has ended. Specifically, 42% and 29% of cancer survivors experience at least subclinical symptoms of anxiety and depression, respectively, and worse mental health compared with the general population [1-3]. Even 10 years after a diagnosis, large population-based studies have shown that cancer survivors are at an elevated risk of experiencing anxiety and depressive symptoms compared with cancer-free, age-matched controls [4]. Advances in diagnosis and treatment have resulted in an increasing number of individuals surviving cancer. Therefore, there is a need to support the ongoing mental health of cancer survivors.

Emotion regulation can be defined as the ability to adapt to one's affective experience, such as maintain, increase, or decrease feelings, behaviors, or physiological responses that comprise an emotional experience [5]. Difficulty with emotion regulation, or emotion dysregulation, is a core transdiagnostic feature underlying the development and maintenance of multiple psychopathologies, including anxiety and depression [6,7]. Emotion regulation capacities may account for one's ability to manage stressful life events, including cancer [8-10]. Strategies for regulating emotions can be categorized as either avoidance-oriented (ie, disengagement-based, such as expressive suppression, experiential avoidance, and denial) or approach-oriented (ie, engagement-based, such as cognitive reappraisals, problem solving, emotional expression, and acceptance). Avoidance-oriented strategies are associated with higher rates of emotional distress than approach-oriented strategies, including anxiety and depressive symptoms among cancer survivors [11-14]. Therefore, upregulating adaptive emotion regulation processes may be an effective way of improving mental health outcomes among cancer survivors.

One cognitive-behavioral intervention designed to target approach-oriented emotion regulation is the Unified Protocol (UP) [15]. The UP is considered transdiagnostic as it effectively improves emotional distress, including symptoms of anxiety and depression, across a range of psychopathologies [16]. Furthermore, pilot studies have demonstrated that the UP may improve depressive symptoms and emotion regulation among people with breast cancer [17]. This suggests that the UP may be effectively adapted for oncological populations. On the basis of these findings, we recently developed the CanCope intervention, an internet-delivered adaptation of the UP's modules, tailored to the needs of cancer survivors of any diagnosis. Each CanCope module was assessed independently in a series of pilot trials. Our results suggested high feasibility, participant satisfaction, and preliminary efficacy of each independent module in improving emotion regulation and mental health symptoms when delivered remotely [18]. These are promising preliminary findings, given that accessibility to face-to-face mental health support for oncological populations is often comprised of geographic location, financial strain, lack of available health care personnel, the iatrogenic effects of cancer treatments, and more recently the COVID-19 pandemic [1,19-24]. This inequality in care indicates the need for evidence-based, remotely delivered, and scalable psychological interventions for cancer survivors.

Although many psychological interventions target the mental health of patients with cancer and cancer survivors [25-27], few have examined the potential underlying mechanisms. This is not specific to psycho-oncology; the lack of well-designed mechanistic research is widespread across intervention research [28,29]. Overall, there is a lack of understanding around *why* and *how* interventions achieve their desired effects. For instance, meta-analytic findings reveal that even though the UP may be effective in improving symptom outcomes, there is a lack of evidence to suggest that these effects are mediated through changes in emotion regulation [16].

Similarly, little is known about the effectiveness of *specific* intervention components, information critical for understanding the causal mechanisms that drive improvements in mental health [30]. Uncovering intervention mechanisms and active components is required to optimize future intervention designs and maximize treatment efficiency and outcomes [29,31]. The UP allows for the assessment of mechanisms, as the protocol adopts a modular approach, where each module targets a distinct emotion regulation skill (eg, identifying and understanding emotions, mindful acceptance of emotions, cognitive reappraisals, and experiential avoidance). One small study assessed the effects of each of these modules when delivered in-person, and the findings support the isolated therapeutic effects of each UP component [32]. The authors' CanCope pilot studies extended these findings, showing that when delivered via the internet, each independently delivered module was associated with improvements in the intended module-specific outcomes [18]. For example, unhealthy beliefs about emotions reduced after participating in the CanCope Understanding Emotions module, and levels of mindfulness increased after taking part in the CanCope Mindful Emotion Awareness module.

In addition, evidence suggests that the UP may improve broader health outcomes and overall quality of life (QoL) [16,33-35]. Compared with the general population, cancer survivors experience inferior QoL. Indeed, up to 75% of survivors experience iatrogenic health deficits associated with reduced QoL and length of survival [22,36]. Emotion regulation is plausibly related to QoL among cancer survivors [37]. How people with cancer regulate emotions is associated with both the physiological and psychological adaptation to cancer, which can in turn impact QoL and disease prognosis [38]. Thus, the UP-adapted and cancer-specific CanCope intervention may not only improve emotion regulation but also overall QoL. By

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assessing intervention effects on QoL, and not simply deficits in mental health, a more holistic and meaningful perspective of health can be examined.

Aims and Hypotheses

To address these limitations, a 2-arm randomized controlled trial was designed to assess the efficacy of an internet-delivered, multimodular UP-based intervention package with all modules combined, titled CanCope Mind (CM). CM was compared with a healthy lifestyle active control intervention, CanCope Lifestyle (CL).

Primary Aim

Aim 1 is to assess the efficacy of CM versus CL in reducing emotion dysregulation (primary outcome) and in improving anxiety and depressive symptoms and QoL (secondary outcomes) in cancer survivors. Hypothesis 1 states that, compared with CL, after treatment (T_4), cancer survivors randomized to CM will experience fewer difficulties regulating emotions as well as lower symptoms of anxiety and depression. Both CM and CL are expected to improve QoL, as CL includes components that target diet, physical activity, relaxation, and sleep. Given that these 4 lifestyle factors are associated with improved QoL, it is unclear whether CM or CL will be more effective in improving QoL.

Secondary Aims

Aim 2 (Exploratory)

Aim 2 is to explore the role of each of the CM modules and whether the intervention is associated with changes in module-specific target outcomes (see Table 1 for CM modules and their associated outcomes).

Table 1. CM[a] module outline and outcomes.

Module	Description	Module-specific outcomes
1. Understanding emotions	• Part 1 (2 days): learn about the adaptive functions of emotions. Day 1[b] is a core activity. • Part 2 (2 days): learn about unhelpful beliefs about emotions. • Part 3 (10 days): learn about the 3-component model of emotional experiences (thoughts, feelings or physical sensations, and behaviors). Explore each component in one's daily life. Day 5[b] is a core activity.	Decrease unhelpful beliefs about emotions (BES[c] [39])
2. Mindful emotion awareness	• Part 1 (7 days): learn about mindfulness and nonjudgment of emotions. Practice mindfulness using daily 10-min guided audios. Day 1[b] is a core activity. • Part 2 (7 days): practice daily "anchoring" techniques to ground oneself in the present moment. Day 8[b] is a core activity.	Increase mindfulness skills (SMQ[d] [40])
3. Flexible thinking	• Part 1 (14 days): learn about common "thinking traps" (ie, cognitive distortions such as catastrophizing) and how to challenge cognitive distortions. Practice daily cognitive reappraisal exercises to develop balanced thinking patterns. Day 1[b] is a core activity.	Increase use of cognitive reappraisal strategies (CERQ[e], UP-CSQ[f] [32,41])
4. Doing things differently	• Part 1 (6 days): learn about the impact of unhelpful EDBs[g] (eg, avoidance) in perpetuating negative thoughts or emotions. Practice identifying one's own EDBs. Day 1[b] is a core activity. • Part 2 (8 days): learn about the importance of challenging EDBs. Practice replacing unhelpful EDBs with healthier alternative actions (eg, approach-oriented rather than avoidance-oriented behaviors). Day 7[b] is a core activity.	Decrease experiential avoidance (MEAQ-30[h] [42])

[a]CM: CanCope Mind.

[b]Each module comprises 1 to 2 *core activities*, which must be completed for participants to finish the module and move on to the next module.

[c]BES: Beliefs About Emotions Scale.

[d]SMQ: Southampton Mindfulness Questionnaire.

[e]CERQ: Cognitive Emotional Regulation Questionnaire.

[f]UP-CSQ: Unified Protocol–Cognitive Skills Questionnaire.

[g]EDBs: emotion-driven behaviors.

[h]MEAQ-30: Multidimensional Experiential Avoidance Questionnaire-30.

Aim 3

If the CM intervention improves emotion dysregulation, we will assess whether changes in emotion dysregulation mediate the effects of CM versus CL on anxiety and depressive symptoms. Hypothesis 2 states that improvements in anxiety and depressive symptoms for CM compared with CL participants —after the treatment will be mediated by greater reductions in emotion dysregulation in CM participants than in CL participants.

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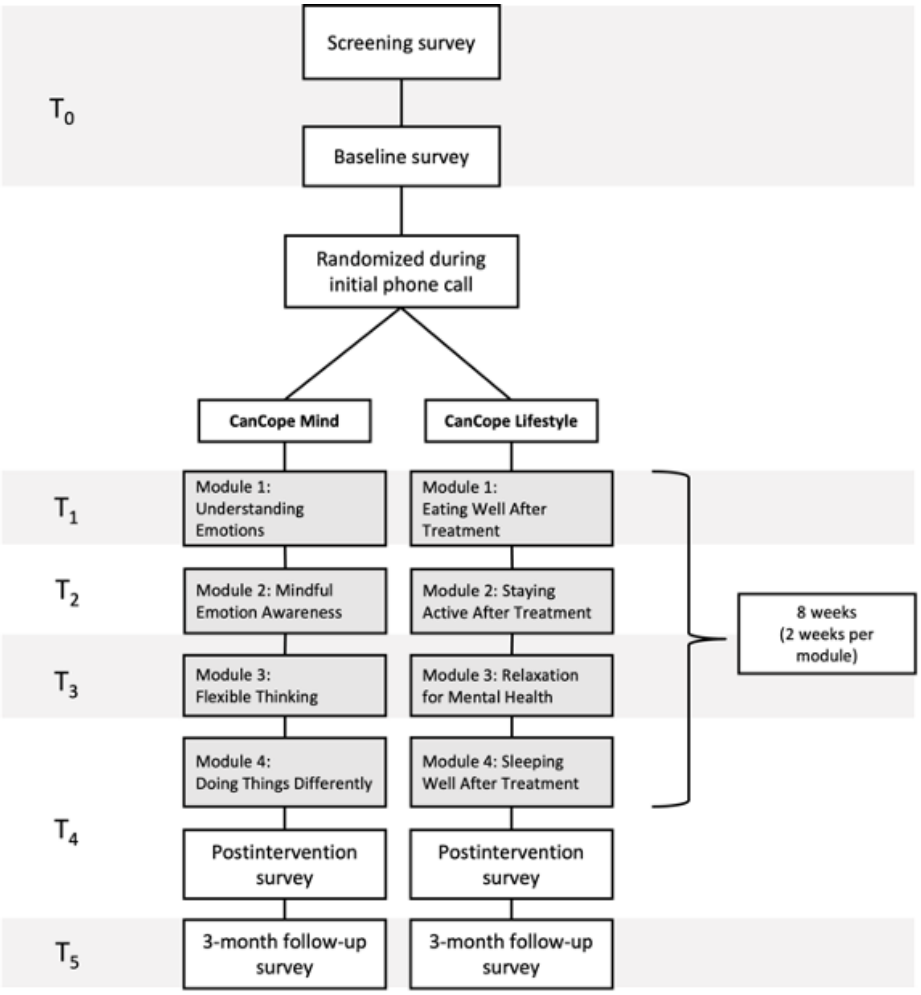
Methods

Study Design and Procedure

This trial is a 2-arm randomized controlled trial. The subsequent sections provide a detailed description of the trial procedures, and Figure 1 provides a visual summary of the assessment time points and participant flow.

Figure 1. Procedure and participant flow diagram. T0: baseline; T1: post-module 1; T2: post-module 2; T3: post-module 3; T4: post-intervention and post-module 4; T5: 3-month follow-up assessment.



Participants and Eligibility Criteria

Participants comprise individuals who have completed their primary cancer treatment (ie, cancer survivors; Textbox 1).

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Textbox 1. Inclusion and exclusion criteria

Inclusion criteria

- Able to read and write in English
- Able to provide informed consent
- Living in Australia, New Zealand, the United Kingdom, the United States, or Canada
- Aged ≥18 years
- Previous diagnosis of cancer (any cancer type)
- ≤2 years since finishing primary cancer treatment (ie, surgery, chemotherapy, and radiotherapy)
- Regular access to the internet and email
- Regular access to a computer, laptop, or smartphone device.

Exclusion criteria

- Currently undergoing or planning to undergo further primary cancer treatment (ie, surgery, chemotherapy, or radiotherapy)
- Cancer is not in remission or is progressing in severity
- Endorses current suicidality and considered high risk for self-harm
- Current episode of psychosis
- Attending regular sessions with a mental health professional (ie, attended sessions with a psychologist or counselor over the past 4 weeks or have scheduled sessions with a psychologist or counselor throughout the 8-week trial)
- Started or changed psychotropic medication or dose within the previous 2 weeks, or plans to start or change psychotropic medication or dose throughout the 8-week trial
- Previously participated in the CanCope pilot trials

No minimum criterion was included for the primary outcomes of emotion dysregulation, as it is not certain that this UP-adaption is only effective in highly dysregulated cancer survivors. By excluding participants based on a minimum cut-off, we would not be able to assess the intervention effects on cancer survivors experiencing high and low difficulties.

Recruitment and Consent

Participants are recruited using multiple methods, including social media platforms (eg, Facebook groups), web-based community forums (eg, Cancer Council), and via organizers of cancer support groups. Embedded within each of these advertisements, participants can access a link to the study's written explanatory statement and consent form hosted on the Research Electronic Data Capture (REDCap) tool [43,44]. Informed consent is obtained by submission of a consent form on the web.

Screening and Initial Phone Call

Consenting participants are automatically redirected to a web-based screening survey to assess eligibility. Subsequently, eligible participants complete the baseline survey and are telephoned to administer the Mini International Neuropsychiatric Interview (MINI) [45] and conduct a risk assessment. Individuals deemed high risk (ie, probable risk of harming themselves) are excluded over the phone and referred to relevant psychiatric services. Eligible participants are randomized to either CM or CL. This group allocation and a summary of their intervention are conveyed to participants over the phone.

Randomization and Blinding

Randomization to CM or CL is conducted using a stratified, block randomization scheme generated in advance and uploaded to REDCap. Variable block sizes (4, 6, or 8) are used to ensure allocation concealment and prior guessing of the allocation sequence at the end of each block. Randomization is stratified by baseline depressive and anxiety symptoms as measured by the Patient-Reported Outcomes Measurement Information System (PROMIS) Anxiety and Depression scales (2 strata: ≥60 for either depression or anxiety, <60 for both depression and anxiety) and the Difficulties in Emotion Regulation Scale–Short Form (2 strata: <45 and ≥45). The randomization scheme is generated and set up in REDCap by a member of the research staff who is not involved in the recruitment or delivery of the intervention nor in the subsequent statistical analysis. The participants are aware of their intervention allocation (ie, CM or CL); thus, they are not blinded. However, participants remain unaware of the study hypotheses regarding which group will improve more on outcomes, and both treatments are presented as potentially effective.

Interventions

Both the CM and CL intervention conditions are internet-delivered programs comprising 4 modules (2 weeks of content per module), which may take participants as few as 8 weeks to complete. Both interventions comprise educational readings and videos followed by activities on the web. The activities include textboxes for participants to provide written responses to encourage active reflections. All intervention materials and activities are delivered on the web via REDCap. Multimedia Appendix 1 illustrates examples of visual snapshots

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of activities in each intervention. All web-based activity responses completed by the participants are available for researchers to view, allowing intervention adherence to be assessed. At the beginning of each intervention and to enhance motivation, all participants are encouraged to set treatment goals. To improve engagement and provide additional support, all participants are offered an optional midintervention phone call (approximately 15 minutes) between modules 2 and 3. Upon completion of T_5, all participants receive the alternative group's intervention material via an email link (ie, combined psychoeducational readings and video links).

Treatment Group: CM

CM is a web-based version of the UP's Transdiagnostic Treatment for Emotional Disorders [15]. The overall goal of the UP is to help individuals understand and recognize their emotions and respond to uncomfortable emotions in a more adaptive manner. Participants allocated to CM receive four UP-adapted modules titled (1) understanding emotions, (2) mindful emotion awareness, (3) flexible thinking, and (4) doing things differently. CM is a reduced format of the UP, as 2 core UP modules (modules 6 and 7) have been excluded from CM owing to their sole focus on exposure therapy, which was deemed inappropriate for remote delivery for individuals experiencing chronic health conditions. In CM, each module comprises 14 daily activities on the web (3-10 minutes each), which allow participants to apply what they have learned from the psychoeducational readings and videos. Participants are not expected to complete *every* daily activity, although they must complete at least 1 to 2 core activities per module before they could move on to the subsequent module. This format aims to mirror a more real-life, clinician-led intervention, where clients would not prematurely progress to a subsequent and more advanced module without first being exposed to fundamental skills from the previous modules (ie, in CM, participants must first learn about what an emotion is [module 1] before they can begin to mindfully engage with their emotional experiences [module 2] and change them [modules 3 and 4]). As a result, participants who reach the end of the entire intervention have been exposed to all core skills. Each module is outlined in subsequent sections, and a summary overview is provided in Table 1.

CM Module 1: Understanding Emotions

Module 1 aims to build an awareness and understanding of emotions through 3 psychoeducational readings, 2 summary videos, and 14 daily activities. *Part 1* explains that emotions are neither *good* nor *bad*, and it outlines the various adaptive functions of common emotions. For instance, anxiety elicits fight-or-flight responses, which is important in times of threat. During the daily activities, participants are encouraged to reflect on their own emotions and their adaptive functions in their lives. *Part 2* describes common unhelpful beliefs or misconceptions around emotions (eg, "showing emotions is a sign of weakness" and "I 'should' feel a certain way in particular situations"). The daily activities encourage participants to explore their own unhelpful beliefs about their emotions. *Part 3* describes the three interrelated components that constitute an emotional experience: (1) thoughts, (2) feelings or bodily sensations, and (3) behaviors. During the daily activities, participants are encouraged to bring awareness to these 3 components in their lives.

CM Module 2: Mindful Emotion Awareness

Module 2 aims to increase mindful awareness of emotions through 2 psychoeducational readings, 2 summary videos, and 14 activities. In *part 1*, participants are encouraged to adopt an accepting and nonjudgmental stance toward primary emotions, as critical judgment of primary emotional responses can perpetuate negative affective states. Participants are provided with 2 emotion-focused guided mindfulness audios and are encouraged to listen to one of them every day for 7 days. *Part 2* teaches a four-step mindful *anchoring* exercise: (1) paying attention to a cue, such as the breath; (2) identifying their thoughts, feelings, and behaviors; (3) considering whether their response is consistent with the present moment; and (4) shifting their response to align with the demands of the present moment. For 7 days, participants are encouraged to practice *anchoring* in *real time*, when experiencing uncomfortable emotions.

CM Module 3: Flexible Thinking

Module 3 aims to increase skills in *flexible thinking* (ie, cognitive flexibility). Flexible thinking involves the ability to (1) identify automatic and unhelpful thoughts and interpretations and subsequently (2) identify an alternative, more balanced appraisal of the given situation. The module comprises 1 reading, 1 summary video, and 14 activities that outline the bidirectional relationship between thoughts and emotions. Participants are taught about common and unhelpful *thinking traps* (ie, cognitive distortions), including catastrophizing, jumping to conclusions, tunnel vision, "should" statements, and all-or-nothing thinking. The daily activities on the web encourage participants to (1) identify their thinking traps, (2) answer multiple questions to challenge the thinking trap (eg, "What evidence supports my negative belief?" "Am I 100% sure these negative outcomes will occur?"), and (3) generate an alternative and more balanced appraisal of the situation.

CM Module 4: Doing Things Differently

The final module aims to build skills in identifying and altering unhelpful emotion-driven behaviors (EDBs) through 2 psychoeducational readings, 2 summary videos, and 14 activities. Unhelpful EDBs are defined as maladaptive ways to try to manage one's emotions, often with the purpose of eliminating an emotion or preventing oneself from feeling an emotion in the first place. *Part 1* focuses on overt and covert avoidance-oriented EDBs (eg, avoiding certain situations or people, procrastinating, denial, ruminating, suppression, and safety behaviors) and their paradoxical effect in increasing negative emotions, such as anxiety. Two other broad categories of EDBs are discussed: reassurance-seeking behaviors (eg, excessive bodychecking for signs of cancer recurrence or excessively seeking external validation and compliments) and defensive behaviors (eg, directing anger and frustration toward others). In activities on the web, participants are encouraged to identify and reflect on these EDBs throughout their lives. *Part 2* teaches participants about *alternative actions*, value-consistent and healthier behaviors that can replace unhelpful EDBs (eg,

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engaging in conversations with loved ones regarding their cancer journey as opposed to avoiding cancer-related discussions owing to anxiety). In daily activities on the web, participants are encouraged to practice replacing their EDBs with alternative actions.

Rationale for Choice of Control Group

To assess the effects of CM on an appropriate comparator, we consulted the National Institute of Health's Pragmatic Model for Comparator Selection in Health-Related Behavioral Trials [46]. According to the model, the best comparator is one that suits the goals of the research trial. Given that (1) the CanCope modules have demonstrated promising results when trialed independently in pilot studies and (2) this is the first efficacy trial to assess the effectiveness of the CM program in its entirety, this trial remains within the preliminary phases of the research process. We defined the goal of this trial as establishing how well CM compares to information currently readily available to cancer survivors seeking support to improve their general well-being.

Currently, patients with cancer and cancer survivors have access to a host of resources that aim to promote general QoL, often with a focus on diet, physical exercise, relaxation, and sleep. These resources are often disseminated freely on the web by cancer-specific (eg, Cancer Council, National Breast Cancer Foundation, Prostate Cancer Foundation Australia) and noncancer-specific (eg, Mind UK, Beyond Blue, and Black Dog Institute) community and government organizations. Therefore, two possible comparator options were considered: (1) a wait-list control condition versus (2) a basic lifestyle and well-being intervention targeting diet, exercise, sleep, and relaxation using free and highly accessible web-based resources.

Both options were evaluated against 7 key characteristics identified in the National Institute of Health model [46], which are summarized in Table 2. On the basis of these considerations, a 4-module web-based well-being or lifestyle comparator was chosen (ie, CL). CL is expected to be widely accepted by participants in comparison to a wait-list control group, which may result in high attrition rates, especially given the number of between-module surveys. Furthermore, a basic well-being program is deemed relevant and highly feasible, as we can draw on information available on the web and preexisting sleep resources used in sleep trials by researchers at Monash University. Most importantly, an active comparator controls for nonspecific components of the intervention, such as contact with researchers and expectancy or placebo effects, allowing for greater stringency in measuring the outcomes of interest. The primary limitation of using CL as a comparator is that improvements in diet, physical exercise, relaxation, and sleep may lead to sizeable improvements in secondary outcomes (ie, anxiety and depressive symptoms and QoL). However, the primary outcome of interest is emotion regulation. Given that the CL intervention does not focus specifically on emotions, we expect that any significantly meaningful improvements in emotion regulation will be smaller than those observed in the CM group.

Table 2. Comparison of potential comparator conditions.

Characteristic	Wait-list control (no intervention for 8 weeks).	CL[a] (four modules: diet, exercise, relaxation, and sleep).
Acceptability	Moderate—participants will eventually be given the CM[b] program, however, they may not be content with completing multiple study assessments during the 8-week waiting period.	High—participants will be provided with a program that targets health areas of interest. All participants will eventually receive the CM intervention material.
Feasibility	High—no intervention needs to be developed.	High—it is easy to access resources on the web to disseminate (from sites such as Cancer Council). Our research group has existing sleep hygiene information specifically designed for oncological populations.
Formidability	Low—no intervention means that outcomes should not change because of the comparator.	Moderate—improving diet, physical activity, relaxation, and sleep can have an impact on lowering depressive and anxiety symptoms and potentially emotion regulation.
Relevance	High—most cancer survivors do not receive a mental health intervention after finishing primary treatment.	High—basic well-being information regarding diet, physical exercise, relaxation, and sleep is commonly disseminated by hospitals and organizations, and is freely available on the web.
Stringency	Low—the absence of a comparator intervention would not control for other factors such as expectancy or placebo effects or contact with researchers.	High—controls for "nonspecific" intervention effects, such as expectancy and placebo effects and contact with researchers. The 4 comparator modules would align with the 4 CM modules, thus closely matching the treatment intervention's timing of modules.
Uniformity	Low—participants would not receive the same information as the treatment group during the assessment period.	High—participants in the comparator group would receive a parallel 4-module program and concurrent assessment surveys.

[a]CL: CanCope Lifestyle.

[b]CM: CanCope Mind.

Control Group: CL

In parallel to the CM modules, the CL group receives four internet-delivered modules that focus on different lifestyle domains: (1) diet, (2) physical activity, (3) relaxation, and (4) sleep. Throughout each 2-week module, participants are sent 2 activity links via email, whereby they are asked to apply what they have learned from the module (eg, *describe how you*

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applied the module material to your lifeover the past week and *describe how you plan to apply the module material to your life over the next week*). Participants may take 3 to 10 minutes to complete each reflective activity on the web. Although the CL participants are sent fewer application activities on the web than the CM participants, they are still encouraged to apply the module material to their daily lives over the 2-week module duration. The content included in CL is publicly available, except for sleep hygiene information, which was developed by the Monash University sleep research group. The content of each module is outlined in the subsequent sections.

CL Module 1: Eating Well After Treatment

Module 1 comprises 1 video and 3 readings. The video was developed by the organization *Mind* (a mental health charity in the United Kingdom established by the National Association for Mental Health) and outlines 8 tips to improve well-being through healthy diet habits (eg, eat regularly, eat healthy fats, keep hydrated, and eat a variety of healthy vegetables). All the 3 readings were developed by the Cancer Council. The readings promote eating a healthy diet rich in fruits, vegetables, and whole grains to maintain well-being and reduce cancer risk and provide healthy recipes. Participants are encouraged to apply the healthy eating habits across the 2-week module.

CL Module 2: Staying Active After Treatment

Module 2 comprises 1 video and 1 reading. The video was developed by the organization *Mind* and outlines tips to encourage physical activity (eg, starting small and adhering to a consistent routine). Participants are directed to the Cancer Council's reading; "Exercise for people living with cancer," which provides various exercises related to strength training, aerobic exercise, flexibility, and strengthening the pelvic floor. Participants are encouraged to choose 2 exercises listed in the reading (eg, strength training) to apply throughout the module.

CL Module 3: Relaxation for Mental Health

Module 3 comprises educational material (1 video and 1 reading) and a link to various guided relaxation audios. The 5-minute YouTube video was developed by the organization *Mind* and outlines 8 tips to aid relaxation (eg, scheduling regular breaks, diaphragmatic breathing, visualization techniques, and listening to music). The reading, titled "Learning to relax," was developed by the Cancer Council and discusses healthy ways to manage emotional stress and aid relaxation (eg, exercising, massage, and yoga). Finally, participants are sent a link to access Beyond Blue's guided relaxation audio clips. Participants could choose from (1) breathing exercises, (2) muscle relaxation, and (3) guided visualizations. Participants are encouraged to listen to any of these audio clips as many times as they would like across the 2-week module.

CL Module 4: Sleeping Well After Treatment

The final module comprises 2 readings focused on sleep and fatigue. The first reading was developed by the Cancer Council and explains fatigue in the context of cancer and ways to manage fatigue. The second reading provides education on sleep (eg, what is sleep, stages of sleep, and the importance of sleep) and various sleep hygiene tips (eg, reducing caffeine intake, reducing light exposure at night, and increasing light exposure in the morning). This informational sheet was developed by researchers at Monash University. Participants are encouraged to apply the sleep hygiene tips across the 2-week module.

Assessment Time Points and Measures

Table 3 summarizes the nature and timing of the assessments in this trial. The research outcomes are assessed via web-based surveys administered via REDCap concurrently to both the CL and CM groups at the following time points: baseline (T_0, approximately 25 minutes), after module 1 (T_1, approximately 10 minutes), after module 2 (T_2, approximately 10 minutes), after module 3 (T_3, approximately 10 minutes), after module 4 (T_4, after the intervention, approximately 25 minutes), and at the 3-month follow-up (T_5, approximately 25 minutes). Participants in the CL are automatically emailed a link to complete each postmodule survey approximately 14 days after starting a given module. For CM participants, the postmodule surveys are automatically scheduled to be sent only once the core activities are completed (core activities are outlined in Table 1). Participants in both CL and CM are unable to begin the subsequent module until they have completed the previous postmodule survey. If participants do not complete their postmodule surveys within 2 weeks of receiving their original survey link, they are withdrawn from the study. Any completed survey responses beyond the 2-week cut-off time point are considered invalid and excluded from the analyses.

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Table 3. Schedule of survey assessments.

Time point	Items per time	Baseline (T_0)[a]	Postallocation[a]				Follow-up (T_5)[a]
			T_1 after module 1	T_2 after module 2	T_3 after module 3	T_4 after module 4	
Intervention groups							
CM[b]	N/A[c]	N/A	✓[d]	✓	✓	✓	N/A
CL[e]	N/A	N/A	✓	✓	✓	✓	N/A
Primary outcome							
DERS-SF[f]	18	✓	✓	✓	✓	✓	✓
Secondary outcomes							
Depression (PROMIS[g])	4	✓	✓	✓	✓	✓	✓
Anxiety (PROMIS)	4	✓	✓	✓	✓	✓	✓
QoL[h] (PROMIS)	30	✓	N/A	N/A	N/A	✓	✓
Module-specific target outcomes							
BES[i]	12	✓	✓	✓	✓	✓	✓
SMQ[j]	16	✓	✓	✓	✓	✓	✓
CERQ[k]	8	✓	✓	✓	✓	✓	✓
UP-CSQ[l]	7	✓	✓	✓	✓	✓	✓
MEAQ-30[m]	30	✓	✓	✓	✓	✓	✓
Other measures							
Depression Risk Questionnaire-7	7	✓	N/A	N/A	N/A	N/A	N/A
Positive Affect Subscale	10	✓	N/A	N/A	N/A	✓	✓
Demographic and cancer information	39	✓	N/A	N/A	N/A	N/A	N/A
Health service use (eg, current medications, mental health treatment)	10	✓	N/A	N/A	N/A	✓	✓
Program evaluation (Client Satisfaction Questionnaire and open feedback)	10	N/A	N/A	N/A	N/A	✓	N/A
Credibility Expectancy Questionnaire	6	✓	N/A	N/A	N/A	N/A	N/A
Adverse events (assessed throughout)	N/A	N/A	✓	✓	✓	✓	✓
COVID-19 pandemic impact and distress	2	✓	N/A	N/A	N/A	✓	N/A
MINI[n]	5 mins	✓	N/A	N/A	N/A	N/A	N/A

[a]Completion times: T0, T4, and T5 were 25 minutes each; T1-T3 were 10 minutes each.

[b]CM: CanCope Mind.

[c]N/A: not applicable.

[d]Measure administered at that time point.

[e]CL: CanCope Lifestyle.

[f]DERS-SF: Difficulties With Emotion Regulation Scale–Short Form.

[g]PROMIS: Patient-Reported Outcomes Measurement Information System. The PROMIS scales are all computer-adaptive tests, which means that they vary in the number of items administered depending on the participants' prior responses.

[h]QoL: quality of life.

[i]BES: Beliefs About Emotions Scale.

[j]SMQ: Southampton Mindfulness Questionnaire.

[k]CERQ: Cognitive Emotional Regulation Questionnaire. "Catastrophizing" and "Refocus on Planning" subscales.

[l]UP-CSQ: Unified Protocol–Cognitive Skills Questionnaire.

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[m]MEAQ-30: Multidimensional Experiential Avoidance Questionnaire-30.

[n]MINI: Mini International Neuropsychiatric Interview.

Screening

The MINI [45] is conducted in an initial phone call and used as a diagnostic tool to assess the presence of a major depressive episode (module A) and generalized anxiety disorder (module N), ruling out organic causes (module O). MINI interviews are recorded, allowing for the assessment of reliability and team discussion of complex cases. Any participant who endorses the criteria for a psychiatric illness is provided with relevant mental health and emergency support numbers.

Primary Outcome

The Difficulties in Emotion Regulation Scale–Short Form (DERS-SF) [47] will be used to assess six domains of emotional regulation (ie, acceptance of emotional responses, emotional awareness, emotional clarity, engagement in goal-directed behaviors, impulse control, and access to emotion regulation strategies). The DERS-SF is an 18-item self-report questionnaire that asks participants to indicate the frequency of emotion-focused behaviors and thoughts on a Likert-type rating scale, with possible responses ranging from 1 (“Almost never”) to 5 (“Almost always”). Example items include “I have difficulty making sense of my feelings” and “When I’m upset, I become out of control.” Scores can range from 18 to 90, with higher scores indicating greater emotional dysregulation. The DERS-SF indicates good concurrent validity for depression, anxiety, and self-harm measures and demonstrates good internal consistency reliability for both the overall scale (Cronbach α=.90) and each individual subscale (Cronbach α ranging from .78 to .89) [48,49]. Moreover, the full version of the Difficulties in Emotion Regulation Scale has been used in prior research to assess emotion dysregulation in oncology populations [50].

Secondary Outcomes

The PROMIS–computer [51,52] adaptive tests for the Anxiety and Depression scales will be used to measure symptom changes. The computer-adaptive test algorithm requires a minimum of 4 items and a maximum of 12, and the test stops when the SE is less than 0.30 [51]. The scales present the statement “over the past 7 days...” followed by items, such as “I felt uneasy” (PROMIS Anxiety) and “I felt helpless” (PROMIS Depression). Each item response is rated on a 5-point Likert-type frequency scale, ranging from 1 (“Never”) to 5 (“Always”). Raw scores for each item are summed and converted into a *T* score (population mean 50, SD 10). Higher scores indicate greater depressive or anxiety symptoms (T<65 = normal-to-mild; T≥65 = moderate to severe symptoms [53]).

The PROMIS QoL Health Utility Score [54] will be calculated using preference-based weights in PROMIS−29+2 Profile (version 2.1) [55] based on computer-adaptive testing to assess QoL. The QoL outcome score is a composite of the following seven domains captured by PROMIS: physical function, pain interference, cognitive function, depression, fatigue, sleep disturbance, and the ability to participate in social roles and activities. The QoL score ranges from −0.022 (“Dead”) to 1.0 (“Full health”) and has achieved good construct validity when measured against the Health Utility Index and the EQ-5D [56].

Module-Specific Target Outcomes

All the module-specific target outcomes and their respective modules are listed in Table 1. The Beliefs About Emotions Scale [39] will be used to assess negative beliefs about emotions and the impact of CM’s module 1. The Southampton Mindfulness Questionnaire [40] will be used to assess mindfulness and the impact of CM’s module 2. The Unified Protocol–Cognitive Skills Questionnaire [32] will be used to assess cognitive reappraisal skills and the impact of CM’s module 3. In addition, the Cognitive Emotional Regulation Questionnaire [41] “Catastrophizing” and “Refocus on Planning” subscales will also be used to assess the impact of CM’s module 3. The Multidimensional Experiential Avoidance Questionnaire-30 [42] will be used to assess levels of emotional (experiential) avoidance and to assess the impact of CM’s module 4.

Intervention Evaluation Outcomes

The Credibility Expectancy Questionnaire [57] will be administered to assess the perceived credibility and expectancy of CM versus CL before commencing the intervention. The Client Satisfaction Questionnaire [58] will be used to assess the participants’ level of satisfaction with CM and CL. Questions will assess factors such as whether the intervention has met participants’ needs and whether participants would return to the service. Higher scores indicate greater satisfaction. With regard to evaluation of treatment fidelity and reliability, because both interventions are delivered in a standardized way via the internet, no additional measures of treatment fidelity or reliability are collected. With regard to adherence, for CM, adherence is measured objectively via the number of completed application activities on the web per module. For CL, adherence is measured via self-reports of whether participants indicate that they have applied the intervention content to their lives that week in the weekly web-based activities.

Other Measures

The Depression Risk Questionnaire-7 [59] is a brief self-reported questionnaire developed as a clinical screening tool for patients with breast cancer at risk of depression. The Positive Affect Subscale from the Positive and Negative Affect Scales [60] will be used to assess positive emotional states (eg, attentiveness, enthusiasm, pride, and interest). Two items assessing (1) impact and (2) distress caused by COVID-19 will be administered, with participants’ self-reported responses indicated on a sliding scale from 0 to 100 (0=no distress or no impact, 100=a lot of distress or a lot of impact).

Participant Compensation

All eligible participants who complete the baseline assessment as well as at least 2 modules and their respective postintervention assessments (ie, half of an intervention, T_1 and T_2) are provided with an e-gift card worth equivalent to Aus $40 (US $30) in their local currency as a token of appreciation. This compensation is provided at the end of their participation.

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Statistical Analysis Plan

Power Analysis

The primary end point for the trial is the immediate postintervention assessment (T_4). As all primary and secondary outcomes are continuous, the primary analyses will be linear regressions with group as a predictor and outcome scores at baseline included as a covariate. We set the type 1 error at Cronbach α=.05 (2-tailed). A Monte Carlo simulation study was conducted to determine the power analysis and required sample size. In the simulation, we varied (1) the correlation between baseline and postintervention outcome scores (*r*) across four values (0.3, 0.4, 0.5, and 0.6) selected from the literature and our pilot research [18] and (2) the standardized mean difference (SMD) between the CM and CL groups at post intervention on outcome scores (primary end point) across 2 values (SMDs of 0.5 and 0.6). The SMDs were selected based on our pilot work [18] where we observed SMDs from before to after the intervention of approximately 0.5 to 1.0 for our primary and secondary outcomes. Our pilot did not include a control group (likely inflating the SMDs) but only tested individual modules separately (likely reducing the SMDs); therefore, we believe that a moderate SMD was reasonable, on average. The code for this Monte Carlo study is publicly available [61]. Results from 10,000 Monte Carlo simulations for each of the conditions and varying sample sizes showed that participants (n=100) with complete data at T_4 will provide more than 80% power to detect a medium (SMD=0.5) group difference—after the intervention, even with only a moderate correlation (*r*=0.3) between baseline and postintervention outcome scores with Cronbach α=.05.

Data Cleaning and Sample Characteristics

Analyses will be conducted in R on an intention-to-treat basis with statistical significance set at Cronbach α=.05 for type 1 error. The tests for primary and secondary outcomes will be 2-sided. The data will be assessed for outliers. If outliers are present, we will use quantile regression to calculate a median estimate or evaluate removing or winsorizing outliers.

Primary Aim

Missing data are ubiquitous in research, and dropout and incomplete data (eg, dropout) are particularly common in web-only trials [62]. For aim 1 analyses, we will address missing data using multiple imputation with a fully conditional specification [63] and predictive mean matching [64]. A total of 20 imputed data sets will be generated. The primary outcome of the trial is the Difficulties in Emotion Regulation Scale (DERS-SF). The primary end point is immediately after the intervention, immediately following module 4 (T_4). Anxiety and depression symptoms as well as overall QoL are secondary outcomes. All outcomes are continuous measures.

The primary analyses will consist of linear regressions on multiple imputed data. Each outcome variable at the primary end point (T_4) will be included as the outcome variable in a linear regression, with group as the main predictor and the outcome variable at baseline (T_0) and stratification factors included as covariates. Adjusted means in each group, as well as the adjusted mean difference, will be calculated. In the event of outliers, quantile regression will be used in place of linear regression and adjusted median differences at the primary end point (T_4), and as exploratory analyses, the other time points will be estimated. Following recent research suggestions [65], we chose to provide randomization-based inferences; that is, statistical significance will be based on Fisher exact *P* values [66] from 100,000 permutations for the adjusted mean differences and uncertainty intervals will be based on 95% Fisher intervals. The sharp null hypothesis tested will be that being randomized to CM has an identical effect on participants' outcomes as being randomized to CL.

Given the conceptual overlap between stratification factors and the outcome measured at baseline, only the stratification factors for anxiety and depression will be included in the linear regression assessment of the primary outcome (DERS-SF). For the linear regression assessment of depression and anxiety symptoms, only the DERS-SF stratification factor will be included. For the linear regression assessing QoL, both stratification factors will be included.

In addition to testing for group differences at the primary end point (T_4), we will explore group differences at T_1, T_2, T_3, and T_5 on the primary and secondary outcomes. The overall sample mean at T_0 will be presented for comparison.

The adjusted SMDs will be calculated as the adjusted group mean difference (CM–CL) divided by the residual SD estimated from the model. In the case of outliers, standardized median difference will be calculated. By using the residual adjusted for baseline outcome scores, this is effectively an effect size on the difference scores or for repeated measures [67].

Secondary Aims

The same analyses, significance tests, sharp null hypothesis, and result reporting described for the primary aim will be used to assess aim 2, the effect of CM versus CL on module-specific target outcomes. The model-specific target outcomes are presented in Table 1. Using regressions (linear if no outliers and quantile if outliers), adjusted differences between CM and CL in module-specific outcome scores will be assessed after each module and at the intervention end point (T_4) adjusted for the score before completing the module.

If intervention effects are observed on the DERS-SF, aim 3 will involve conducting mediation analyses to assess whether greater improvements on the DERS-SF (primary outcome), in the CM versus CL condition, mediate the effects of CM versus CL on anxiety and depression symptoms (secondary outcomes).

Sensitivity Analyses

Planned sensitivity analyses will include (1) calculating parametric and asymptotic *P* values and CIs, (2) generalized additive models to examine whether results differ when allowing nonlinear associations between baseline and postintervention symptoms, (3) per-protocol analyses based only on participants who completed all core intervention components, and (4) assessing group differences in intervention duration and the impact of intervention completion time on outcomes.

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Ethics Approval and Adverse Events

This study received ethics approval from the Human Research Ethics Committee at Monash University (ethics ID number: 25825). Any protocol modifications will be communicated to the Human Research Ethics Committee and participants. The primary investigator will make safety and progress reports to the ethics committee at least annually and within 3 months of study completion. Adverse events will be tracked in the following ways: (1) a >10-point worsening (at any time point compared with the previous time points) in PROMIS T scores on the anxiety or depressive symptom outcomes; (2) two questions administered at both T_2 and T_4 to assess the side effects due to the intervention and negative experiences, such as inappropriateness or unhelpfulness of the intervention; and (3) monitoring for any unsolicited reports of adverse events or serious adverse events (eg, mental health–related hospital admissions). In the consent form, participants are informed that the survey questions, including PROMIS anxiety and depressive symptom surveys, ask sensitive information and may be confronting, triggering temporary elevations in distress for some individuals. If this occurs, all participants are provided with relevant mental health support numbers to contact, and they could report this to the researchers.

Results

Recruitment for this trial began in September 2020 and all follow-up data were collected in April 2022. A total of 224 patients were randomized to the CM (n=110, 49.1%) and CL (n=114, 50.9%) groups. In total, 61 CM participants and 75 CL participants have completed the intervention and postintervention assessment surveys.

Discussion

This manuscript outlines the protocol for a novel randomized controlled trial evaluating the efficacy of a multicomponent, emotion-focused, internet-delivered intervention (CM) compared with an active comparator intervention (CL) in improving emotion regulation, symptoms of anxiety and depression, and QoL in cancer survivors. The findings from this trial will extend previous pilot results, which suggested that each CM module may be independently effective in improving cancer survivors' mental health and emotion regulation [18].

Limitations

The results of this trial will be interpreted in the context of its limitations. For instance, as the treatment group's effects will not be compared against the absence of any intervention (eg, wait-list control), we will not be able to assess whether improvements in either group are due to the actual interventions or a result of naturalistic tendencies (eg, natural improvement in mental health symptoms over time). In addition, the intervention intensity and thus the potential duration of CM and CL differ. Unlike in CL, CM includes mandatory core activities in each module, which must be completed before participants can progress to the subsequent modules. This means that CM participants are likely to take longer to complete the intervention, which could impact the outcomes and attrition rates. Finally, CM and CL are English language–based interventions, and the trial excludes those who cannot read or write in English, which may limit the generalizability of findings to English-speaking populations only.

Strengths and Significance

Despite these limitations, this is the first randomized controlled trial to evaluate an emotion-focused, UP-adapted, and internet-delivered intervention designed for cancer survivors to improve their mental health and QoL. Considering (1) that most of those diagnosed with cancer survive their diagnosis [68], (2) that cancer survivors experience elevated symptoms of psychological distress and lower QoL [1,36], and (3) that cancer survivors may face economic and geographic barriers to accessing mental health support [21,23,69], the development of web-based and affordable interventions that are highly accessible is paramount. Finally, as CM is internet-guided, it is also expected to have a low therapist burden and is considered highly scalable.

Another strength of this study relates to its unique study design. The trial will allow not only an assessment of symptom improvement but also an evaluation of factors that account for symptom changes. Specifically, by concurrently measuring emotion regulation and psychopathological symptoms at all time points, the design will enable the assessment of more nuanced relationship patterns between these closely linked variables. Thus far, few studies assessing applications of the UP have been able to clearly decipher whether improvements in emotion dysregulation are truly mediating symptom improvements.

Furthermore, the study will allow a detailed assessment and comparison of each module's effects in the treatment versus control conditions. This mechanistic analysis allows for greater treatment optimization. For example, if the target outcome of one module is found to contribute minimally compared with the other modules, then theoretically, the less effective module may be removed or decreased in intensity to reduce intervention duration and improve treatment efficiency.

In addition, the CL intervention material may prove to be a rather formidable control comparator. This is because lifestyle factors, such as diet [70], exercise [71], relaxation [72], and sleep [73], are highly correlated with mental health outcomes. Therefore, if CM is more efficacious than CL in improving emotion regulation and anxiety and depressive symptoms, such findings will speak to the strength and magnitude of the effects of CM.

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Data Availability

Deidentified data for this trial will be made available once collected and analyzed within 7 years of the final publication and shared on Monash University's web-base [74]. Data sharing is not applicable to this protocol paper, as no data sets were generated or analyzed.

Conflicts of Interest

None declared.

Multimedia Appendix 1
Supplementary materials including visual snapshots of intervention activities.
[PDF File (Adobe PDF File), 6922 KB - resprot_v11i7e36658_app1.pdf]

References

1. Carreira H, Williams R, Müller M, Harewood R, Stanway S, Bhaskaran K. Associations between breast cancer survivorship and adverse mental health outcomes: a systematic review. J Natl Cancer Inst 2018 Dec 01;110(12):1311-1327 [FREE Full text] [doi: 10.1093/jnci/djy177] [Medline: 30403799]
2. Linden W, Vodermaier A, Mackenzie R, Greig D. Anxiety and depression after cancer diagnosis: prevalence rates by cancer type, gender, and age. J Affect Disord 2012 Dec 10;141(2-3):343-351. [doi: 10.1016/j.jad.2012.03.025] [Medline: 22727334]
3. van Stam MA, van der Poel HG, Bosch JL, Tillier CN, Horenblas S, Mols F, et al. Prevalence and correlates of mental health problems in prostate cancer survivors: a case-control study comparing survivors with general population peers. Urol Oncol 2017 Aug;35(8):531.e1-531.e7. [doi: 10.1016/j.urolonc.2017.03.028] [Medline: 28457651]
4. Lu D, Andersson TM, Fall K, Hultman CM, Czene K, Valdimarsdóttir U, et al. Clinical diagnosis of mental disorders immediately before and after cancer diagnosis: a nationwide matched cohort study in Sweden. JAMA Oncol 2016 Sep 01;2(9):1188-1196. [doi: 10.1001/jamaoncol.2016.0483] [Medline: 27124325]
5. Gross JJ. Emotion regulation: past, present, future. Cogn Emotion 1999 Sep;13(5):551-573. [doi: 10.1080/026999399379186]
6. Kring AM, Sloan DM. Emotion Regulation and Psychopathology: A Transdiagnostic Approach to Etiology and Treatment. New York, NY, USA: The Guilford Press; 2010.
7. Sloan E, Hall K, Moulding R, Bryce S, Mildred H, Staiger PK. Emotion regulation as a transdiagnostic treatment construct across anxiety, depression, substance, eating and borderline personality disorders: a systematic review. Clin Psychol Rev 2017 Nov;57:141-163. [doi: 10.1016/j.cpr.2017.09.002] [Medline: 28941927]
8. Kangas M, Gross JJ. The affect regulation in cancer framework: understanding affective responding across the cancer trajectory. J Health Psychol 2020 Jan;25(1):7-25. [doi: 10.1177/1359105317748468] [Medline: 29260595]
9. Moreno PI, Wiley JF, Stanton AL. Coping through emotional approach: the utility of processing and expressing emotions in response to stress. In: Snyder CR, Lopez SJ, Edwards LM, Marques SC, editors. The Oxford Handbook of Positive Psychology. 3rd edition. Oxford, UK: Oxford University Press; 2017. [doi: 10.1093/oxfordhb/9780199396511.013.19]
10. Troy A, Mauss I. Resilience in the face of stress: emotion regulation as a protective factor. In: Southwick S, Litz B, Charney D, Friedman M, editors. Resilience and Mental Health: Challenges Across the Lifespan. Cambridge, MA, USA: Cambridge University Press; 2011:30-44.
11. Hoyt MA, Nelson CJ, Darabos K, Marín-Chollom A, Stanton AL. Mechanisms of navigating goals after testicular cancer: meaning and emotion regulation. Psychooncology 2017 Jun;26(6):747-754 [FREE Full text] [doi: 10.1002/pon.4068] [Medline: 26765203]
12. Kvillemo P, Bränström R. Coping with breast cancer: a meta-analysis. PLoS One 2014 Nov 25;9(11):e112733 [FREE Full text] [doi: 10.1371/journal.pone.0112733] [Medline: 25423095]
13. Lee J, Youn S, Kim C, Yeo S, Chung S. The influence of sleep disturbance and cognitive emotion regulation strategies on depressive symptoms in breast cancer patients. Sleep Med Res 2019 Jun;10(1):36-42. [doi: 10.17241/smr.2019.00388]
14. Stanton AL, Wiley JF, Krull JL, Crespi CM, Hammen C, Allen JJ, et al. Depressive episodes, symptoms, and trajectories in women recently diagnosed with breast cancer. Breast Cancer Res Treat 2015 Nov;154(1):105-115 [FREE Full text] [doi: 10.1007/s10549-015-3563-4] [Medline: 26420401]
15. Barlow DH, Farchione TJ, Sauer-Zavala S, Murray-Latin H, Ellard KK, Bullis JR, et al. Unified Protocol for Transdiagnostic Treatment of Emotional Disorders: Therapist Guide. 2nd edition. Oxford, UK: Oxford University Press; 2018.
16. Sakiris N, Berle D. A systematic review and meta-analysis of the Unified Protocol as a transdiagnostic emotion regulation based intervention. Clin Psychol Rev 2019 Aug;72:101751. [doi: 10.1016/j.cpr.2019.101751] [Medline: 31271848]

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17. Weihs KL, McConnell MH, Wiley JF, Crespi CM, Sauer-Zavala S, Stanton AL. A preventive intervention to modify depression risk targets after breast cancer diagnosis: design and single-arm pilot study. Psychooncology 2019 Apr;28(4):880-887 [FREE Full text] [doi: 10.1002/pon.5037] [Medline: 30803095]
18. Smith IS, Wellecke C, Weihs KL, Bei B, Wiley JF. Piloting CanCope: an Internet-delivered transdiagnostic intervention to improve mental health in cancer survivors. Psychooncology 2022 Jan;31(1):107-115. [doi: 10.1002/pon.5787] [Medline: 34425036]
19. Fallowfield L, Jenkins V. Psychosocial/survivorship issues in breast cancer: are we doing better? J Natl Cancer Inst 2014 Nov 27;107(1):335. [doi: 10.1093/jnci/dju335] [Medline: 25432407]
20. Harrington CB, Hansen JA, Moskowitz M, Todd BL, Feuerstein M. It's not over when it's over: long-term symptoms in cancer survivors--a systematic review. Int J Psychiatry Med 2010;40(2):163-181. [doi: 10.2190/PM.40.2.c] [Medline: 20848873]
21. Jong KE, Vale PJ, Armstrong BK. Rural inequalities in cancer care and outcome. Med J Aust 2005 Jan 03;182(1):13-14. [doi: 10.5694/j.1326-5377.2005.tb06546.x] [Medline: 15651940]
22. Ness S, Kokal J, Fee-Schroeder K, Novotny P, Satele D, Barton D. Concerns across the survivorship trajectory: results from a survey of cancer survivors. Oncol Nurs Forum 2013 Jan;40(1):35-42. [doi: 10.1188/13.ONF.35-42] [Medline: 23269768]
23. Sharp L, Carsin AE, Timmons A. Associations between cancer-related financial stress and strain and psychological well-being among individuals living with cancer. Psychooncology 2013 Apr;22(4):745-755. [doi: 10.1002/pon.3055] [Medline: 22411485]
24. Edge R, Mazariego C, Li Z, Canfell K, Miller A, Koczwara B, et al. Psychosocial impact of COVID-19 on cancer patients, survivors, and carers in Australia: a real-time assessment of cancer support services. Support Care Cancer 2021 Sep;29(9):5463-5473 [FREE Full text] [doi: 10.1007/s00520-021-06101-3] [Medline: 33694089]
25. Faller H, Schuler M, Richard M, Heckl U, Weis J, Küffner R. Effects of psycho-oncologic interventions on emotional distress and quality of life in adult patients with cancer: systematic review and meta-analysis. J Clin Oncol 2013 Feb 20;31(6):782-793. [doi: 10.1200/JCO.2011.40.8922] [Medline: 23319686]
26. Murphy MJ, Newby JM, Butow P, Kirsten L, Allison K, Loughnan S, et al. iCanADAPT Early protocol: randomised controlled trial (RCT) of clinician supervised transdiagnostic internet-delivered cognitive behaviour therapy (iCBT) for depression and/or anxiety in early stage cancer survivors -vs- treatment as usual. BMC Cancer 2017 Mar 15;17(1):193 [FREE Full text] [doi: 10.1186/s12885-017-3182-z] [Medline: 28298187]
27. Newby TA, Graff JN, Ganzini LK, McDonagh MS. Interventions that may reduce depressive symptoms among prostate cancer patients: a systematic review and meta-analysis. Psychooncology 2015 Dec;24(12):1686-1693. [doi: 10.1002/pon.3781] [Medline: 25753507]
28. Lemmens LH, Müller VN, Arntz A, Huibers MJ. Mechanisms of change in psychotherapy for depression: an empirical update and evaluation of research aimed at identifying psychological mediators. Clin Psychol Rev 2016 Dec;50:95-107. [doi: 10.1016/j.cpr.2016.09.004] [Medline: 27770716]
29. Windgassen S, Goldsmith K, Moss-Morris R, Chalder T. Establishing how psychological therapies work: the importance of mediation analysis. J Ment Health 2016;25(2):93-99. [doi: 10.3109/09638237.2015.1124400] [Medline: 26732531]
30. Cuijpers P, Cristea IA, Karyotaki E, Reijnders M, Hollon SD. Component studies of psychological treatments of adult depression: a systematic review and meta-analysis. Psychother Res 2019 Jan;29(1):15-29. [doi: 10.1080/10503307.2017.1395922] [Medline: 29115185]
31. Stanton AL, Luecken LJ, MacKinnon DP, Thompson EH. Mechanisms in psychosocial interventions for adults living with cancer: opportunity for integration of theory, research, and practice. J Consult Clin Psychol 2013 Apr;81(2):318-335. [doi: 10.1037/a0028833] [Medline: 22663900]
32. Sauer-Zavala S, Cassiello-Robbins C, Conklin LR, Bullis JR, Thompson-Hollands J, Kennedy KA. Isolating the unique effects of the Unified Protocol treatment modules using single case experimental design. Behav Modif 2017 Mar;41(2):286-307. [doi: 10.1177/0145445516673827] [Medline: 28198196]
33. Maia AC, Braga AA, Nunes CA, Nardi AE, Silva AC. Transdiagnostic treatment using a unified protocol: application for patients with a range of comorbid mood and anxiety disorders. Trends Psychiatry Psychother 2013;35(2):134-140 [FREE Full text] [doi: 10.1590/s2237-60892013000200007] [Medline: 25923304]
34. de Ornelas Maia AC, Sanford J, Boettcher H, Nardi AE, Barlow D. Improvement in quality of life and sexual functioning in a comorbid sample after the unified protocol transdiagnostic group treatment. J Psychiatr Res 2017 Oct;93:30-36. [doi: 10.1016/j.jpsychires.2017.05.013] [Medline: 28575646]
35. Gallagher MW, Sauer-Zavala SE, Boswell JF, Carl JR, Bullis J, Farchione TJ, et al. The impact of the Unified Protocol for emotional disorders on quality of life. Int J Cogn Ther 2013 Mar 01;6(1):57-72 [FREE Full text] [doi: 10.1521/ijct.2013.6.1.57] [Medline: 24358405]
36. Jefford M, Ward AC, Lisy K, Lacey K, Emery JD, Glaser AW, et al. Patient-reported outcomes in cancer survivors: a population-wide cross-sectional study. Support Care Cancer 2017 Oct;25(10):3171-3179. [doi: 10.1007/s00520-017-3725-5] [Medline: 28434095]

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37. Conley CC, Bishop BT, Andersen BL. Emotions and emotion regulation in breast cancer survivorship. Healthcare (Basel) 2016 Aug 10;4(3):56 [FREE Full text] [doi: 10.3390/healthcare4030056] [Medline: 27517969]
38. Brandão T, Tavares R, Schulz MS, Matos PM. Measuring emotion regulation and emotional expression in breast cancer patients: a systematic review. Clin Psychol Rev 2016 Feb;43:114-127. [doi: 10.1016/j.cpr.2015.10.002] [Medline: 26520599]
39. Rimes KA, Chalder T. The Beliefs about Emotions Scale: validity, reliability and sensitivity to change. J Psychosom Res 2010 Mar;68(3):285-292. [doi: 10.1016/j.jpsychores.2009.09.014] [Medline: 20159215]
40. Chadwick P, Hember M, Symes J, Peters E, Kuipers E, Dagnan D. Responding mindfully to unpleasant thoughts and images: reliability and validity of the Southampton mindfulness questionnaire (SMQ). Br J Clin Psychol 2008 Nov;47(Pt 4):451-455. [doi: 10.1348/014466508X314891] [Medline: 18573227]
41. Garnefski N, Kraaij V. The Cognitive Emotion Regulation Questionnaire: psychometric features and prospective relationships with depression and anxiety in adults. Eur J Psychol Assess 2007 Jan;23(3):141-149. [doi: 10.1027/1015-5759.23.3.141]
42. Sahdra BK, Ciarrochi J, Parker P, Scrucca L. Using genetic algorithms in a large nationally representative American sample to abbreviate the Multidimensional Experiential Avoidance Questionnaire. Front Psychol 2016 Feb 24;7:189 [FREE Full text] [doi: 10.3389/fpsyg.2016.00189] [Medline: 26941672]
43. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)--a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform 2009 Apr;42(2):377-381 [FREE Full text] [doi: 10.1016/j.jbi.2008.08.010] [Medline: 18929686]
44. Harris KR, Norton PJ. Transdiagnostic cognitive behavioral therapy for the treatment of emotional disorders: a preliminary open trial. J Behav Ther Exp Psychiatry 2019 Dec;65:101487. [doi: 10.1016/j.jbtep.2019.101487] [Medline: 31132511]
45. Sheehan D, Lecrubier Y, Harnett Sheehan K, Janavs J, Weiller E, Keskiner A, et al. The validity of the Mini International Neuropsychiatric Interview (MINI) according to the SCID-P and its reliability. Eur Psychiatr 1997;12(5):232-241. [doi: 10.1016/s0924-9338(97)83297-x]
46. Freedland KE, King AC, Ambrosius WT, Mayo-Wilson E, Mohr DC, Czajkowski SM, National Institutes of Health Office of Behavioral and Social Sciences Research Expert Panel on Comparator Selection in Behavioral and Social Science Clinical Trials. The selection of comparators for randomized controlled trials of health-related behavioral interventions: recommendations of an NIH expert panel. J Clin Epidemiol 2019 Jun;110:74-81 [FREE Full text] [doi: 10.1016/j.jclinepi.2019.02.011] [Medline: 30826377]
47. Kaufman EA, Xia M, Fosco G, Yaptangco M, Skidmore CR, Crowell SE. The Difficulties in Emotion Regulation Scale Short Form (DERS-SF): validation and replication in adolescent and adult samples. J Psychopathol Behav Assess 2015 Nov 23;38(3):443-455. [doi: 10.1007/s10862-015-9529-3]
48. Hallion LS, Steinman SA, Tolin DF, Diefenbach GJ. Psychometric properties of the Difficulties in Emotion Regulation Scale (DERS) and its short forms in adults with emotional disorders. Front Psychol 2018 Apr 19;9:539 [FREE Full text] [doi: 10.3389/fpsyg.2018.00539] [Medline: 29725312]
49. Skutch JM, Wang SB, Buqo T, Haynos AF, Papa A. Which brief is best? Clarifying the use of three brief versions of the difficulties in emotion regulation scale. J Psychopathol Behav Assess 2019 Sep 15;41(3):485-494 [FREE Full text] [doi: 10.1007/s10862-019-09736-z] [Medline: 34446987]
50. Vaughan E, Koczwara B, Kemp E, Freytag C, Tan W, Beatty L. Exploring emotion regulation as a mediator of the relationship between resilience and distress in cancer. Psychooncology 2019 Jul;28(7):1506-1512. [doi: 10.1002/pon.5107] [Medline: 31087804]
51. Pilkonis PA, Yu L, Dodds NE, Johnston KL, Maihoefer CC, Lawrence SM. Validation of the depression item bank from the Patient-Reported Outcomes Measurement Information System (PROMIS) in a three-month observational study. J Psychiatr Res 2014 Sep;56:112-119 [FREE Full text] [doi: 10.1016/j.jpsychires.2014.05.010] [Medline: 24931848]
52. Pilkonis PA, Choi SW, Reise SP, Stover AM, Riley WT, Cella D, PROMIS Cooperative Group. Item banks for measuring emotional distress from the Patient-Reported Outcomes Measurement Information System (PROMIS®): depression, anxiety, and anger. Assessment 2011 Sep;18(3):263-283 [FREE Full text] [doi: 10.1177/1073191111411667] [Medline: 21697139]
53. Cella D, Choi S, Garcia S, Cook KF, Rosenbloom S, Lai JS, et al. Setting standards for severity of common symptoms in oncology using the PROMIS item banks and expert judgment. Qual Life Res 2014 Dec;23(10):2651-2661 [FREE Full text] [doi: 10.1007/s11136-014-0732-6] [Medline: 24938431]
54. Dewitt B, Feeny D, Fischhoff B, Cella D, Hays RD, Hess R, et al. Estimation of a preference-based summary score for the patient-reported outcomes measurement information system: the PROMIS-preference (PROPr) scoring system. Med Decis Making 2018 Aug;38(6):683-698 [FREE Full text] [doi: 10.1177/0272989X18776637] [Medline: 29944456]
55. Hays RD, Spritzer KL, Schalet BD, Cella D. PROMIS-29 v2.0 profile physical and mental health summary scores. Qual Life Res 2018 Jul;27(7):1885-1891 [FREE Full text] [doi: 10.1007/s11136-018-1842-3] [Medline: 29569016]
56. Hanmer J, Dewitt B, Yu L, Tsevat J, Roberts M, Revicki D, et al. Cross-sectional validation of the PROMIS-Preference scoring system. PLoS One 2018 Jul 31;13(7):e0201093 [FREE Full text] [doi: 10.1371/journal.pone.0201093] [Medline: 30063733]
57. Devilly GJ, Borkovec TD. Psychometric properties of the credibility/expectancy questionnaire. J Behav Ther Exp Psychiatry 2000 Jun;31(2):73-86. [doi: 10.1016/s0005-7916(00)00012-4] [Medline: 11132119]

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58. Larsen DL, Attkisson C, Hargreaves WA, Nguyen TD. Assessment of client/patient satisfaction: development of a general scale. Eval Program Plann 1979;2(3):197-207. [doi: 10.1016/0149-7189(79)90094-6] [Medline: 10245370]
59. Weihs KL, Wiley JF, Crespi CM, Krull JL, Stanton AL. Predicting future major depression and persistent depressive symptoms: development of a prognostic screener and PHQ-4 cutoffs in breast cancer patients. Psychooncology 2018 Feb;27(2):420-426 [FREE Full text] [doi: 10.1002/pon.4472] [Medline: 28600855]
60. Watson D, Clark LA, Tellegen A. Development and validation of brief measures of positive and negative affect: the PANAS scales. J Pers Soc Psychol 1988 Jun;54(6):1063-1070. [doi: 10.1037//0022-3514.54.6.1063] [Medline: 3397865]
61. Wiley JF. Public Planning Repository for CanCope RCT. Behavioural Medicine Lab. 2020 Aug 5. URL: https://github.com/behavioralmedicinelab/CanCope_RCTPlanning [accessed 2022-07-08]
62. Karyotaki E, Kleiboer A, Smit F, Turner DT, Pastor AM, Andersson G, et al. Predictors of treatment dropout in self-guided Web-based interventions for depression: an 'individual patient data' meta-analysis. Psychol Med 2015 Oct;45(13):2717-2726. [doi: 10.1017/S0033291715000665] [Medline: 25881626]
63. van Buuren S. Multiple imputation of discrete and continuous data by fully conditional specification. Stat Methods Med Res 2007 Jun;16(3):219-242. [doi: 10.1177/0962280206074463] [Medline: 17621469]
64. van Buuren S. Flexible Imputation of Missing Data. 2nd edition. Boca Raton, FL, USA: CRC Press; 2018.
65. Bind MC, Rubin DB. When possible, report a Fisher-exact P value and display its underlying null randomization distribution. Proc Natl Acad Sci U S A 2020 Aug 11;117(32):19151-19158 [FREE Full text] [doi: 10.1073/pnas.1915454117] [Medline: 32703808]
66. Imbens GW, Rubin DB. Fisher's exact P-values for completely randomized experiments. In: Imbens GW, Rubin DB, editors. Causal Inference for Statistics, Social, and Biomedical Sciences: An Introduction. Cambridge, UK: Cambridge University Press; 2015:57-82. [doi: 10.1017/CBO9781139025751]
67. Lakens D. Calculating and reporting effect sizes to facilitate cumulative science: a practical primer for t-tests and ANOVAs. Front Psychol 2013 Nov 26;4:863 [FREE Full text] [doi: 10.3389/fpsyg.2013.00863] [Medline: 24324449]
68. Cancer data in Australia. Australian Institute of Health and Welfare, Australian Government. 2020 Jul 1. URL: https://www.aihw.gov.au/reports/cancer/cancer-data-in-australia/contents/cancer-survival-data-visualisation [accessed 2021-11-10]
69. Paul CL, Hall AE, Carey ML, Cameron EC, Clinton-McHarg T. Access to care and impacts of cancer on daily life: do they differ for metropolitan versus regional hematological cancer survivors? J Rural Health 2013 Aug;29 Suppl 1:s43-s50. [doi: 10.1111/jrh.12020] [Medline: 23944279]
70. Godos J, Currenti W, Angelino D, Mena P, Castellano S, Caraci F, et al. Diet and mental health: review of the recent updates on molecular mechanisms. Antioxidants (Basel) 2020 Apr 23;9(4):346 [FREE Full text] [doi: 10.3390/antiox9040346] [Medline: 32340112]
71. Mikkelsen K, Stojanovska L, Polenakovic M, Bosevski M, Apostolopoulos V. Exercise and mental health. Maturitas 2017 Dec;106:48-56. [doi: 10.1016/j.maturitas.2017.09.003] [Medline: 29150166]
72. Fung CN, White R. Systematic review of the effectiveness of relaxation training for depression. Int J Appl Psychol 2012 Apr 31;2(2):8-16. [doi: 10.5923/j.ijap.20120202.02]
73. Ratcliff CG, Zepeda SG, Hall MH, Tullos EA, Fowler S, Chaoul A, et al. Patient characteristics associated with sleep disturbance in breast cancer survivors. Support Care Cancer 2021 May;29(5):2601-2611 [FREE Full text] [doi: 10.1007/s00520-020-05777-3] [Medline: 32964261]
74. Monash University research repository: BRIDGES. Monash University. URL: https://bridges.monash.edu/ [accessed 2022-07-08]

Abbreviations

CL: CanCope Lifestyle
CM: CanCope Mind
DERS-SF: Difficulties With Emotion Regulation Scale–Short Form
EDB: emotion-driven behavior
MINI: Mini International Neuropsychiatric Interview
PROMIS: Patient-Reported Outcomes Measurement Information System
QoL: quality of life
REDCap: Research Electronic Data Capture
SMD: standardized mean difference
UP: Unified Protocol

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Protocol

Utilizing Technology for Diet and Exercise Change in Complex Chronic Conditions Across Diverse Environments (U-DECIDE): Protocol for a Randomized Controlled Trial

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Abstract

Background: The metabolic syndrome is common across many complex chronic disease groups. Advances in health technology have provided opportunities to support lifestyle interventions.

Objective: The purpose of this study is to test the feasibility of a health technology-assisted lifestyle intervention in a patient-led model of care.

Methods: The study is a single-center, 26-week, randomized controlled trial. The setting is specialist kidney and liver disease clinics at a large Australian tertiary hospital. The participants will be adults with a complex chronic condition who are referred for dietetic assessment and display at least one feature of the metabolic syndrome. All participants will receive an individualized assessment and advice on diet quality from a dietitian, a wearable activity monitor, and standard care. Participants randomized to the intervention group will receive access to a suite of health technologies from which to choose, including common base components (text messages) and optional components (online and mobile app–based nutrition information, an online home exercise program, and group-based videoconferencing). Exposure to the optional aspects of the intervention will be patient-led, with participants choosing their preferred level of engagement. The primary outcome will be the feasibility of delivering the program, determined by safety, recruitment rate, retention, exposure uptake, and telehealth adherence. Secondary outcomes will be clinical effectiveness, patient-led goal attainment, treatment fidelity, exposure demand, and participant perceptions. Primary outcome data will be assessed descriptively and secondary outcomes will be assessed using an analysis of covariance. This study

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will provide evidence on the feasibility of the intervention in a tertiary setting for patients with complex chronic disease exhibiting features of the metabolic syndrome.

Results: The study was funded in 2019. Enrollment has commenced and is expected to be completed by June 2022. Data collection and follow up are expected to be completed by December 2022. Results from the analyses based on primary outcomes are expected to be submitted for publication by June 2023.

Conclusions: The study will test the implementation of a health technology–assisted lifestyle intervention in a tertiary outpatient setting for a diverse group of patients with complex chronic conditions. It is novel in that it embeds patient choice into intervention exposure and will inform health service decision-makers in regards to the feasibility of scale and spread of technology-assisted access to care for a broader reach of specialist services.

Trial Registration: Australian New Zealand Clinical Trial Registry ACTRN12620001282976; https://www.anzctr.org.au/Trial/Registration/TrialReview.aspx?id=378337

International Registered Report Identifier (IRRID): DERR1-10.2196/37556

(JMIR Res Protoc 2022;11(7):e37556) doi:10.2196/37556

KEYWORDS

lifestyle intervention; telehealth service delivery; digital disruption; complex chronic disease; liver disease; kidney disease; transplant; metabolic syndrome; metabolism; diabetes; obesity; mobile health; health technology; chronic disease

Introduction

The metabolic syndrome (MetS) is a combination of clinical risk factors, including central obesity, hypertension, dyslipidemia, and hyperglycemia [1]. Presence of the MetS is associated with increased risk of cardiometabolic complications, including cardiovascular disease and type 2 diabetes [2]. On a global scale, the MetS represents a substantial treatment burden due to increased costs and medication expenditure, hospitalization, and utilization of outpatient services [3,4]. The prevalence of the MetS is up to 60% in tertiary health care settings among patients with complex chronic conditions, including kidney and liver disease [5-7].

Specific components of the MetS may warrant pharmacotherapy, but this should only occur on a background of lifestyle intervention with a focus on diet quality and exercise [8-11]. Previous diet and exercise interventions in people with chronic disease have shown a cardioprotective effect [12-18]. However, the implementation of community-based diet and exercise management programs for complex chronic diseases has traditionally been challenging. Patients with chronic kidney or liver disease often have multimorbidity, potentially further compounding metabolic risk [19,20]. Management has traditionally required contact with multiple specialist teams across a siloed system, creating a significant burden for patients and caregivers [17,21]. Diet and exercise services have traditionally been delivered in condition-specific specialist settings, often with insufficient resources to deliver adequate services to address the health issues [22-24]. An integrated approach for the delivery of exercise and diet interventions through a unified complex chronic disease model of care could support improvement of cardiometabolic risk in tertiary care across specialist groups.

Advances in health technology have provided new opportunities to assist lifestyle interventions and improve the management of the MetS [13,17]. Asynchronous (eg, online information and resources) and synchronous (eg, telehealth appointments with health professionals) technology interventions have emerged as viable options for delivery of health care. These have the potential to address current barriers to service delivery, particularly in rural areas, including continuity of care, availability of resources, and location of services [25]. A range of factors within complex tertiary care systems, including patient-related factors (eg, values, goals, motivations, skills, and knowledge), organizational-related factors (eg, culture, priorities, and structural systems), and external factors (eg, health care funding), must be considered when assessing the feasibility of disruptive service change [26]. Patient-led approaches allow for the patient's perspective to be considered when receiving health care [27]. These approaches ideally assist patients in individualizing their self-management plans through selecting which services they want to engage with and through what means.

This study will expand on the current literature by testing the implementation of a health technology–assisted lifestyle intervention for people with complex chronic disease. The primary aim will be to test the feasibility of this intervention, determined by safety, recruitment rate, retention, exposure uptake, and telehealth adherence. The secondary aims include assessing the clinical effectiveness of the intervention, (including metabolic syndrome severity, dietary quality, physical activity and sedentary behavior, exercise capacity, neuromuscular fitness, muscular pain, clinical parameters, quality of life, perceived confidence, fatigue, and sleep quality and quantity), patient-led goal attainment, treatment fidelity, exposure demand, and participant perceptions. We hypothesize that delivery of lifestyle interventions using health technology is feasible, can address the barriers to service delivery, and will demonstrate improved clinical outcomes over standard care.

Methods

Study Design and Setting

This is a single-center, 26-week, randomized controlled trial. The study is being conducted in a public hospital in a major metropolitan city in Queensland, Australia. The study design and flow are shown in Figure 1.

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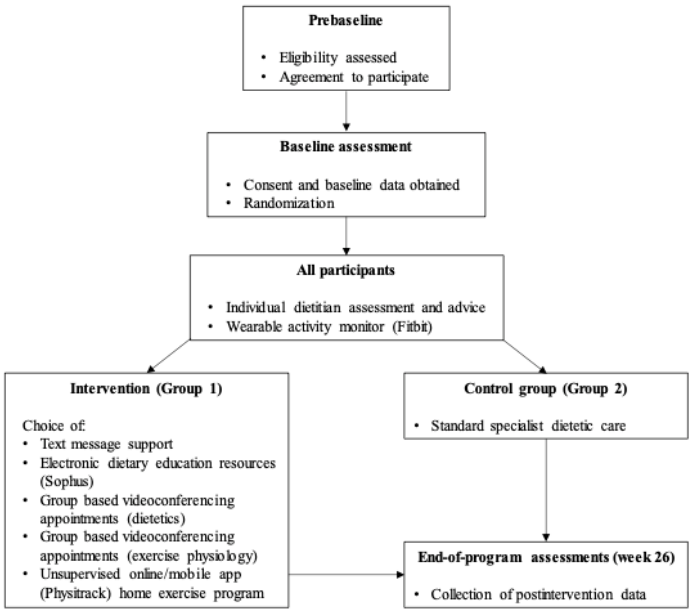
Figure 1. Study design and participant flow, indicating the base components offered to all participants and the additional technology-assisted components offered to the intervention group.



Participants and Eligibility Criteria

Adults living with kidney or liver disease who are at increased cardiometabolic risk and receiving specialist care at the Princess Alexandra Hospital in Brisbane, Australia, will be included. Eligibility criteria are shown in Textbox 1.

Textbox 1. Eligibility criteria.

Inclusion criteria

- Under the outpatient care of at least one of the following specialist Princess Alexandra Hospital clinics: kidney or liver transplant, chronic kidney disease, hemodialysis, peritoneal dialysis, or hepatology
- Have (or be undergoing treatment for) at least one of the features of the metabolic syndrome, as defined by the harmonized criteria [1]:
  - Elevated blood pressure (or on medication to treat) (systolic blood pressure ≥130 mm Hg and/or diastolic blood pressure ≥85 mm Hg)
  - Elevated waist circumference (population- and country-specific definitions [1])
  - Reduced high-density lipoprotein cholesterol (or on medication to treat) (<1.0 mmol/L in males; <1.3 mmol/L in females)
  - Elevated fasting blood glucose (or on medication to treat) (≥5.6 mmol/L)
  - Elevated triglycerides (or on medication to treat) (≥1.7 mmol/L)
- Deemed suitable to participate by treating medical specialist
- Screened as capable to participate by an exercise professional
- Have current access to a mobile device or computer hardware with internet access and webcam capability

Exclusion criteria

- Non–English speaking or unable to read and write in English
- Documented malnutrition
- Under 18 or over 80 years of age
- Currently pregnant or breastfeeding
- Life expectancy less than 6 months

Recruitment

The recruitment target will be 168 participants. Potentially eligible patients will be sourced via screening referrals to the dietetics department from a medical specialist. Referrals will be initially screened by the research project officer, and potentially eligible people will be contacted by phone to complete eligibility screening and be invited to participate. If a patient agrees to participate, a baseline appointment will be scheduled by the research project officer. Participant information and consent forms will be provided to patients via email prior to the baseline assessment, and written informed consent will

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be obtained at the baseline appointment. Age, sex, referring clinic, and inclusion and exclusion information for patients deemed ineligible or who decline to participate will be collected from electronic medical records. Ineligible patients will continue with the process of standard dietetic care as per usual practice guidelines. Demographic and medical data (Table 1) will be collected via online forms, review of medical charts, and phone calls prior to the baseline assessment. This is deemed a low-risk study, with expectations of behavior change no different from current usual care.

Randomization and Allocation

Participants will be randomized 1:1 to the intervention group (group 1) or to a control group (group 2) that will receive standard care and individualized dietetic advice to support improvements in diet quality [28]. Computer-generated randomization will be completed using the REDCap research management system [29]. Groups will be stratified by referral source: (1) chronic kidney disease clinic, (2) hepatology clinic, or (3) liver or kidney posttransplant clinic. Participants will be informed of their group allocation following baseline assessment by the research project officer.

Assessors and Blinding

Baseline assessments will occur prior to randomization. Assessors performing end-of-program clinical assessments will be blinded to group allocations. Assessor blinding will be verified by questionnaire at time of completion for each participant (Likert scale 1-5). This questionnaire will evaluate whether assessors have remained blinded to participant allocation. Participants will be reminded by the research project officer prior to end-of-program assessments to not disclose their group allocation to assessors.

Quantitative Data Collection

Baseline demographic and medical history data that will be collected are listed in Table 1. Research outcomes and the associated measurement methods are outlined in Table 2. Primary outcomes will be assessed once all participants have finished the trial, and secondary outcomes will be collected at baseline and end-of-program assessments. Once a participant is randomized, the research staff will make every reasonable effort (eg, via phone calls, text messages, and emails) to follow the participant for the entire study period for collection of data.

Table 1. Demographic and medical data collected prior to the baseline assessment.

Demographic and medical data	Measurements
Sex	Male or female
Date of birth	Date
Ethnicity	Caucasian, Indigenous, European, Anglo-Saxon, Asian, other, unknown/not reported
Marital status	Single or never married, living together, de facto or married, separated or divorced, widowed
Highest education level completed	Primary school, less than grade 10, grade 10, grade 12, vocational school or college, university
Employment status	Full-time, part-time, unemployed, self-employed, student, retired
Medication use	Listed medication intake including type, dose, and frequency
Menopause status	Yes, no, not applicable
Allergies	Yes, no, listed allergies
Cigarette smoking history	Former, current, never
Alcohol consumption	Number of standard drinks per week
Need for assistance to read written health materials[a]	Never, rarely, sometimes, often, always
eHealth literacy	eHealth Literacy Scale (eHEALS)[b] questionnaire [30]

[a]Assessed through the following question via online form: "How often do you need to have someone help you when you read instructions, pamphlets, or other written material from your doctor or pharmacy?"

[b]eHEALS is a validated 8-question digital health literacy questionnaire that evaluates the ability to find the right type of health information online, where and how to find and use it, possession of the skills and confidence to evaluate the quality of online health information, and the perception of the usefulness and importance of accessing online information for health [30]. This will be administered via an online form.

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Table 2. Primary and secondary outcomes and their associated measurements.

Outcomes	Measurements
Primary outcomes	
Safety	• Number of study-related serious adverse events
Recruitment rate	• Number of patients recruited as a proportion of all referred eligible patients
Retention	• Number of intervention participants undergoing end-of-program assessment
Exposure uptake	• Frequency of dietetic and exercise specialist contact (within public hospital system) as a proportion of total scheduled contacts
Telehealth adherence	• Attendance to online exercise and dietetic sessions as a proportion of total scheduled contacts
Secondary outcomes	
Clinical effectiveness	
Metabolic Syndrome Severity Score [31]	• Algorithm score comprising systolic blood pressure, diastolic blood pressure, waist circumference, triglycerides, high-density lipoprotein cholesterol, and fasting blood glucose
Dietary quality	• Diet quality assessed by food group intake (frequency per day or week), fiber intake (grams per day), unsaturated oils (grams per day), and discretionary food intake (grams per day)
Physical activity and sedentary behavior	• Time (intensity-weighted minutes) spent in past week as assessed by International Physical Activity Questionnaire (Short Form) and Fitbit weekly physical activity heart rate data
Exercise capacity	• 6-Minute Walk Test score
Neuromuscular fitness	• Single chair stand, Five Times Sit to Stand test, hand grip strength
Muscular pain	• Modified Nordic Musculoskeletal Questionnaire
Quality of life	• European Quality of Life Five Dimension Five Level Scale
Nutrition and physical activity management self-efficacy	• Likert confidence scales
Fatigue	• Functional Assessment of Chronic Illness Fatigue Scale score
Sleep quality and quantity	• Pittsburgh Sleep Quality Index score, total Fitbit weekly sleep data
Additional clinical parameters	• Resting heart rate, BMI, serum biochemical analytes (Multimedia Appendix 1)
Goal attainment	• Goal Attainment Scale score
Treatment fidelity	• Treatment notes[a] • Staff attendance at professional support and case discussions
Exposure demand	• Selection of health technology options
Participant perceptions	• Feedback survey • Qualitative individual interview data (subsample)

[a]Participant session notes taken by health professionals from telehealth-facilitated sessions with the intervention group.

Primary Outcome

The primary outcome is feasibility (Table 2), which will be used to inform future service delivery. Feasibility success will be confirmed if the intervention is safe (defined as a similar number of study-related serious adverse events [SAEs] between groups) and if three of the following four criteria are fulfilled: (1) ≥50% of all referred eligible patients are recruited (recruitment), (2) ≥70% of intervention participants undergo an end-of-program assessment (retention), (3) ≥75% of intervention participants have a higher frequency of specialist outpatient dietetic and exercise specialist contact than the controls (exposure uptake), and (4) videoconferencing-facilitated dietetic and exercise sessions have an attendance rate of ≥80% of the total scheduled contacts (telehealth adherence).

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Safety

Safety will be determined from adverse event reporting. SAE categories and adverse events of special interest are detailed in Textbox 2. SAEs will be classified by event category, the outcome of the event, the relationship to the study, and by whether they were planned or unplanned. The relationship of the SAE to the study will be determined by medical review. All adverse events will be monitored and recorded via the REDCap research management system throughout the study [29]. In addition, all participants will be asked by a member of the research staff at the end-of-program assessment whether any unreported SAE or adverse event had occurred during the study period.

Textbox 2. List of serious adverse events and adverse events of special interest to be recorded and monitored during the study period.

Serious adverse event categories [32]

- Death
- Life-threatening event
- Hospitalization (acute or prolonged), including planned admissions
- Event resulting in persistent or significant disability or incapacity
- Important medical event (eg, adverse drug reaction)
- Pregnancy

Adverse events of special interest [32]

- Hypoglycemic episode requiring assistance from another individual
- Fall
- Musculoskeletal injury requiring medical or allied health attention
- Hyperkalemia (newly diagnosed or requiring intervention)
- Episode of low blood pressure requiring medical attention
- Chest pain requiring medical attention

Secondary Outcomes

The secondary outcomes that will be evaluated are clinical effectiveness (including metabolic syndrome severity, dietary quality, physical activity and sedentary behavior, exercise capacity, neuromuscular fitness, muscular pain, clinical parameters, quality of life, nutrition and physical activity self-efficacy, fatigue, and sleep quality and quantity), patient-led goal attainment, treatment fidelity, exposure demand, and participant perceptions (Table 2).

Clinical Effectiveness

All clinical effectiveness data will be collected at baseline and end-of-program assessments.

Metabolic Syndrome Severity Score

The metabolic syndrome severity score (MetSSS) is a continuous risk assessment score for quantifying severity of the MetS. It will be calculated using an algorithm developed from an Australian population that includes systolic blood pressure, diastolic blood pressure, waist circumference, and fasting blood measures (triglycerides, high-density lipoprotein cholesterol, and glucose) [31].

Dietary Quality

Habitual dietary intake of the participants will be collected via a 3-day self-administered diet record (2 weekdays and 1 weekend day) using the Research Food Diary mobile app (Xyris Software [Australia] Pty Ltd) [33]. Participants will be asked to record information on the type, portion, and brand of all consumed foods. This includes condiments, oils, herbs and spices, and beverages. The app is blinded such that participants cannot access any nutrient or composition information of foods. Participants will be asked to send their diet record data via the email function, and it will be verified via phone by a study dietitian before analysis. FoodWorks 10 Professional (Xyris) will be used for nutritional analysis of the diet records using the AusFoods 2019 and AusBrands 2019 databases, including estimated intakes of energy, macronutrients, micronutrients, and food groups [34]. Dietary intake data will be used to compare dietary quality of both study groups at baseline and end-of-program assessments. This includes servings or grams per day of food groups (fruit, vegetables, whole grains, legumes, nuts and seeds, and fish and seafood), fiber, unsaturated oils, and discretionary foods (processed meats, solid fats, added sugars, and alcoholic drinks). To minimize inaccurate self-reporting, participants with implausible intakes of <500 or >3500 kcal/day will be excluded [35].

Physical Activity and Sedentary Behavior

The International Physical Activity Questionnaire Short Form (IPAQ-SF) [36] will be used to assess self-reported behavior in the previous week. The survey will be administered by a health professional with experience in physical activity research in an interview setting. Participants will be guided through the questionnaire to gain an understanding of how much time they spend per week being sedentary and performing different intensities of physical activity. IPAQ-SF results will be reported in metabolic equivalent (MET) minutes per week of total activity and minutes per week for sedentary behavior, moderate physical

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activity, and vigorous physical activity. Heart rate (HR) data from a wearable activity monitor will be used to objectively measure weekly minutes of moderate- to vigorous-intensity physical activity throughout the study. The monitor allows for this intensity range to be preset in a custom heart rate zone. Participants will be provided with information about how to use and synchronize the device at the baseline assessment.

Exercise Capacity

The 6-Minute Walk Test (6MWT) will be used to assess exercise capacity. The test will be conducted indoors with temperature control on a 20-meter track under the supervision of a health professional. It will be conducted according to a standardized protocol [37]. The result of the 6MWT will be distance walked, rounded to the nearest meter.

Neuromuscular Fitness

The single and repeated chair stand tests will be used to assess functional lower limb neuromuscular strength and endurance. The single chair stand test requires the participant to start in a seated position with the hands crossed against the chest, stand, and then return to a seated posture as quickly as possible. The repeated chair stand test records the time it takes for the participant to complete 5 stands (5xSTS) [37]. One trial will be allotted for this test. The hand grip strength test will be completed using a grip dynamometer 3 times for each hand, with the highest result recorded for both the dominant and nondominant hand. All tests will be conducted under the supervision of a health professional, according to standardized protocols [37].

Muscular Pain

Participants will complete the Modified Nordic Musculoskeletal Questionnaire (MNMQ) [38] to quantify musculoskeletal pain. This will be administered via an online form provided by email prior to the baseline and end-of-program assessments.

Clinical Parameters

Body mass and height will be measured by a member of the research team with a calibrated weight scale and stadiometer. BMI will be calculated for each participant. Duplicate waist circumference will be measured at a level midway between the lower rib margin and iliac crest in the horizontal plane [37], and the mean will be recorded. If there is a greater than 1.5% difference between waist measures, a third measure will be taken and the median will be recorded [37]. Resting heart rate, systolic blood pressure, and diastolic blood pressure will be measured. Triplicate blood pressure and heart rate measurements will be taken approximately 2 minutes apart, with the participant in a seated position and having rested for at least 10 minutes. Participants will be asked when they last took medication or consumed caffeine. The first blood pressure measurement will be discarded and the mean of the last 2 readings will be used. Biochemical blood analytes will be measured at accredited pathology laboratories (Multimedia Appendix 1).

Quality of Life and Self-Efficacy

The EQ-5D-5L scale will be administered via online survey prior to physical assessments and will be used to evaluate quality of life [39]. Four-point validated Likert scales, ranging from 1 (very uncertain) to 4 (very certain), will be used to assess self-efficacy in overcoming barriers related to eating healthy food and carrying out exercise intentions and will be administered under the supervision of a health professional [40].

Sleep Quality and Quantity and Fatigue

The Pittsburgh Sleep Quality Index (PSQI) survey will be administered via online survey prior to in-person assessments to quantify sleep quality and duration [41]. Weekly sleep data will be collected using a wearable activity monitor. The monitor records total sleep time and time in sleep stages (deep, light, rapid eye movement, and wakefulness). Participants will be asked to wear the monitor during the night to capture sleep data. The Functional Assessment of Chronic Illness Fatigue Scale (FACIT; version 4) [42] will be administered via online survey prior to in-person assessments to evaluate fatigue.

Goal Attainment Score

Goal setting will be facilitated at the baseline assessment for all participants. Participants will be encouraged to set SMART (specific, measurable, achievable, realistic, timely) goals [43]. The goal attainment scaling method will be used to compare goal attainment between the intervention and control groups at end-of-program assessments [44].

Treatment Fidelity

Treatment fidelity will be assessed throughout the trial across three areas: training provided, delivery of treatment, and receipt of treatment [45]. Attendance of clinical staff at standardized orientation training and refresher training sessions, as well as regular professional support and case discussions, will be recorded. For delivery of dietetic treatment, the clinicians will summarize the topics covered at the end of each group telehealth session (eg, healthy snacks, vegetables and fruits, and legumes) and the frequency of topics and themes discussed over the course of the project will be described. For delivery of exercise treatment, a record of each training session prescription will be captured.

Exposure Demand

Exposure demand will be assessed descriptively by summarizing the frequency of each technology option chosen by the intervention group at baseline and summarizing the different combinations of technologies chosen by the intervention group at baseline.

Participant Perceptions

Quantitative and qualitative feedback from participants will be collected at end-of-program assessments. Prior to assessment day, participants will be asked to complete an online questionnaire using a 5-point Likert scale to assess the acceptability of different aspects of the intervention received, its usability, and their satisfaction with it. Quantitative data from the surveys will be analyzed using simple descriptive statistics.

A subsample of participants from both groups will be deliberately selected to achieve maximum demographic diversity for age, sex, and disease group, and they will be invited to provide feedback regarding the model of care received. Semistructured one-on-one interviews will be conducted by a

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health professional with experience in qualitative research training and no role in delivering the service model. We will interview the participants in-person at the end-of-program assessment visit or via telephone at a time convenient to the participant. Questions will be designed to capture the participant's impressions of the service model they experienced; potential barriers and facilitators to the diet and exercise recommendations; their perspectives on the technology-assisted delivery methods, usability, and acceptability; and their self-reported intentions for future use of diet monitoring technology after completion of the study period. All interviews will be audio recorded, transcribed verbatim, and thematically analyzed with an iterative and inductive approach.

All Participants

All participants will receive usual medical and specialist care and may choose to discontinue contact with the health professionals at any time during the study period. All participants will be offered an individualized in-person appointment with a dietitian, review appointments, and a wearable activity monitor. Patients do not currently have access to exercise physiology services as part of standard care.

Individual Dietitian Assessment and Advice

All participants will receive a personalized nutrition assessment and dietary advice aligned with principles of healthy eating for reducing cardiometabolic risk [28]. These principles are informed by evidence-based dietary patterns, including Mediterranean-style and DASH (dietary approaches to stop hypertension) diets [28], and focus on eating fruit, vegetables, whole grain cereals, healthy protein sources (especially fish, legumes, nuts, and seeds), unflavored dairy foods, healthy fats and oils (including extra virgin olive oil), and the use of herbs and spices instead of salt. This advice will be provided by an accredited practicing dietitian (APD) in an in-person appointment. The advice will be tailored to personal preferences and goals.

Wearable Activity Monitor

All participants will be provided with a Fitbit Inspire HR (Fitbit, Inc) device and its accompanying mobile app to monitor physical activity. The heart rate reserve (HRR) method will be used to quantify moderate-to vigorous-intensity physical activity (40-89% HRR), with resting heart rate measured at baseline and maximal heart rate estimated as follows: 208 – (0.7 × age) [46]. For participants taking beta-blocker medication, which affects heart rate, a more representative equation will be used: 168 – (0.51 × age) [47]. At the baseline assessment, participants will be instructed on how to use the Fitbit, including how to download the app and synchronize the device, and will be provided with an information booklet. Each participant will have a Fitbit account established with a study-specific email address that will be accessible to study staff. This will permit appropriate real-time data extraction for the study. If no device data is present for 7 days during the study period, participants will be contacted via text or phone call to troubleshoot. Participants will keep the device after the end-of-program assessments.

Intervention

Participants randomized to the intervention group will be offered access to a suite of health technology options with both core (text message support) and optional (electronic dietary education resources, group-based exercise physiology and dietetics videoconferencing appointments, and an unsupervised online or mobile app home exercise program) components. Exposure to the frequency of text messages and the number and type of optional components will be patient-led, with participants choosing their preferred level of engagement (Figure 1). Participants will choose their components after randomization and the research project officer will confirm their choice via phone call in week 1. The core and optional components are described in the following sections.

Text Message Support

All intervention participants will receive lifestyle-related text messages. The text messages will be semipersonalized and unidirectional (Table 3). They will reflect selected behavior change techniques to help facilitate change in dietary and physical activity patterns [48,49]. Participants will be able to select the desired frequency of text messages: once, twice, or three times per week for the duration of the intervention.

Table 3. Text messages and relation to behavior change technique constructs.

Behavior change technique constructs	Text message examples
Social support	"Telling your helpful family and friends about your goals will help you achieve them"
Prompt specific goal setting	"2 serves of fruit every day is an important goal"
Behavior substitution	"Swapping 2 red meat meals for fish is a great way to get healthy sources of protein and fats!"
Prompt self-monitoring of behavior	"Monitor your resistance and aerobic exercise training sessions using the Fitbit watch and app"
Provide information about behavior-health link	"Resistance exercise twice a week increases muscle size and strength, helping you lose weight and keep healthy"
Problem solving	"Are you finding it hard to get 30 minutes of physical activity every day? Start with a smaller amount and build from there. Every little bit helps!"
Provide instruction	"To get more fiber from fruit, keep the skin on and aim for 2 serves per day"

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Option 1: Electronic Dietary Education Resources

Participants can choose to have access to online and mobile app–based nutrition information from Sophus (Sophus Health Pty Ltd). These include nutrition fact sheets, nutrition information videos, personal journals, and recipes promoting the principles of healthy eating for reducing cardiometabolic risk [28].

Option 2: Group Based Videoconferencing Appointments (Dietetics)

Participants can choose to have access to group dietitian telehealth sessions (maximum 6 participants per group) via the Queensland Health telehealth portal. Sessions will be run by an APD and will be offered monthly. Sessions will last for 45 minutes and focus on principles of healthy eating for reducing cardiometabolic risk.

Option 3: Group Based Videoconferencing Appointments (Exercise Physiology)

Participants can choose to have access to group exercise telehealth sessions (maximum 6 participants per group) via the Queensland Health telehealth portal. Sessions will be run by an accredited exercise physiologist (AEP) and will be offered weekly. Sessions will last for 60 minutes. Participants will also be offered a personalized home exercise program prescribed through Physitrack (Physitrack Ltd, London, UK).

Option 4: Unsupervised Online and Mobile App Home Exercise Program

Participants can choose to access an unsupervised personalized home exercise program prescribed through Physitrack. This option does not include exercise telehealth sessions with an AEP. Home programs will be individually updated monthly by an AEP.

Exercise Intervention

Further details for the exercise intervention can be seen in Multimedia Appendix 2. In brief, participants opting into one of the two exercise options will be asked to achieve a minimum of 150 minutes of moderate- to vigorous-intensity aerobic exercise, and complete two 30-minute resistance exercise sessions per week. Participants who choose either exercise option will be provided with equipment (resistance bands with light and medium resistance grades) to facilitate resistance exercise. The prescribed videoconferencing exercise sessions will consist of 20 minutes of aerobic exercise, 30 minutes of resistance exercise, and 5-minute warm ups and cool downs. The AEP will remind the participants of their target heart rate zone and ask them to monitor their heart rate during the training session with their wearable activity monitor. The repetitions in reserve (RiR) method will be utilized for prescribing resistance exercise intensity via autoregulation [50]. Autoregulation allows resistance training to be adjusted in response to an individual's performance in the session [51]. The prescribed exercise sessions will include 2 to 4 sets of a load between 1 to 4 RiR utilizing the provided equipment or body weight exercises. Participants who choose either exercise option will be provided with a personalized home exercise program following the same plan as the videoconferencing sessions.

Statistical Analysis

Sample Size

As this will be a feasibility study, a sample size calculation was not performed for the primary outcome. To allow for reliable findings, the sample size calculation was conducted using the MetSSS for clinical effectiveness as a secondary outcome. Assuming a correlation of 0.5 between baseline and 26-week MetSSS and an effect size of 0.42 (representing a change of 0.8 in the intervention group and no change in the control group, with a pooled standard deviation of 1.9), the Stata procedure "sampsi" suggests that 67 participants per arm will be required to achieve 80% power to detect a significant difference at the 5% level (2-sided) using an analysis of covariance (ANCOVA). Allowing for 20% dropout, the required number of participants to be recruited will be 168 (84 per arm).

Primary Analysis

The primary analysis will evaluate the feasibility of the intervention. As mentioned previously, the feasibility of the intervention will be determined by evaluating safety and if three of the following four criteria are achieved: (1) recruitment rate ≥50%, (2) retention ≥70%, (3) exposure uptake ≥75%, and (4) telehealth adherence ≥80%. Safety will be assessed by comparing the number of study-related SAEs in the intervention and control groups using a chi-square test of homogeneity. The safety of the intervention will be assumed if there are no statistical differences between the groups.

Secondary Analyses

Analysis for continuous clinical outcomes will be conducted via an ANCOVA to compare change values between study groups, adjusted for baseline values and patient population (ie, patients with chronic kidney disease, hepatology, and kidney and liver posttransplant). No imputation of missing values will occur.

Supplementary descriptive analysis of participant technology choices and patient-led goal attainment will be conducted. Summative statistics for the proportion of engagement among participants in the intervention arm will be collected and analyzed postintervention. A significance level of $P<.05$ will be used for all analyses.

Patient and Public Involvement

Significant consumer engagement was undertaken in the design of the research question and health priorities; this involved focus groups and interviews [21,24,49,52,53]. This informed the design of the intervention, particularly the inclusion of patient choice in how to engage with technology and the acceptability of using telehealth options for diet and exercise support. Patients were not involved in the recruitment or conduct of the study and did not assess the burden of the intervention. Written summaries of the results will be sent to participants upon completion of the study.

Ethics Approval

This trial has been approved by the Metro South Human Research Ethics Committee (HREC/2019/QMS/58285) and The University of Queensland Human Research Ethics

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Committee (2020000127). The trial adheres to the Helsinki declaration and has been prospectively registered with the Australian New Zealand Clinical Trial Registry (ACTRN12620001282976).

Results

The study was funded in 2019 and has been approved by the Metro South Human Research Ethics Committee and The University of Queensland Human Research Ethics Committee. Due to the COVID-19 pandemic, study enrollment was delayed for 6 months. Participant enrollment has commenced and will continue through June 2022. End-of-program assessments will continue through December 2022, when data collection is expected to be completed. Analysis, interpretation, and preliminary dissemination of results are planned for January 2023 to June 2023 through scientific conferences. The main results are expected to be published by August 2023.

Discussion

This trial will test the implementation of a technology-assisted lifestyle intervention for a diverse group of patients with complex chronic conditions who receive specialist outpatient care from the tertiary health system. While telehealth delivery of dietary interventions has been shown to be cost-effective in research settings [54], this mixed methods approach incorporates feasibility and effectiveness outcomes, as well as patient engagement strategies to evaluate service redesign in a real-world clinical setting. While trials of technology such as telephone coaching or video-enabled telehealth counselling sessions have generally been deemed feasible for some complex conditions [13,48], patients' desire for greater choice and to lead decision-making around engagement with a diverse suite of technologies is clear [21,52]. We expect that the intervention will be able to address a number of barriers to engaging with lifestyle interventions in the hospital and health care system, and that it will allow improved access to specialist care compared to standard practice. The results of this project will be of interest to researchers and policy makers who are strategically investing in a transition to telehealth models of care. This is especially pertinent in the context of the global COVID-19 pandemic, which challenged traditional health care delivery models. Patient-led health technology approaches to lifestyle intervention may be instrumental to the future of health service design. Recruitment in this study will be limited to patients referred to dietetic services as part of their usual tertiary hospital outpatient care, and results may thus lack generalizability to other settings. The results will be broadly disseminated (locally, nationally and internationally) through established networks of the investigator team. There will be no restrictions placed on publication of any results. There is no intention for the use of professional writers. All authors will meet journal requirements for authorship.

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Data Availability

After completion and publication of the trial results, data requests can be submitted to the researchers at the Department of Nutrition and Dietetics at the Princess Alexandra Hospital, Brisbane, Australia.

Authors' Contributions

IJH, GAM, KLC, JSC, NMI, MMC, HLM, DKJ, and SEK contributed to study conception. RCCB, MMC, JTK, AB, NWB, GAM, SEK, JSC, NMI, KLC, HMS, and IJH contributed to study design. RCCB, MMC, JTK, AB, NWB, GAM, SEK, JSC, DKJ, NMI, KLC, HLM, HMS, and IJH provided input into the development of the study tools. RCCB, HLM, DKJ, JSC, SEK, and IJH were responsible for the initial drafting of the first manuscript. RCCB, DKJ, MMC, HLM, JTK, LW, AB, HMS, NWB, NMI, GAM, KLC, JSC, SEK, and IJH contributed to manuscript editing and review. All authors read and approved the final protocol.

Conflicts of Interest

None declared.

Multimedia Appendix 1
Biochemical analytes.
[DOCX File , 13 KB - resprot_v11i7e37556_app1.docx]

Multimedia Appendix 2
Detailed description of telehealth exercise intervention.

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[DOCX File , 20 KB - resprot_v11i7e37556_app2.docx]

References

1. Alberti KGMM, Eckel RH, Grundy SM, Zimmet PZ, Cleeman JI, Donato KA, International Diabetes Federation Task Force on Epidemiology and Prevention, National Heart, Lung, and Blood Institute, American Heart Association, World Heart Federation, International Atherosclerosis Society, International Association for the Study of Obesity. Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. Circulation 2009 Oct 20;120(16):1640-1645. [doi: 10.1161/CIRCULATIONAHA.109.192644] [Medline: 19805654]
2. Mottillo S, Filion KB, Genest J, Joseph L, Pilote L, Poirier P, et al. The metabolic syndrome and cardiovascular risk a systematic review and meta-analysis. J Am Coll Cardiol 2010 Sep 28;56(14):1113-1132 [FREE Full text] [doi: 10.1016/j.jacc.2010.05.034] [Medline: 20863953]
3. Marangos PJ, Okamoto LJ, Caro JJ. Economic Burden of the Components of the Metabolic Syndrome. In: Preedy VR, Watson RR, editors. Handbook of Disease Burdens and Quality of Life Measures. New York, NY: Springer; 2010:1135-1149.
4. Scholze J, Alegria E, Ferri C, Langham S, Stevens W, Jeffries D, et al. Epidemiological and economic burden of metabolic syndrome and its consequences in patients with hypertension in Germany, Spain and Italy; a prevalence-based model. BMC Public Health 2010 Sep 02;10:529 [FREE Full text] [doi: 10.1186/1471-2458-10-529] [Medline: 20813031]
5. McCoy SM, Campbell KL, Lassemillante AM, Wallen MP, Fawcett J, Jarrett M, et al. Changes in dietary patterns and body composition within 12 months of liver transplantation. Hepatobiliary Surg Nutr 2017 Oct;6(5):317-326 [FREE Full text] [doi: 10.21037/hbsn.2017.01.12] [Medline: 29152478]
6. Murray EM, McCoy SM, Campbell KL, Hickman IJ. Dietitians' practices and perspectives on nutrition priorities for liver transplant recipients. Nutr Diet 2013 Oct 03;71(2):86-91. [doi: 10.1111/1747-0080.12079]
7. European Association for the Study of the Liver. EASL Clinical Practice Guidelines: Liver transplantation. J Hepatol 2016 Feb;64(2):433-485. [doi: 10.1016/j.jhep.2015.10.006] [Medline: 26597456]
8. Yamaoka K, Tango T. Effects of lifestyle modification on metabolic syndrome: a systematic review and meta-analysis. BMC Med 2012 Nov 14;10:138 [FREE Full text] [doi: 10.1186/1741-7015-10-138] [Medline: 23151238]
9. Prasad GVR. Metabolic syndrome and chronic kidney disease: Current status and future directions. World J Nephrol 2014 Nov 06;3(4):210-219 [FREE Full text] [doi: 10.5527/wjn.v3.i4.210] [Medline: 25374814]
10. Rahimi RS, Landaverde C. Nonalcoholic fatty liver disease and the metabolic syndrome: clinical implications and treatment. Nutr Clin Pract 2013 Feb;28(1):40-51. [doi: 10.1177/0884533612470464] [Medline: 23286927]
11. Fatourou EM, Tsochatzis EA. Management of metabolic syndrome and cardiovascular risk after liver transplantation. Lancet Gastroenterol Hepatol 2019 Sep;4(9):731-741. [doi: 10.1016/S2468-1253(19)30181-5] [Medline: 31387736]
12. Gremeaux V, Drigny J, Nigam A, Juneau M, Guilbeault V, Latour E, et al. Long-term lifestyle intervention with optimized high-intensity interval training improves body composition, cardiometabolic risk, and exercise parameters in patients with abdominal obesity. Am J Phys Med Rehabil 2012 Nov;91(11):941-950. [doi: 10.1097/PHM.0b013e3182643ce0] [Medline: 22854902]
13. Hickman IJ, Hannigan AK, Johnston HE, Elvin-Walsh L, Mayr HL, Staudacher HM, et al. Telehealth-delivered, Cardioprotective Diet and Exercise Program for Liver Transplant Recipients: A Randomized Feasibility Study. Transplant Direct 2021 Mar;7(3):e667 [FREE Full text] [doi: 10.1097/TXD.0000000000001118] [Medline: 33564717]
14. Howden EJ, Leano R, Petchey W, Coombes JS, Isbel NM, Marwick TH. Effects of exercise and lifestyle intervention on cardiovascular function in CKD. Clin J Am Soc Nephrol 2013 Sep;8(9):1494-1501 [FREE Full text] [doi: 10.2215/CJN.10141012] [Medline: 23970136]
15. Dinu M, Pagliai G, Casini A, Sofi F. Mediterranean diet and multiple health outcomes: an umbrella review of meta-analyses of observational studies and randomised trials. Eur J Clin Nutr 2018 Jan;72(1):30-43. [doi: 10.1038/ejcn.2017.58] [Medline: 28488692]
16. Ikizler TA, Robinson-Cohen C, Ellis C, Headley SAE, Tuttle K, Wood RJ, et al. Metabolic Effects of Diet and Exercise in Patients with Moderate to Severe CKD: A Randomized Clinical Trial. J Am Soc Nephrol 2018 Jan;29(1):250-259 [FREE Full text] [doi: 10.1681/ASN.2017010020] [Medline: 29038285]
17. Howden EJ, Coombes JS, Strand H, Douglas B, Campbell KL, Isbel NM. Exercise training in CKD: efficacy, adherence, and safety. Am J Kidney Dis 2015 Apr;65(4):583-591. [doi: 10.1053/j.ajkd.2014.09.017] [Medline: 25458662]
18. Kantartzis K, Thamer C, Peter A, Machann J, Schick F, Schraml C, et al. High cardiorespiratory fitness is an independent predictor of the reduction in liver fat during a lifestyle intervention in non-alcoholic fatty liver disease. Gut 2009 Sep;58(9):1281-1288. [doi: 10.1136/gut.2008.151977] [Medline: 19074179]
19. Fraser SDS, Taal MW. Multimorbidity in people with chronic kidney disease: implications for outcomes and treatment. Curr Opin Nephrol Hypertens 2016 Nov;25(6):465-472. [doi: 10.1097/MNH.0000000000000270] [Medline: 27490909]
20. Patel PJ, Hayward KL, Rudra R, Horsfall LU, Hossain F, Williams S, et al. Multimorbidity and polypharmacy in diabetic patients with NAFLD: Implications for disease severity and management. Medicine (Baltimore) 2017 Jun;96(26):e6761 [FREE Full text] [doi: 10.1097/MD.0000000000006761] [Medline: 28658094]

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21. Hickman IJ, Coran D, Wallen MP, Kelly J, Barnett A, Gallegos D, et al. 'Back to Life'-Using knowledge exchange processes to enhance lifestyle interventions for liver transplant recipients: A qualitative study. Nutr Diet 2019 Sep;76(4):399-406. [doi: 10.1111/1747-0080.12548] [Medline: 31083821]
22. Bonner A, Gillespie K, Campbell KL, Corones-Watkins K, Hayes B, Harvie B, et al. Evaluating the prevalence and opportunity for technology use in chronic kidney disease patients: a cross-sectional study. BMC Nephrol 2018 Feb 02;19(1):28 [FREE Full text] [doi: 10.1186/s12882-018-0830-8] [Medline: 29394930]
23. Cotugno JD, Ferguson M, Harden H, Colquist S, Stack AA, Zimmerman JI, et al. "I wish they could be in my shoes": patients' insights into tertiary health care for type 2 diabetes mellitus. Patient Prefer Adherence 2015;9:1647-1655 [FREE Full text] [doi: 10.2147/PPA.S91214] [Medline: 26604714]
24. Kelly JT, Campbell KL, Hoffmann T, Reidlinger DP. Patient Experiences of Dietary Management in Chronic Kidney Disease: A Focus Group Study. J Ren Nutr 2018 Nov;28(6):393-402. [doi: 10.1053/j.jrn.2017.07.008] [Medline: 29146140]
25. Street TD, Somoray K, Richards GC, Lacey SJ. Continuity of care for patients with chronic conditions from rural or remote Australia: A systematic review. Aust J Rural Health 2019 Jun;27(3):196-202 [FREE Full text] [doi: 10.1111/ajr.12511] [Medline: 31074919]
26. Harvey G, Kitson A. PARIHS revisited: from heuristic to integrated framework for the successful implementation of knowledge into practice. Implement Sci 2016 Mar 10;11:33 [FREE Full text] [doi: 10.1186/s13012-016-0398-2] [Medline: 27013464]
27. McNichol E. Patient-led innovation in healthcare: The value of the ‘user’ perspective. Int J Healthc Manag 2013 Jul 18;5(4):216-222. [doi: 10.1179/2047971912y.0000000020]
28. Dietary Position Statement: Heart Healthy Eating Patterns. National Heart Foundation of Australia. URL: https://tinyurl.com/3h2samvv [accessed 2022-06-24]
29. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)--a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform 2009 Apr;42(2):377-381 [FREE Full text] [doi: 10.1016/j.jbi.2008.08.010] [Medline: 18929686]
30. Norman CD, Skinner HA. eHEALS: The eHealth Literacy Scale. J Med Internet Res 2006 Nov 14;8(4):e27 [FREE Full text] [doi: 10.2196/jmir.8.4.e27] [Medline: 17213046]
31. Wiley JF, Carrington MJ. A metabolic syndrome severity score: A tool to quantify cardio-metabolic risk factors. Prev Med 2016 Jul;88:189-195. [doi: 10.1016/j.ypmed.2016.04.006] [Medline: 27095322]
32. Common Terminology Criteria for Adverse Events (CTCAE) Version 5. U.S. Department of Health and Human Services. URL: https://ctep.cancer.gov/protocoldevelopment/electronic_applications/docs/ctcae_v5_quick_reference_8.5x11.pdf [accessed 2022-06-24]
33. Ambrosini GL, Hurworth M, Giglia R, Trapp G, Strauss P. Feasibility of a commercial smartphone application for dietary assessment in epidemiological research and comparison with 24-h dietary recalls. Nutr J 2018 Jan 09;17(1):5 [FREE Full text] [doi: 10.1186/s12937-018-0315-4] [Medline: 29316930]
34. What are the Xyris food groups? Foodworks Support. URL: https://support.xyris.com.au/hc/en-us/articles/205716319-What-are-the-Xyris-food-groups- [accessed 2022-06-24]
35. Rhee JJ, Sampson L, Cho E, Hughes MD, Hu FB, Willett WC. Comparison of methods to account for implausible reporting of energy intake in epidemiologic studies. Am J Epidemiol 2015 Feb 15;181(4):225-233 [FREE Full text] [doi: 10.1093/aje/kwu308] [Medline: 25656533]
36. Craig CL, Marshall AL, Sjöström M, Bauman AE, Booth ML, Ainsworth BE, et al. International physical activity questionnaire: 12-country reliability and validity. Med Sci Sports Exerc 2003 Aug;35(8):1381-1395. [doi: 10.1249/01.MSS.0000078924.61453.FB] [Medline: 12900694]
37. Coombes J, Skinner T. ESSA's Student Manual for Health, Exercise and Sport Assessment. London, UK: Elsevier Health Sciences APAC; 2014.
38. Kuorinka I, Jonsson B, Kilbom A, Vinterberg H, Biering-Sørensen F, Andersson G, et al. Standardised Nordic questionnaires for the analysis of musculoskeletal symptoms. Appl Ergon 1987 Sep;18(3):233-237. [doi: 10.1016/0003-6870(87)90010-x] [Medline: 15676628]
39. Herdman M, Gudex C, Lloyd A, Janssen M, Kind P, Parkin D, et al. Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). Qual Life Res 2011 Dec;20(10):1727-1736 [FREE Full text] [doi: 10.1007/s11136-011-9903-x] [Medline: 21479777]
40. Buysse DJ, Reynolds CF, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. Psychiatry Res 1989 May;28(2):193-213. [doi: 10.1016/0165-1781(89)90047-4] [Medline: 2748771]
41. Schwarzer R, Renner B. Health-Specific Self-Efficacy Scales. Freie Universität Berlin. URL: http://userpage.fu-berlin.de/~health/healself.pdf [accessed 2022-06-24]
42. Webster K, Cella D, Yost K. The Functional Assessment of Chronic Illness Therapy (FACIT) Measurement System: properties, applications, and interpretation. Health Qual Life Outcomes 2003 Dec 16;1:79 [FREE Full text] [doi: 10.1186/1477-7525-1-79] [Medline: 14678568]

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43. Bovend'Eerdt TJH, Botell RE, Wade DT. Writing SMART rehabilitation goals and achieving goal attainment scaling: a practical guide. Clin Rehabil 2009 Apr;23(4):352-361. [doi: 10.1177/0269215508101741] [Medline: 19237435]
44. Turner-Stokes L. Goal attainment scaling (GAS) in rehabilitation: a practical guide. Clin Rehabil 2009 Apr;23(4):362-370. [doi: 10.1177/0269215508101742] [Medline: 19179355]
45. Bellg AJ, Borrelli B, Resnick B, Hecht J, Minicucci DS, Ory M, Treatment Fidelity Workgroup of the NIH Behavior Change Consortium. Enhancing treatment fidelity in health behavior change studies: best practices and recommendations from the NIH Behavior Change Consortium. Health Psychol 2004 Sep;23(5):443-451. [doi: 10.1037/0278-6133.23.5.443] [Medline: 15367063]
46. Tanaka H, Monahan KD, Seals DR. Age-predicted maximal heart rate revisited. J Am Coll Cardiol 2001 Jan;37(1):153-156 [FREE Full text] [doi: 10.1016/s0735-1097(00)01054-8] [Medline: 11153730]
47. Godlasky E, Hoffman T, Weber-Peters S, Bradford R, Miller N, Kunselman AR, et al. Effects of β-Blockers on Maximal Heart Rate Prediction Equations in a Cardiac Population. J Cardiopulm Rehabil Prev 2018 Mar;38(2):111-117. [doi: 10.1097/HCR.0000000000000328] [Medline: 29465497]
48. Kelly JT, Conley M, Hoffmann T, Craig JC, Tong A, Reidlinger DP, et al. A Coaching Program to Improve Dietary Intake of Patients with CKD: ENTICE-CKD. Clin J Am Soc Nephrol 2020 Mar 06;15(3):330-340 [FREE Full text] [doi: 10.2215/CJN.12341019] [Medline: 32111701]
49. Kelly JT, Warner MM, Conley M, Reidlinger DP, Hoffmann T, Craig J, et al. Feasibility and acceptability of telehealth coaching to promote healthy eating in chronic kidney disease: a mixed-methods process evaluation. BMJ Open 2019 Jan 29;9(1):e024551 [FREE Full text] [doi: 10.1136/bmjopen-2018-024551] [Medline: 30700482]
50. Zourdos MC, Klemp A, Dolan C, Quiles JM, Schau KA, Jo E, et al. Novel Resistance Training-Specific Rating of Perceived Exertion Scale Measuring Repetitions in Reserve. J Strength Cond Res 2016 Jan;30(1):267-275. [doi: 10.1519/JSC.0000000000001049] [Medline: 26049792]
51. Greig L, Stephens Hemingway BH, Aspe RR, Cooper K, Comfort P, Swinton PA. Autoregulation in Resistance Training: Addressing the Inconsistencies. Sports Med 2020 Nov;50(11):1873-1887 [FREE Full text] [doi: 10.1007/s40279-020-01330-8] [Medline: 32813181]
52. Barnett A, Campbell KL, Mayr HL, Keating SE, Macdonald GA, Hickman IJ. Liver transplant recipients' experiences and perspectives of a telehealth-delivered lifestyle programme: A qualitative study. J Telemed Telecare 2021 Oct;27(9):590-598. [doi: 10.1177/1357633X19900459] [Medline: 31986966]
53. Warner MM, Tong A, Campbell KL, Kelly JT. Patients' Experiences and Perspectives of Telehealth Coaching with a Dietitian to Improve Diet Quality in Chronic Kidney Disease: A Qualitative Interview Study. J Acad Nutr Diet 2019 Aug;119(8):1362-1374. [doi: 10.1016/j.jand.2019.01.023] [Medline: 30979633]
54. Law L, Kelly JT, Savill H, Wallen MP, Hickman IJ, Erku D, et al. Cost-effectiveness of telehealth-delivered diet and exercise interventions: A systematic review. J Telemed Telecare 2022 Feb 02. [doi: 10.1177/1357633X211070721] [Medline: 35108135]

Abbreviations

5xSTS: repeated chair stand test
6MWT: 6-Minute Walk Test
AEP: accredited exercise physiologist
ANCOVA: analysis of covariance
APD: accredited practicing dietitian
DASH: dietary approaches to stop hypertension
FACIT: Functional Assessment of Chronic Illness Fatigue
HR: heart rate
HRR: heart rate reserve
IPAQ-SF: International Physical Activity Questionnaire Short Form
MET: metabolic equivalent
MetS: metabolic syndrome
MetSSS: Metabolic Syndrome Severity Score
MNMQ: Modified Nordic Musculoskeletal Questionnaire
PSQI: Pittsburgh Sleep Quality Index
RiR: repetitions in reserve
SAE: serious adverse event
SMART: specific, measurable, achievable, realistic, timely

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Protocol

A Stress and Pain Self-management mHealth App for Adult Outpatients With Sickle Cell Disease: Protocol for a Randomized Controlled Study

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Abstract

Background: This paper describes the research protocol for a randomized controlled trial of a self-management intervention for adults diagnosed with sickle cell disease (SCD). People living with SCD experience lifelong recurrent episodes of acute and chronic pain, which are exacerbated by stress.

Objective: This study aims to decrease stress and improve SCD pain control with reduced opioid use through an intervention with self-management relaxation exercises, named You Cope, We Support (YCWS). Building on our previous findings from formative studies, this study is designed to test the efficacy of YCWS on stress intensity, pain intensity, and opioid use in adults with SCD.

Methods: A randomized controlled trial of the short-term (8 weeks) and long-term (6 months) effects of YCWS on stress, pain, and opioid use will be conducted with 170 adults with SCD. Patients will be randomized based on 1:1 ratio (stratified on pain intensity [≤5 or >5]) to be either in the experimental (self-monitoring of outcomes, alerts or reminders, and use of YCWS [relaxation and distraction exercises and support]) or control (self-monitoring of outcomes and alerts or reminders) group. Patients will be asked to report outcomes daily. During weeks 1 to 8, patients in both groups will receive system-generated alerts or reminders via phone call, text, or email to facilitate data entry (both groups) and intervention use support (experimental). If the participant does not enter data after 24 hours, the study support staff will contact them for data entry troubleshooting (both groups) and YCWS use (experimental). We will time stamp and track patients' web-based activities to understand the study context and conduct exit interviews on the acceptability of system-generated and staff support. This study was approved by our institutional review board.

Results: This study was funded by the National Institute of Nursing Research of the National Institutes of Health in 2020. The study began in March 2021 and will be completed in June 2025. As of April 2022, we have enrolled 45.9% (78/170) of patients. We will analyze the data using mixed effects regression models (short term and long term) to account for the repeated measurements

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over time and use machine learning to construct and evaluate prediction models. Owing to the COVID-19 pandemic, the study was modified to allow for mail-in consent process, internet-based consent process via email or Zoom videoconference, devices delivered by FedEx, and training via Zoom videoconference.

Conclusions: We expect the intervention group to report reductions in pain intensity (primary outcome; 0-10 scale) and in stress intensity (0-10 scale) and opioid use (Wisepill event medication monitoring system), which are secondary outcomes. Our study will contribute to advancing the use of nonopioid therapy such as guided relaxation and distraction techniques for managing SCD pain.

Trial Registration: ClinicalTrials.gov NCT04484272; https://clinicaltrials.gov/ct2/show/NCT04484272

International Registered Report Identifier (IRRID): PRR1-10.2196/33818

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KEYWORDS

sickle cell disease; self-management; stress; pain; opioid use; analgesics; intervention; support; protocol; randomized controlled trial

Introduction

Background

Sickle cell disease (SCD) is an orphan disease with multifactorial impact. In the United States, the incident rate of SCD has remained constant [1]. However, SCD is projected to increase from 304,800 newborns annually to 404,200 newborns by 2050 worldwide [2]. SCD is the most common inherited blood disorder in the United States [3], with annual health care cost of US $2.4 billion [4] for 100,000 diagnosed Americans. Current human diasporas and massive migration from Africa, Middle East, Mediterranean region, Central and South America, and India contribute to the sickle cell gene pool in the United States, as does a growing Hispanic population [2]. People living with SCD were once destined for recurrent morbidity or early death, but now, live into their forties and beyond [5]. In the United States, for people with HbSS, HbSβ^0, or HbSD, the median age of survival is 48 (95% CI 44.4-58.4) years and for people with HbSC or HbSβ^+, the median age of survival is 54.7 (95% CI 38.6-62.9) years [6]. People living with SCD have lifelong recurrent episodes of acute pain and substantial persistent pain together with other symptoms including respiratory threats, organ failure, stroke risk, and stress and disruption in their lives and those of their family [7-15]. Evidence indicates that patients with SCD who survive beyond childhood continue to live most days with persistent pain that can affect any organ owing to ischemia [13].

The chronic pain associated with SCD is often rated as more intense than childbirth pain and persists for years [16]. Recurrent, unpredictable, and disabling episodes of vaso-occlusive pain was the primary reason for >100,000 annual SCD emergency department (ED) encounters and hospitalizations [17]. People with SCD have an average of 2.59 (95% CI 2.53-2.65) ED visits or hospitalizations per year [17]. ED visit and hospitalization rates are 2 to 6 and 7 to 30 times higher, respectively, among African American individuals with SCD visits than those without SCD [18].

Other studies report strong positive relationship between the frequency and severity of pain and death [13,19-22]. Currently, the only cure for SCD is allogeneic hematopoietic stem cell transplantation, with limited availability owing to the risk of transplantation-related mortality [23]. Potential cures for SCD include transferring the causal β-globin gene, editing sickle β-globin mutation, or reactivating fetal hemoglobin, the research for which is still ongoing [24]. As stem cell transplantation is not without considerable risk, it is usually reserved for patients with severe symptoms of SCD [25]. Given the strong association between severe SCD pain and death [13], there is an urgent need to find readily available therapies for controlling SCD pain.

Stress, associated with pain in patients with SCD, is correlated with overactivation of the hypothalamic-pituitary-adrenal axis hormones or neurotransmitters (eg, cortisol, norepinephrine, and epinephrine), which trigger the fight-or-flight responses and intensify responses to nociceptive pain (somatic and visceral tissue damage) [26-28]. Stress can also activate neuropathic pain mechanisms (neural tissue damage) implicated as part of SCD pain [16]. In patients with pain, the perception of stress can lead to stress-induced hyperalgesia (increased pain from a painful stimulus) [29]. Findings from studies of patients with SCD [30,31] and other pain conditions [32] show small to medium positive associations between stress and pain. In a pilot study of 52 adult patients with SCD, we found that compared with patients who perceived low psychological stressors from their physicians, those who perceived high stressors from their physicians also reported greater stress (P<.001) and pain (P=.002) [30]. Results were similar for psychological stressors from nurses (perceived stress: P<.001 and pain: P=.02) [30]. Others found that patients with SCD who reported high stress also reported high average pain [31], and increased stress intensity was associated with increased same-day pain in patients with SCD [33]. Cumulative findings from these studies provide strong evidence of the association of stress with pain in patients with SCD. The hypothalamic-pituitary-adrenal axis theory posits that stress reduction interventions have the potential to reduce SCD pain.

Nondrug Therapy for Self-management of Pain in SCD

The use of pain self-management in SCD has gained much attention in recent years. Pain self-management techniques can include deep breathing exercises, progressive relaxation, and guided imagery [34]. Patients with SCD are ideally suited for

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nondrug therapies. In a recent study of 227 patients with SCD, approximately 92% reported using nondrug therapy in the previous 6 months to manage pain [35]. Studies of nondrug therapies in patients with SCD found reduced perceived pain intensity [36] and reduced clinical pain [37,38]. Guided relaxation, which is one of many tools used in cognitive behavioral therapy, is designed to help patients identify triggers for pain, modify problematic emotions or behaviors, and develop coping skills [39]. By using relaxation and stress management to guide patients away from negative feelings and behaviors, we can weaken the inclination to use opioids as the only method of pain management and strengthen their repertoire of strategies with alternative healthy actions, thereby improving their day-to-day relationship with pain.

Current Drug Therapy for Managing SCD Pain (Opioids)

The use of opioids as the mainstay of therapy for both acute and persistent SCD is not ideal. Opioid analgesics are known to cause severe side effects, including death from overdose. They are frequently prescribed for SCD pain; however, accumulating evidence suggests the need to incorporate nondrug therapies as strategies for managing SCD pain systematically [40]. A recent study characterized opioid analgesic use in patients with SCD and showed that 40% of them were prescribed opioids in the previous 12 months [41]. Furthermore, 3% of pediatric patients and 23% of adult patients used high doses (>30 mg of oral morphine equivalence [OME] daily) [41]. Findings also suggest that patients with vaso - occlusive pain crisis (acute) and avascular necrosis (chronic) reported using high-dose opioid use [41].

Patients who use high opioid doses were more likely to use nonsteroidal anti - inflammatory drugs, visit acute health care facilities, and indicate that they experienced pain on most days [42]. The opioid epidemic in the United States stems from heavy reliance on opioid therapy for controlling all pain types, including persistent pain, a practice against the Center for Disease Control recommendation that nondrug therapies are preferable for treating chronic pain [43]. Compared with the national average, patients with SCD have lower opioid addiction rates and fewer deaths from overdose [44]. Between 1993 and 2013, a total of 174,959 individuals in the United States died from opioid prescription overdose. During the same period, 95 patients with SCD died from opioid prescription overdose [44]. To mitigate the risk of death from opioid overdose and other side effects of opioids in patients with SCD, behavior change strategies are sorely needed, which will empower patients to embrace self-management principles, including the systematic use of nondrug therapies as complements to opioids.

Providing behavior change strategies via mobile health (mHealth) apps or internet-delivered interventions aligns with the Federal Pain Research Strategy to promote and enable pain self-management [45]. In a previous study, Ezenwa et al [37] found that an internet-enabled, stand-alone distraction and relaxation intervention demonstrated the feasibility and acceptability of the intervention in adult outpatients with SCD. As in this previous study [37], the design for this study is based on a multidimensional theory of pain supported by decades of research [46]. Operating within this theoretical framework, participants with SCD will continue taking opioid analgesics during the study period. A well-designed study, such as ours, will provide a behavior strategy with the potential of reducing opioid use.

Study Aims and Hypotheses

The focus of this study is to evaluate the effectiveness of a self-management intervention that promotes the use of relaxation and distraction exercises (RDEs) in reducing pain, stress, and opioid dependency among adult outpatients with SCD. Specifically, the aims of this study are the following:

1. Determine the *short-term* effects of You Cope, We Support (YCWS). Hypothesis: In the first 8 weeks, compared with the control group, the experimental group will report reductions in the primary outcome—pain intensity (0-10 scale) and in the secondary outcomes—stress intensity (0-10 scale) and opioid use (OME).
2. Determine the *long-term* effects of YCWS. Hypothesis: During months 3 to 6, compared with the control group, the experimental group will report reductions in the primary outcome—pain intensity (0-10 scale) and in the secondary outcomes—stress intensity (0-10 scale) and opioid use (OME).
3. Use machine learning to develop and evaluate models that predict patient outcomes based on their group assignment and their personal (eg, self-efficacy, sex, education, family income, and computer experience) and environmental characteristics (eg, distance from care and quality of internet connection). The results will provide insight into the heterogeneity of intervention's effects and the patients most likely to benefit from YCWS.

Methods

Study Design

The study is a randomized controlled trial (RCT) of the short-term (8 weeks) and long-term (6 months) effects of YCWS on efficacy outcomes (pain, stress, and opioid use), designed to determine the short-term and long-term effects of the YCWS intervention and to evaluate models that predict patient outcomes based on their group assignment and their personal and environmental characteristics.

Study Setting

We are recruiting patients both in person and internet-based throughout the state of Florida, including the University of Florida (UF) Health-Shands in Gainesville and UF Health-Shands in Jacksonville. Thus, data collection and intervention delivery occur throughout Florida, with UF Health-Shands in Gainesville as the primary site for data collection, intervention delivery, and data analysis.

Ethics Approval

The UF institutional review board (IRB) is the approving IRB of record and has approved all the recruitment and study procedures (IRB202000984).

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Recruitment

We will recruit from the UF Health-Gainesville and UF Health-Jacksonville hematology clinics and the UF Health-Jacksonville transition program. The UF Health-Shands Hospital, Gainesville, adult sickle cell program has a clinic panel of 497 adult patients with SCD. Of the 497 patients, (283/497, 57%) are women and (452/497, 91%) are African American individuals. The adult SCD program consists of a multidisciplinary team including 5 medical hematologists, 2 advanced registered nurse practitioners, 1 physician assistant, and 1 registered nurse. The UF Health-Jacksonville adult sickle cell program has a clinic panel of 569 adult patients with SCD. Of the 569 patients, 318 (56%) are women and 540 (95%) are African American individuals. The UF Health-Jacksonville adult SCD program consists of a multidisciplinary team including 1 medical hematologist and 1 advanced registered nurse practitioner.

The study is registered on ClinicalTrials.gov. We will use web-based recruitment processes, including posting recruitment information on the UF study Facebook page and various internet listservs to identify and recruit adults with SCD from across Florida. We will also use colorful posters, flyers, and brochures developed for this study and distribute them in sickle cell clinics and health fairs and through university bulletin boards. In addition, we will work directly with sickle cell organizations, community-based organizations, health care networks, and churches to post recruitment flyers aimed at encouraging adults to participate in and advertise the study within their networks throughout Florida.

Eligibility Criteria

Inclusion Criteria

To be included in the study, patients must be adults with a diagnosis of SCD (eg, HbSS, HbSC, HbSβ^0 thalassemia, and HbSβ^+ thalassemia), report moderate to severe level of pain (>3 on 0-10 scale) related to SCD within previous 24 hours, use opioid analgesics on *as-needed* or *continuous* basis, speak and read English, and be ≥18 years.

Exclusion Criteria

Patients will be excluded if they are legally blind or physically unable to complete the procedures or have previously participated in our relaxation and distraction intervention feasibility study.

Sample Size

For those who meet the eligibility criteria, we anticipate enrolling 195 participants to retain 170 (87.2%) participants with complete data at 8 weeks, based on a 13% attrition rate observed in our previous longitudinal studies in which follow-up was more than a year. We will strive for a sample in which 95% participants have African descent and approximately 50% are women. Our team has been exceptionally successful in conducting longitudinal studies using tablet technology with this vulnerable population and recruiting and retaining patients with SCD for pain research [16,47-50].

Screening and Consent

This is an internet-based study, with all screening and consent processes completed by the research specialist (RS) or the community health worker either in person, internet-based, through email, or through US postal service, depending on the patient's needs. The RS or community health worker will explain the study to the patients and ascertain their willingness to participate. Patients will be informed that their participation is voluntary and that a decision to decline participation will not affect their care. Patients who choose to participate will be asked to sign a written consent form. We will use one of the following methods: (1) patient will sign the consent form in person and will be given a copy, which they may keep for their record; (2) we will email the consent form for the patient to sign and email back to the RS; or (3) we will send 2 copies of the consent form with a self-addressed envelope with paid postage to the patient using the address provided. The patient will sign the consent form, keep a copy for their record, and mail a copy back to us. Patients recruited via phone or email will sign the written consent form on the day of their first study visit, if occurring in person. Otherwise, patients will sign the consent form electronically or via the other consenting methods described previously. The RS who will assist individuals in these screening and consent processes will be trained in good clinical practices for research and IRB and Health Insurance Portability and Accountability Act procedures. The training includes role-playing with the principal investigator (PI) and retraining if the staff deviate from the proper processes.

Randomization

We will use permuted block randomization with stratification based on worst pain intensity (≤5 or >5) to assign the 195 consecutively selected patients to the 2 study groups. The assignment will be blind until a sealed electronic envelope is opened after the patient completes the pretest data collection procedures.

Study Retention and Adherence

An important retention strategy is to engage the patients as active partners in the study by explaining the importance of their contribution. We have built trusting relationships with the clinic staff and patient panel, which facilitated the success of our feasibility study and an 18-month longitudinal study (1R01HL124945) that have resulted in several publications [50-55]. Other important retention and adherence strategies include contacting participants for data collection and updating contact information every month. We hired a health care worker from the community to serve as the study support staff for the YCWS intervention. We will send electronic birthday cards and birthday wishes via email and text message. We will also obtain participants' addresses, telephone numbers, and 3 other secondary contacts to track them during the 6-month study. We will provide incentives to motivate individuals to enroll in the study, maintain interest, and sustain participation for 6 months of self-monitoring or YCWS. All participants will retain the US $150 Galaxy tablet they use for the study as acknowledgment of their time and participation. We will pay US $50 per month as internet access costs for each participant for 6 months. At the end of 6 months, the total incentive is US

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$450 per participant, which includes the study tablet and accessory cost. In addition, we will use other general study procedures, including (1) text messaging, video messaging, emailing, or calling participants to remind them if they have not provided data for the day and to encourage them to do so and (2) updating patient addresses and phone numbers as needed during each contact.

Interventions

Experimental Arm

The experimental arm includes self-monitoring of pain and stress, electronic monitoring of opioid use, alerts or reminders, and use of YCWS (3 video banks of RDE and support). The YCWS app features self-monitoring, video banks, and support elements, which comprise the YCWS intervention (Tables 1 and 2).

When patients log in to the system, they can select the stress intensity scale (0-10) and pain intensity scale (0-10), set plans, or video banks subtabs that display on the screen consecutively (Figure 1). Patients will touch the screen to record their stress and pain intensities. Once their stress or pain intensity is recorded, they will receive instantaneous feedback via graphical readout (Figure 2 presents an approximate model of the graphical readout) showing their stress and pain during the past week (including the present day), pain goals, and daily YCWS use. An auxiliary icon under self-monitoring shows *Set your plans (Goal setting)*. The patient can use this auxiliary icon to revise optimal and tolerable pain goals and time of day to complete study activities including support and to set alerts or reminders. When patients click *video banks* (Table 3), 3 subicons (basic, everyday, and favorite) will be displayed.

Table 1. Proposed links between YCWS[a] app features, examples of YCWS self-management intervention, and self-management skills.

YCWS module	YCWS app features	Examples of YCWS intervention self-management activities	Self-management skills
1	View or update and self-monitor goals, profile, and activities	• Patient self-monitors, that is, sets goals for time of day for daily tracking of stress, pain, and opioids use; uses YCWS intervention; or searches for other video links for everyday videos. Patient sets pain control goals regarding optimal pain goal and tolerable pain goal. Patient sets time of day to receive system-generated alerts and reminders, if they have not completed data entry for the day. • Patient records self-monitoring data for stress, pain, and opioids use. Patient records searches for other video links for the everyday videos. Patient records time to contact study support staff for troubleshooting issues with YCWS app.	Goal setting and action planning
2	Use video banks for stress and pain reduction	• Patient views videos as needed. Patient identifies which of the video links produce stress and pain reduction that met their optimal and tolerable pain goals that were set in module 1 and decides whether to use the same video link multiple times or try another video link.	Action planning and decision-making
3	Get support; patient control panel; receive system-generated alerts or reminders; and contact from study staff, if no data are entered after 24 hours	• Patient reviews reminders (eg, how many minutes are left before the next recording of stress, pain, opioids use or to use video banks) or documents questions for study support staff about barriers to and facilitators of self-management. • If the patient does not enter data after 24 hours, the study support staff will contact them 2 hours before the next data collection time for troubleshooting. • Patient conducts study for the day or responds to support staff about any barriers to completing the study activities as set in self-monitoring goals.	Action planning, problem solving, and decision-making

[a]YCWS: You Cope, We Support.

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Table 2. Proposed links between YCWS[a] app features and examples of control self-management activities.

YCWS module	YCWS app features	Examples of control self-management activities
1	View or update and self-monitor	• Patient self-monitors by daily tracking of stress and pain. • Patient records self-monitoring data for stress and pain.
2	Get support, patient control panel, and receive system-generated alerts or reminders	• Patient reviews alerts or reminders (eg, how many minutes are left before the next recording of stress and pain). • If the patient does not enter data after 24 hours, the study support staff will contact them 2 hours before the next data collection time for troubleshooting.

[a]YCWS: You Cope, We Support.

Figure 1. Screenshot of daily stress and pain monitoring for the experimental group.

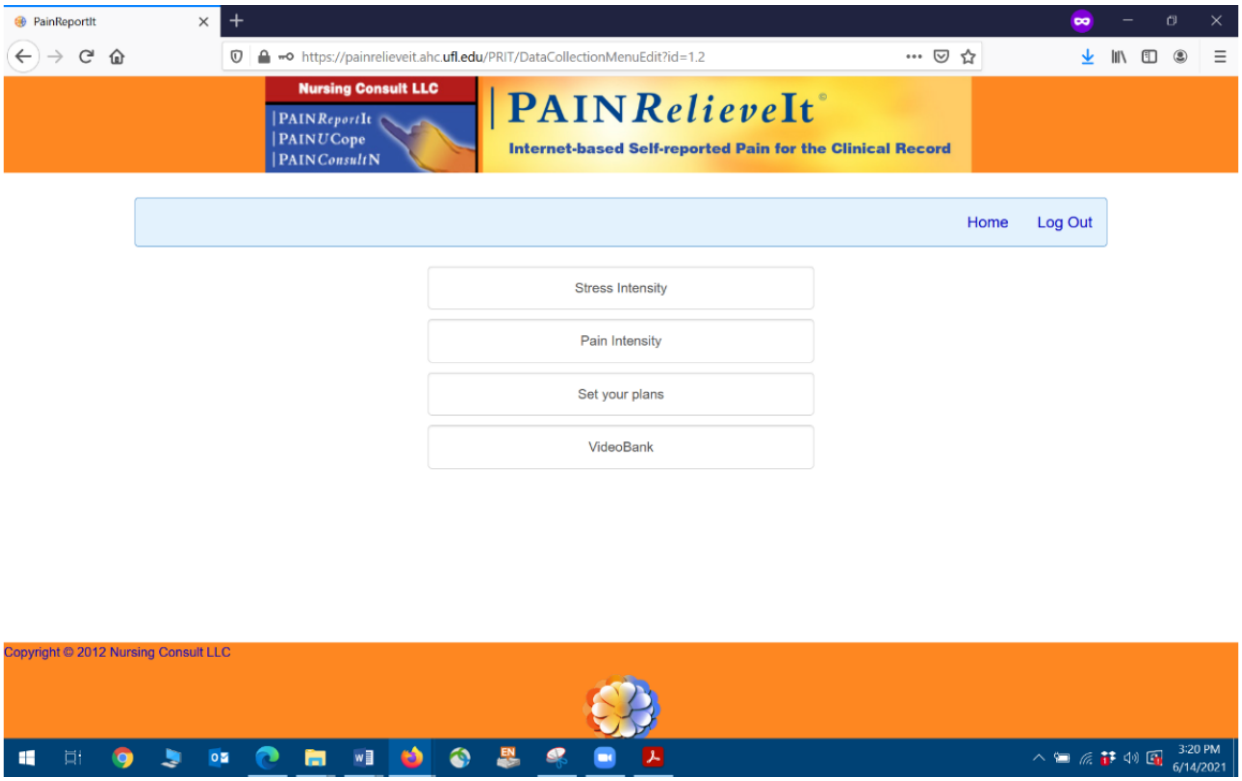

Figure 2. Exemplar Feedback via Graphical Readout for Pain Intensity. YCWS: You Cope, We Support.

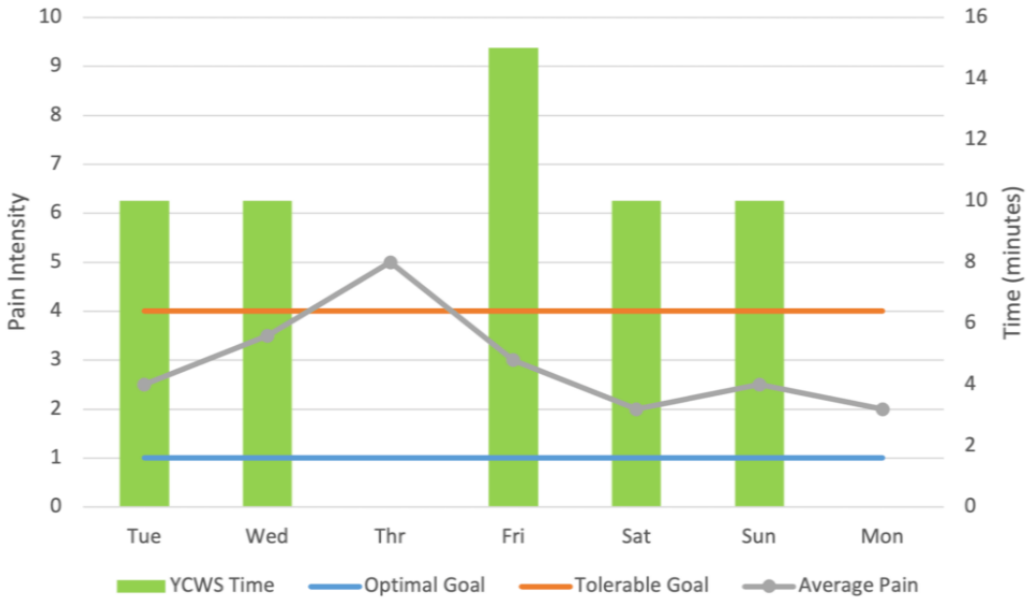

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Table 3. Description of You Cope, We Support banks of video links.

Study period and basic videos	Everyday videos	Favorite videos
Short term		
• A total of 6 video clips of guided relaxation and distraction exercises of various lengths: 2, 5, 8, 10, 15, and 20 minutes	• Links to investigator-vetted relaxation and distraction exercises of various lengths that are freely available on YouTube	• Initially, it will be an empty portfolio. • Patients will store their favorite relaxation and distraction video links, which they can choose from basic videos and everyday videos.
• Used all through week 1 to become familiar with the intervention and learn deep breathing exercise through instructions	• Used during weeks 2-8	• Used during weeks 2-8.

• A total of 4 active components of the relaxation and distraction exercises:
  • Soothing female voice
  • Smoke images that change shape
  • Deep breathing exercise
  • Background sound
	• A total of 4 active components varied across two categories. Category 1:
	  • Either male or female voices
	  • Variety of nature images
	  • Background nature sounds
	  • Deep breathing exercise
	• Category 2
	  • Variety of nature images
	  • Background nature sounds
	  • No voice
	  • No deep breathing exercise
		• On the basis of patients' preference.
		• Investigators do not control the active components.

Long term		
• Patients will continue to use video bank	• Patients will continue to use video bank	• Patients will continue to use video bank. • Patients will have the ability to find their favorite video clips on the web and add them to favorite videos for personal use and recommend them via the investigators to the community of patients with sickle cell disease. • Investigator will sequester and vet links that are not from basic videos and everyday videos to ascertain that they work and are valid before other patients can view them.

Individuals can click on any of the 3 banks to choose a video to watch. The YCWS intervention can be customized by choosing video clips based on female or male voice, type of nature images, background sound, or lengths and by finding their own video clips. Patients can watch as many video clips as needed. Patients would be able to discern whether they received stress or pain relief after using the videos and determine which of the videos provided them with the most stress or pain relief. According to individual preference, we will send system-generated alerts or reminders to patients or a research staff will call, text, or email the patients to facilitate data entry and intervention use every 24 hours. The patient can also connect with our support staff about issues related to YCWS intervention use (experimental group only) and technical difficulties with study device or app for advice on what to do (both groups). Our support staff will monitor our database daily. If the patient does not enter data after 24 hours of system-generated alerts or reminders or messages via staff cell phone, the study support staff will contact them for data entry troubleshooting and, for the experimental group, for YCWS use as they indicated in their goals. During the short-term trial (weeks 1-8), patients will monitor their stress and pain daily, as described previously.

We will provide experimental group members access to 3 video banks from which they can choose their daily intervention. Patients will use only basic videos during week 1 to become familiar with the intervention and learn deep breathing and relaxation exercises through instructions. For example, one of the basic video clips entitled *Breathing out worry, breathing in light* guides the patients to "Notice the cloud-like formations on the screen. Observe how the images drift and change. As you breathe deeply, let your concerns and tensions (which worry you go) out into the atmosphere where they can dissolve just as the cloud-like formations on the screen dissolve and vanish from view. It is all right to let go of your worries. In fact, it is important to your health that you do so. Just breathe out problems and worries. See them drift off, walking by, and off the screen, no longer a part of you. Now, breathe in sunshine and healing energy." This requirement is critical and supported by recent evidence showing that the respiratory control center communicates directly with and controls a brain center linked to attention, arousal, and panic [56]. Corless et al [57-60] (Corless, B, unpublished data, January 2022) used these

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approaches in psychoneuroimmunology studies in patients with cancer or HIV, and we used them in our feasibility studies in patients with SCD. Some of the active components in the basic videos include colorful images similar to smoke or other nature images that slowly change shape against a dark background (images that do not represent any concept with known negative connotations), soothing female or male voice, deep breathing exercise, and slow-paced guided relaxation and distraction instructions. During weeks 2 to 8, patients will also have access to everyday videos and favorite videos.

During weeks 1 to 8, we will send system-generated alerts or reminders or messages every 24 hours to patients in the experimental group via phone call, text, or email to facilitate intervention use. If the patient does not enter data after 24 hours, the study support staff, who will be from the community or RS, will contact them 2 hours before the next data collection time for troubleshooting. The support staff will contact patients via chat, text, email, phone call, or FaceTime based on patients' preferences to facilitate participation and troubleshoot. Owing to travel burdens including worsening of their pain in cold or hot weather, patient attendance in the monthly SCD support group is extremely low (1-2 patients per month). Patients with SCD report a preference for active remote support as opposed to face-to-face peer or social support because of weather, travel, and parking issues involved with receiving the support at an academic health center. Remote support also empowers them to participate in the study without the additional burden of traveling to the location of any peer or social support as recommended by the Chronic Disease Self-Management Program [61]. We specifically designed the support component of YCWS to incorporate the recommendations from our patient team members to address these issues and refine feedback messages and format.

During the long-term period (months 3-6), only system-generated alerts or reminders via messaging service or staff cell phone will be available. Patients will have the ability to find their favorite video clips on the web, add them to *favorite videos* for personal use, and recommend them via the investigators to other patients with SCD. We will vet these recommendations before releasing them to other patients. Throughout the study period, we will time stamp and track the patients' YCWS web-based activities to capture data on system use.

Control Arm

The control arm includes self-monitoring of pain and stress, electronic monitoring of opioid use, and alerts or reminders. During the efficacy trial (weeks 1-8), similar to patients in the experimental group, patients will monitor their stress, pain, and opioid use daily. We will send system-generated alerts or reminders every 24 hours to patients via phone call, text, or email to facilitate data entry. If the patient does not enter the data after 24 hours of alerts or reminders, the study support staff will contact them for data entry troubleshooting. During the long-term period (months 3-6), patients will continue to self-monitor their daily stress and pain and use the electronic opioid use monitoring device. Patients will also continue to receive system-generated alerts or reminders via messaging service or staff cell phone. Throughout the study period, we will time stamp and track patients' web-based activities to capture data on system use and outcome variables.

Protocol Adherence Check for the Fidelity of the Control and YCWS Interventions

The PI will conduct reliability assessments for the RS's implementation of the protocol on a random sample of 20% of the study measures. Although this assessment cannot be blinded, the RS will not be informed of the reliability check until the baseline data collection procedure is underway. If there are any deviations from the protocol, the RS will undergo additional training and supervised data collection to ensure protocol adherence.

Intervention Fidelity

To improve fidelity, we will ensure that participants use the YCWS intervention as intended by monitoring the participants' YCWS system use on the web. During the first 8 weeks, we will call or text participants 2 hours before the next data collection time if the patient does not enter data after 24 hours of system-generated alerts or reminders and has missed the period they indicated for completing the study, to encourage the use of YCWS. We will also ascertain if they are having trouble with accessing the program and will troubleshoot with the participants to resolve any issues. We will also monitor the participants' self-monitoring of stress, pain, and opioid use in both groups. As a measure of intervention fidelity, the use of the system and measures will be documented by the app software that automatically writes time-stamped data to a SQL database. The fidelity of our pilot feasibility protocol is rigorous as the program is computerized and consistently implemented. In addition, we will monitor mobile device use, and time of use will be documented in the database to determine the intervention dose.

Outcome Measures

Primary Outcome (Pain)

Pain, the primary outcome, will be measured using the pain intensity scale. This 3-item scale asks patients to report their current, least, and worst pain intensity in the past 24 hours on a scale of 0 (no pain) to 10 (pain as bad as it could be). We will calculate the average of the 3 scores to obtain an average pain intensity score, which has an internal consistency (α) of .85 [62] and predictive validity (Ezenwa, M, unpublished data, April 2022) in the population with SCD.

Secondary Outcomes (Stress and Opioid Use)

Stress

Stress will be measured using the stress intensity scale. This 3-item scale asks patients to report their current, least, and worst stress intensity in the past 24 hours on a scale of 0 (no stress) to 10 (stress as bad as it could be). We will calculate the average of the 3 scores to obtain an average stress intensity score. The internal consistency (α) of the stress intensity in the SCD sample was .82 [37]. It showed moderate, but not significant, correlation (r=0.41; P=.07) with the participants' Perceived Stress

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Questionnaire (PSQ)-Recent score, demonstrating fair construct validity [37].

Opioid Use

We will use PAINReportIt [63-65] software program (Nursing Consult LLC) to collect data on drug names and doses of scheduled and as-needed opioid analgesics at baseline, and the data will be updated at week 8 and month 6. We will track opioid refills through patients' pharmacies. We will use the Wisepill medication event monitoring system to collect data on opioid use. The Wisepill records the quantity of the medications. Each patient will receive 2 Wisepill devices, one for scheduled opioids and the other for as-needed opioids. The Wisepill medication event monitoring system was designed to monitor medication adherence and provide instant feedback via cellphone and internet technologies. The Wisepill has been used by patients with various health conditions, including tuberculosis [66], HIV [67], depression [68], and SCD [69]. The dispenser was designed such that it would be compelling and easy to use. It holds approximately 30 large pills or 60 small pills in a 7-compartment inner container and is powered by a 1100 mA lithium polymer rechargeable battery. We will use the Wisepill to record patients' opioid use. Each week, the patient will fill the Wisepill with their scheduled and as-needed opioid medications on the day of the week indicated in their goals. Subsequently, patients will dispense their daily doses of medication from the Wisepill. Each time the compartment is opened, a cellular signal is sent and recorded in real time on a web-based server. The data are immediately accessible to the research staff for downloading via a secure internet interface. Lucero et al [67] have used this device in previous studies.

Descriptive and Process Measures

PSQ-Recent

PSQ-Recent [70] is a 30-item tool that measures general perceived stress in the past week. The response options are 1 (almost never) to 4 (usually). Overall perceived stress index score is computed by subtracting 30 from the raw sum score and, then, dividing by 90, yielding scores that range from 0 to 1. High scores indicate great perceived stress. PSQ-Recent has demonstrated good test-retest reliability of 0.82 and good construct validity with the Perceived Stress Scale by Cohen (r=0.73) [70]. The internal consistency (α) reliability of the PSQ-Recent in our SCD sample was .94 [30]. We will collect these data to understand the context of our intervention.

System-Based Daily Activity

We will collect data on patients' daily activities, such as the time spent on the YCWS intervention, including the time spent in using the video banks of RDE. The software will capture these activities by time-stamped data in the SQL database.

Demographic Characteristics

Questions regarding demographic characteristics and analgesics are also included in PAINReportIt [63-65]. Patients will report their age, sex, ethnicity, marital status, level of education, family income, weight, height, physical activity levels (per week), smoking status, stage in the menstrual cycle (women), previous use of computers, current access to computers, distance from care, and quality of internet connection. These data will be collected as composite demographic data to assess the participants' representativeness and for prediction modeling.

Sickle Cell Self-efficacy Scale

The Sickle Cell Self-Efficacy Scale is a 9-item tool that measures patients' beliefs in their ability to engage in daily activities despite having SCD and coping with obstacles or setbacks associated with SCD. For example, one of the items asks patients, "How sure are you that you can reduce your SCD pain by using methods other than taking extra pain medication?" The response options are 1 (not at all sure) to 4 (very sure). The total self-efficacy score is the sum of the 9 items, with scores ranging from 9 to 36. High scores indicate great self-efficacy. The Sickle Cell Self-Efficacy Scale has been validated in patients with SCD who are ≥11 years and has an internal consistency (α) of .87 in the population with SCD [71].

Study Acceptability Scale

Patients will also be asked to complete a 6-item questionnaire that focuses on the acceptability of the study [65]. Response options depend on the question. For example, the first question queries "Was participating in this study too hard?" The response choices are (1) not hard at all, (2) somewhat hard, and (3) too hard. This tool has been validated in the population with SCD in a study in which pen tablets were used [65] and in the preliminary study supporting this RCT. This scale provides data on the patients' thoughts about the study processes and will help plan effectiveness or implementation studies.

Exit Interview Guide

This measure contains open-ended questions to solicit patients' experiences with using a tablet for data collection (3 questions) and opinions (experimental group only) about the YCWS video clips and how they can be improved (3 questions). We will conduct an exit interview about staff support's acceptability (1 question) and system-generated support (1 question). We will conduct the exit interview at week 8 (RCT-exit; short term) and month 6 (RCT-exit; long term). The exit interview will be audiotaped and transcribed verbatim. We used this measure in our feasibility study. We will use patients' feedback to modify and improve our protocol for future studies.

Data Collection and Management

The research data will be collected electronically using laptop and pen tablet computers. All the study surveys may be completed via the web using an app developed for this study. This application will contain PAINReportIt, a computer program developed by DJW to collect participants' pain information and other surveys in electronic format. Participants' data will be written directly to that server and will not reside, even temporarily, on the laptop or pen tablet computer. We will use HTTPS for encrypted data transfer to the College of Nursing server. The data will be stored in a secure College of Nursing server with access restricted to the immediate study personnel. All patients will be assigned a code number, and the research team will identify their data only with that code number. The link of the code numbers to the participant identifiers will be kept separate from the study data. Only the investigators and key personnel will have access to the code or master key. Any

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hard data collected will be stored in a locked office at the College of Nursing.

The software design will make every effort to reduce user errors; all data will be entered directly by the participant using an interface tested with cognitive interview methods that informed the final interface design. Consistency checks are built into the software so that inconsistent data (eg, out of range or logically inconsistent) are flagged immediately to inform the users and assess their intent. In addition, there will be more comprehensive consistency checks before data analysis. Inconsistent data points will be treated as missing. On the basis of our previous studies with this web application, we expect the percentage of inconsistent data values to be very low (<0.5%).

Statistical Analysis

Overview

The study biostatistician will perform data management and analysis in collaboration with the PI and coinvestigators. The data will be stored in an SQL database and exported to the statistical software R for analysis. We will use an intention-to-treat approach, which includes all randomized participants in our analysis. We will consider $P<.025$ as statistically significant for intervention efficacy tests (short term and long term) on the primary outcome of pain intensity. For other inferences, we will consider $P<.05$ to be statistically significant. We will compute descriptive statistics (frequencies, means, SDs, etc) of baseline patient characteristics data, including demographics, pain, stress, and analgesic use before the test and compare the control group and the experimental group using chi-square tests or 2-tailed *t* tests. We expect no significant difference between the 2 randomly generated groups.

Aim 1 Analysis

To study the short-term effect of the intervention on the primary outcome (pain intensity) and secondary outcomes (stress intensity and opioid use), all of which are measured daily, we will use linear mixed effects models. Fixed effect terms in the models include the group variable to represent the treatment effect and baseline outcome measurement. Participant-specific random effect terms will be used to account for within-participant correlation in repeat measures. Note that we do not include the time variable in our models because we are primarily interested in the treatment effect on the average pain, stress, and opioid use over time. We do not anticipate significant time trends, but will explore them in the secondary analysis.

Aim 2 Analysis

To estimate the long-term effects of the intervention, we will again use linear mixed effects models. Fixed effect terms in the models include the group variable to represent the treatment effect and baseline outcome measurement. Participant-specific random effect terms will be used to account for within-participant correlation in repeat measures.

Aim 3 Analysis

We will construct machine learning models, in particular, random forest models, to predict outcomes based on patient group assigned, patient's personal characteristics (eg, self-efficacy, sex, education, family income, and computer experience), and environmental factors (eg, distance from care and quality of internet connection). A random forest model consists of a large ensemble of regression trees and the average prediction of these trees will be output as the prediction of the model. Regression trees can accommodate nonlinearity and complex interaction without manual specification by researchers, but have the disadvantage of noisiness. Random forest retains the advantage of tree, while reducing noise by introducing randomness in the form of training each component tree with a bootstrap sample of the original training data and randomly selecting a subset of predictors as candidate for splitting at each split of the tree, to reduce the correlation between the trees and the variance of average prediction. We will use a random 70/30 partition (stratified by group and baseline pain) to reserve 30% of the patient sample as the test set, with the remaining 70% as the training set. We will use cross validation to optimize the parameters (minimal node size and number of random features selected for each split) for the random forest prediction models. The models, trained and optimized on the training data set, will be assessed using the reserved test data set to obtain an unbiased estimate of its performance when applied to new data. These models will allow us to identify individuals most likely to benefit from the proposed intervention and the modifiable environmental factors to improve the effects of the intervention.

Missing Data

Random effect models can accommodate longitudinal data with missing visits. For visits with partial data (item-level missing data), we will use multiple imputation by fully conditional specification to generate multiple completed data sets, on each of which statistical inference will be performed separately and then aggregated using Rubin rule [72]. This allows us to fully use the information provided by the participants.

Sample Power

The success of this study lies on its short-term and long-term efficacy on the primary outcome of pain intensity. We conservatively assume an SD of 3 for pain intensity based on values we observed in earlier studies. With a 2-sided type I error of 0.025, the proposed sample of 170 patients provides 80% power to detect a pain reduction of 1.5, below the minimal pain reduction of 2, which is considered as clinically meaningful.

Results

The project was funded by the National Institutes of Health and National Institute of Nursing Research. Our IRB approved the study on May 14, 2020.

Study recruitment started on March 29, 2021. As of April 2022, we had enrolled 45.9% (78/170) participants in the study. Of the 78 participants, 65 (83%) participants have completed baseline, 53 (68%) have completed the postintervention assessment after 8 weeks, and 28 (36%) have completed the 6-month study.

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Discussion

Study Significance

As technology advances, the use of mHealth apps is becoming an integral part of daily life, including for self-management of chronic conditions. Web-based interventions and technologies are reported to have high usability and acceptability as a tool to monitor and self-report daily pain [73-75], monitor medication adherence [76-79], increase SCD reproductive knowledge scores [80,81], and reduce current pain and stress levels [37]. To the best of our knowledge, we are the first to use an mHealth intervention with self-management RDEs to reduce stress and improve SCD pain control, with a concomitant reduction in opioid use.

This protocol paper presents the design of the RADIANCE study, an RCT with the long-term goal to reduce stress and improve pain control in patients with SCD with less opioid use. The intervention with self-management RDEs, YCWS, can offer interactive learning that allows sustained or repeated sessions. Although the intervention may have no direct benefit to individual participants, it may provide individuals with previously unrecognized insights about their stress, pain, and opioid use and options for self-management of these symptoms.

Strengths and Limitations

A strength of this guided relaxation study is its web-based design and implementation that provides patients with the ability to interact with the program at their convenience in real-world settings. By providing the tools to reduce their pain, it may help patients with SCD to feel empowered. Given that the guided relaxation is web-based, the patients may have a sense of control and empowerment. However, the web-based design can also be a limitation if internet connection becomes an issue. We attempt to mitigate this potential effect by making the intervention platform independent and allowing patients to go to the library and use the library computer or use their other smart devices for the study. Furthermore, the findings of this study will be generalized only to the state of Florida and not nationwide.

Although recruiting patients from health care networks and churches is a new strategy for us in Gainesville, Florida, this will likely be an opportunity for access to affected communities (ie, college students and other young adults). We will report on the patients' YCWS web-based activities, data on system use, and pain and stress intensity. The study has the potential for assisting people to develop the confidence necessary to self-manage stress that could intensify their acute or persistent SCD pain. If demonstrated to be effective, this internet-based and web-based intervention could be made available nationwide and, eventually, worldwide.

Dissemination Plan

To maximize the dissemination of this study, we will share methodological approaches, data, and results generated from this study by publishing our findings in research journals that are indexed by PubMed and generally accessible to the research community. We will also present the findings and methodologies at national and international research and health care conferences in accordance with the proposed study time line.

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Authors' Contributions

MOE designed the study in collaboration with YY and DJW. All authors are involved in data collection and writing the manuscript.

Conflicts of Interest

None declared.

References

1. Centers for Disease Control and Prevention. 2022 May 2. URL: http://genes-r-us.uthscsa.edu/newborn_reports [accessed 2022-06-06]
2. Piel FB, Hay SI, Gupta S, Weatherall DJ, Williams TN. Global burden of sickle cell anaemia in children under five, 2010-2050: modelling based on demographics, excess mortality, and interventions. PLoS Med 2013;10(7):e1001484 [FREE Full text] [doi: 10.1371/journal.pmed.1001484] [Medline: 23874164]
3. Prevalence and incidence of sickle cell disease. Healthgrades. 2006. URL: http://www.wrongdiagnosis.com/s/sickle_cell_anemia/prevalence.htm#prevalence_intro [accessed 2006-10-13]
4. Lanzkron S, Carroll CP, Haywood Jr C. The burden of emergency department use for sickle-cell disease: an analysis of the national emergency department sample database. Am J Hematol 2010 Oct;85(10):797-799 [FREE Full text] [doi: 10.1002/ajh.21807] [Medline: 20730795]

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5. Lee A, Thomas P, Cupidore L, Serjeant B, Serjeant G. Improved survival in homozygous sickle cell disease: lessons from a cohort study. BMJ 1995 Dec 16;311(7020):1600-1602 [FREE Full text] [doi: 10.1136/bmj.311.7020.1600] [Medline: 8555802]
6. DeBaun MR, Ghafuri DL, Rodeghier M, Maitra P, Chaturvedi S, Kassim A, et al. Decreased median survival of adults with sickle cell disease after adjusting for left truncation bias: a pooled analysis. Blood 2019 Feb 07;133(6):615-617 [FREE Full text] [doi: 10.1182/blood-2018-10-880575] [Medline: 30530750]
7. Atkin K, Ahmad WI. Living a 'normal' life: young people coping with thalassaemia major or sickle cell disorder. Soc Sci Med 2001 Sep;53(5):615-626. [doi: 10.1016/s0277-9536(00)00364-6] [Medline: 11478541]
8. Casey RL, Brown RT. Psychological aspects of hematologic diseases. Child Adolesc Psychiatr Clin N Am 2003 Jul;12(3):567-584. [doi: 10.1016/s1056-4993(03)00025-7] [Medline: 12910823]
9. Gladwin MT, Sachdev V, Jison ML, Shizukuda Y, Plehn JF, Minter K, et al. Pulmonary hypertension as a risk factor for death in patients with sickle cell disease. N Engl J Med 2004 Feb 26;350(9):886-895. [doi: 10.1056/NEJMoa035477] [Medline: 14985486]
10. Lemanek KL, Buckloh LM, Woods G, Butler R. Diseases of the circulatory system: sickle cell disease and hemophilia. In: Roberts MC, editor. Handbook of Pediatric Psychology. 2nd ed. New York, NY, USA: The Guilford Press; 1995:286-309.
11. Logan DE, Radcliffe J, Smith-Whitley K. Parent factors and adolescent sickle cell disease: associations with patterns of health service use. J Pediatr Psychol 2002;27(5):475-484. [doi: 10.1093/jpepsy/27.5.475] [Medline: 12058011]
12. Moskowitz JT, Butensky E, Harmatz P, Vichinsky E, Heyman MB, Acree M, et al. Caregiving time in sickle cell disease: psychological effects in maternal caregivers. Pediatr Blood Cancer 2007 Jan;48(1):64-71. [doi: 10.1002/pbc.20792] [Medline: 16622841]
13. Platt OS, Brambilla DJ, Rosse WF, Milner PF, Castro O, Steinberg MH, et al. Mortality in sickle cell disease. Life expectancy and risk factors for early death. N Engl J Med 1994 Jun 09;330(23):1639-1644. [doi: 10.1056/NEJM199406093302303] [Medline: 7993409]
14. Powars D, Weidman JA, Odom-Maryon T, Niland JC, Johnson C. Sickle cell chronic lung disease: prior morbidity and the risk of pulmonary failure. Medicine (Baltimore) 1988 Jan;67(1):66-76. [Medline: 3336282]
15. While AE, Mullen J. Living with sickle cell disease: the perspective of young people. Br J Nurs 2004;13(6):320-325. [doi: 10.12968/bjon.2004.13.6.12528] [Medline: 15126965]
16. Wilkie DJ, Molokie R, Boyd-Seal D, Suarez ML, Kim YO, Zong S, et al. Patient-reported outcomes: descriptors of nociceptive and neuropathic pain and barriers to effective pain management in adult outpatients with sickle cell disease. J Natl Med Assoc 2010 Jan;102(1):18-27 [FREE Full text] [doi: 10.1016/s0027-9684(15)30471-5] [Medline: 20158132]
17. Brousseau DC, Owens PL, Mosso AL, Panepinto JA, Steiner CA. Acute care utilization and rehospitalizations for sickle cell disease. JAMA 2010 Apr 07;303(13):1288-1294. [doi: 10.1001/jama.2010.378] [Medline: 20371788]
18. Shankar SM, Arbogast PG, Mitchel E, Cooper WO, Wang WC, Griffin MR. Medical care utilization and mortality in sickle cell disease: a population-based study. Am J Hematol 2005 Dec;80(4):262-270 [FREE Full text] [doi: 10.1002/ajh.20485] [Medline: 16315251]
19. Liebeskind JC. Pain can kill. Pain 1991 Jan;44(1):3-4. [doi: 10.1016/0304-3959(91)90141-J] [Medline: 2038486]
20. Page GG. The medical necessity of adequate pain management. Pain Forum 1996 Dec;5(4):227-233. [doi: 10.1016/s1082-3174(96)80001-8]
21. Page GG, Ben-Eliyahu S. Pain kills: animal models and neuro-immunological links. In: Payne R, Patt RB, Hill CS, editors. Assessment and Treatment of Cancer Pain - Progress in Pain Research and Management. Seattle, WA, USA: IASP Press; 1998.
22. Page JC, Chen EY. Management of painful diabetic neuropathy. A treatment algorithm. J Am Podiatr Med Assoc 1997 Aug;87(8):370-379. [doi: 10.7547/87507315-87-8-370] [Medline: 9274092]
23. Bernaudin F, Socie G, Kuentz M, Chevret S, Duval M, Bertrand Y, SFGM-TC. Long-term results of related myeloablative stem-cell transplantation to cure sickle cell disease. Blood 2007 Oct 01;110(7):2749-2756 [FREE Full text] [doi: 10.1182/blood-2007-03-079665] [Medline: 17606762]
24. Hoban MD, Orkin SH, Bauer DE. Genetic treatment of a molecular disorder: gene therapy approaches to sickle cell disease. Blood 2016 Feb 18;127(7):839-848 [FREE Full text] [doi: 10.1182/blood-2015-09-618587] [Medline: 26758916]
25. Krishnamurti L, Neuberg DS, Sullivan KM, Kamani NR, Abraham A, Campigotto F, et al. Bone marrow transplantation for adolescents and young adults with sickle cell disease: results of a prospective multicenter pilot study. Am J Hematol 2019 Apr;94(4):446-454 [FREE Full text] [doi: 10.1002/ajh.25401] [Medline: 30637784]
26. Brotman DJ, Golden SH, Wittstein IS. The cardiovascular toll of stress. Lancet 2007 Sep 22;370(9592):1089-1100. [doi: 10.1016/S0140-6736(07)61305-1] [Medline: 17822755]
27. Makino S, Hashimoto K, Gold PW. Multiple feedback mechanisms activating corticotropin-releasing hormone system in the brain during stress. Pharmacol Biochem Behav 2002 Aug;73(1):147-158. [doi: 10.1016/s0091-3057(02)00791-8] [Medline: 12076734]
28. Selye H. A syndrome produced by diverse nocuous agents. 1936. J Neuropsychiatry Clin Neurosci 1998;10(2):230-231. [doi: 10.1176/jnp.10.2.230a] [Medline: 9722327]

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29. McEwen BS, Kalia M. The role of corticosteroids and stress in chronic pain conditions. Metabolism 2010 Oct;59 Suppl 1:S9-15. [doi: 10.1016/j.metabol.2010.07.012] [Medline: 20837196]
30. Ezenwa MO, Molokie RE, Wilkie DJ, Suarez ML, Yao Y. Perceived injustice predicts stress and pain in adults with sickle cell disease. Pain Manag Nurs 2015 Jun;16(3):294-306 [FREE Full text] [doi: 10.1016/j.pmn.2014.08.004] [Medline: 25439119]
31. Porter LS, Gil KM, Sedway JA, Ready J, Workman E, Thompson Jr RJ. Pain and stress in sickle cell disease: an analysis of daily pain records. Int J Behav Med 1998;5(3):185-203. [doi: 10.1207/s15327558ijbm0503_1] [Medline: 16250701]
32. Petrelluzzi KF, Garcia MC, Petta CA, Grassi-Kassisse DM, Spadari-Bratfisch RC. Salivary cortisol concentrations, stress and quality of life in women with endometriosis and chronic pelvic pain. Stress 2008 Sep;11(5):390-397. [doi: 10.1080/10253890701840610] [Medline: 18800310]
33. Gil KM, Carson JW, Porter LS, Scipio C, Bediako SM, Orringer E. Daily mood and stress predict pain, health care use, and work activity in African American adults with sickle-cell disease. Health Psychol 2004 May;23(3):267-274. [doi: 10.1037/0278-6133.23.3.267] [Medline: 15099167]
34. Clarke TC, Black LI, Stussman BJ, Barnes PM, Nahin RL. Trends in the use of complementary health approaches among adults: United States, 2002-2012. Natl Health Stat Report 2015 Feb 10(79):1-16 [FREE Full text] [Medline: 25671660]
35. Thompson WE, Eriator I. Pain control in sickle cell disease patients: use of complementary and alternative medicine. Pain Med 2014 Feb;15(2):241-246. [doi: 10.1111/pme.12292] [Medline: 24524842]
36. Gil KM, Wilson JJ, Edens JL, Webster DA, Abrams MA, Orringer E, et al. Effects of cognitive coping skills training on coping strategies and experimental pain sensitivity in African American adults with sickle cell disease. Health Psychol 1996 Jan;15(1):3-10. [doi: 10.1037//0278-6133.15.1.3] [Medline: 8788535]
37. Ezenwa MO, Yao Y, Engeland CG, Molokie RE, Wang ZJ, Suarez ML, et al. A randomized controlled pilot study feasibility of a tablet-based guided audio-visual relaxation intervention for reducing stress and pain in adults with sickle cell disease. J Adv Nurs 2016 Jun;72(6):1452-1463. [doi: 10.1111/jan.12895] [Medline: 26768753]
38. Thomas VN, Wilson-Barnett J, Goodhart F. The role of cognitive-behavioural therapy in the management of pain in patients with sickle cell disease. J Adv Nurs 1998 May;27(5):1002-1009. [doi: 10.1046/j.1365-2648.1998.00584.x] [Medline: 9637327]
39. Kleber HD, Weiss RD, Anton Jr RF, George TP, Greenfield SF, Kosten TR, et al. Practice guideline for the treatment of patients with substance use disorders. 2nd edition. American Psychiatric Association. 2006 Aug. URL: https://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/substanceuse.pdf [accessed 2022-03-08]
40. Anie KA, Green J. Psychological therapies for sickle cell disease and pain. Cochrane Database Syst Rev 2015 May 08;2015(5):CD001916 [FREE Full text] [doi: 10.1002/14651858.CD001916.pub3] [Medline: 25966336]
41. Han J, Zhou J, Saraf SL, Gordeuk VR, Calip GS. Characterization of opioid use in sickle cell disease. Pharmacoepidemiol Drug Saf 2018 May;27(5):479-486 [FREE Full text] [doi: 10.1002/pds.4291] [Medline: 28815799]
42. Smith WR, Bovbjerg VE, Penberthy LT, McClish DK, Levenson JL, Roberts JD, et al. Understanding pain and improving management of sickle cell disease: the PiSCES study. J Natl Med Assoc 2005 Feb;97(2):183-193. [Medline: 15712781]
43. Dowell D, Haegerich TM, Chou R. CDC guideline for prescribing opioids for chronic pain - United States, 2016. MMWR Recomm Rep 2016 Mar 18;65(1):1-49. [doi: 10.15585/mmwr.rr6501e1] [Medline: 26987082]
44. Ruta NS, Ballas SK. The opioid drug epidemic and sickle cell disease: guilt by association. Pain Med 2016 Oct;17(10):1793-1798. [doi: 10.1093/pm/pnw074] [Medline: 27152018]
45. Federal Pain Research Strategy. The National Institutes of Health Interagency Pain Research Coordinating Committee. 2021. URL: https://www.iprcc.nih.gov/federal-pain-research-strategy-overview [accessed 2022-03-15]
46. Ahles TA, Blanchard EB, Ruckdeschel JC. The multidimensional nature of cancer-related pain. Pain 1983 Nov;17(3):277-288. [doi: 10.1016/0304-3959(83)90100-8] [Medline: 6657288]
47. Abudawood K. Quantification of patient-reported pain locations: development of an automated measurement method. Computers, Informatics, Nursing (In press) 2021.
48. Dyal BW, Ezenwa MO, Yao Y, Molokie RE, Wang ZJ, Ballas SK, et al. Randomized clinical trial of computerized PAINRelieveIt® for patients with sickle cell disease: PAINReportIt® and PAINUCope®. Patient Educ Couns 2020 Jan;103(1):136-144 [FREE Full text] [doi: 10.1016/j.pec.2019.08.021] [Medline: 31451364]
49. Ezenwa MO, Molokie RE, Wang ZJ, Yao Y, Suarez ML, Angulo V, et al. Outpatient pain predicts subsequent one-year acute health care utilization among adults with sickle cell disease. J Pain Symptom Manage 2014 Jul;48(1):65-74 [FREE Full text] [doi: 10.1016/j.jpainsymman.2013.08.020] [Medline: 24636960]
50. Suarez ML, Schlaeger JM, Angulo V, Shuey DA, Carrasco J, Roach KL, et al. Keys to recruiting and retaining seriously ill African Americans with sickle cell disease in longitudinal studies: respectful engagement and persistence. Am J Hosp Palliat Care 2020 Feb;37(2):123-128 [FREE Full text] [doi: 10.1177/1049909119868657] [Medline: 31394904]
51. Dyal BW, Ezenwa MO, Yoon SL, Fillingim RB, Yao Y, Schlaeger JM, et al. Relationship of pain quality descriptors and quantitative sensory testing: sickle cell disease. Nurs Res 2019;68(5):365-373 [FREE Full text] [doi: 10.1097/NNR.0000000000000375] [Medline: 31283720]

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52. Dyal BW, Ezenwa MO, Yoon SL, Fillingim RB, Yao Y, Schlaeger JM, et al. A QST-based pain phenotype in adults with sickle cell disease: sensitivity and specificity of quality descriptors. Pain Pract 2020 Feb;20(2):168-178 [FREE Full text] [doi: 10.1111/papr.12841] [Medline: 31553824]
53. Molokie RE, Wang ZJ, Yao Y, Powell-Roach KL, Schlaeger JM, Suarez ML, et al. Sensitivities to thermal and mechanical stimuli: adults with sickle cell disease compared to healthy, pain-free African American controls. J Pain 2020;21(9-10):957-967 [FREE Full text] [doi: 10.1016/j.jpain.2019.11.002] [Medline: 31733363]
54. Powell-Roach K, Yao Y, Ezenwa MO, Schlaeger JM, Suarez ML, Molokie RE, et al. Neuropathic pain screening: construct validity in patients with sickle cell disease. West J Nurs Res 2020 Feb;42(2):125-130 [FREE Full text] [doi: 10.1177/0193945919836446] [Medline: 30900520]
55. Powell-Roach KL, Yao Y, Rutherford JN, Schlaeger JM, Patil CL, Suarez ML, et al. Thermal and mechanical quantitative sensory testing values among healthy African American adults. J Pain Res 2019 Aug 9;12:2511-2527 [FREE Full text] [doi: 10.2147/JPR.S211855] [Medline: 31496792]
56. Yackle K, Schwarz LA, Kam K, Sorokin JM, Huguenard JR, Feldman JL, et al. Breathing control center neurons that promote arousal in mice. Science 2017 Mar 31;355(6332):1411-1415 [FREE Full text] [doi: 10.1126/science.aai7984] [Medline: 28360327]
57. Corless IB, Abrams D, Nicholas PK, McGibbon CA. The use of complementary and alternative therapies. AACN Clin Issues 2000 Feb;11(1):4-6. [doi: 10.1097/00044067-200002000-00002] [Medline: 11040547]
58. Corless IB, Abrams D, Biglieri E, Dodd M. View from within - coping with isolated thrombocytic purpura. In: Proceedings of the 3rd International Conference on AIDS. 1987 Presented at: ICA '87; June 1-5, 1987; Washington, DC, USA.
59. Corless IB, Abrams D, Biglieri E, Dodd M. Men with isolated thrombocytic purpura: the impact of a psychophysiological intervention on platelet count. In: Proceedings of the 3rd International Conference on AIDS. 1987 Presented at: ICA '87; June 1-5, 1987; Washington, DC, USA.
60. Corless IB. For healthful, loving living, video and discussion. In: Funk SG, Tornquist EM, Champagne MT, editors. Key Aspects of Comfort: Management of Pain, Fatigue, and Nausea. Chapel Hill, NC, USA: University of North Carolina-Chapel Hill; 1988.
61. Lorig KR, Sobel DS, Stewart AL, Brown Jr BW, Bandura A, Ritter P, et al. Evidence suggesting that a chronic disease self-management program can improve health status while reducing hospitalization: a randomized trial. Med Care 1999 Jan;37(1):5-14. [doi: 10.1097/00005650-199901000-00003] [Medline: 10413387]
62. Jha A, Suarez ML, Ferrans CE, Molokie R, Kim YO, Wilkie DJ. Cognitive testing of PAINReportIt in adult African Americans with sickle cell disease. Comput Inform Nurs 2010;28(3):141-150 [FREE Full text] [doi: 10.1097/NCN.0b013e3181d7820b] [Medline: 20431356]
63. Huang HY, Wilkie DJ, Zong SP, Berry D, Hairabedian D, Judge MK, et al. Developing a computerized data collection and decision support system for cancer pain management. Comput Inform Nurs 2003;21(4):206-217. [doi: 10.1097/00024665-200307000-00011] [Medline: 12869874]
64. Wilkie DJ, Huang HY, Berry DL, Schwartz A, Lin YC, Ko NY, et al. Cancer symptom control: feasibility of a tailored, interactive computerized program for patients. Fam Community Health 2001 Oct;24(3):48-62. [Medline: 11563944]
65. Wilkie DJ, Judge MK, Berry DL, Dell J, Zong S, Gilespie R. Usability of a computerized PAINReportIt in the general public with pain and people with cancer pain. J Pain Symptom Manage 2003 Mar;25(3):213-224 [FREE Full text] [doi: 10.1016/s0885-3924(02)00638-3] [Medline: 12614956]
66. Liu X, Blaschke T, Thomas B, De Geest S, Jiang S, Gao Y, et al. Usability of a Medication Event Reminder Monitor System (MERM) by providers and patients to improve adherence in the management of tuberculosis. Int J Environ Res Public Health 2017 Sep 25;14(10):1115 [FREE Full text] [doi: 10.3390/ijerph14101115] [Medline: 28946683]
67. Lucero R, Williams R, Esalomi T, Alexander-Delpech P, Cook C, Bjarnadottir RI. Using an electronic medication event-monitoring system for antiretroviral therapy self-management among African American women living with HIV in rural Florida: cohort study. JMIR Form Res 2020 Feb 19;4(2):e14888 [FREE Full text] [doi: 10.2196/14888] [Medline: 32130114]
68. Andersen LS, Magidson JF, O'Cleirigh C, Remmert JE, Kagee A, Leaver M, et al. A pilot study of a nurse-delivered cognitive behavioral therapy intervention (Ziphamandla) for adherence and depression in HIV in South Africa. J Health Psychol 2018 May;23(6):776-787 [FREE Full text] [doi: 10.1177/1359105316643375] [Medline: 27121977]
69. Ingerski LM, Loew M, Porter JS, Su Y, Zhang H, Hankins JS, et al. Use of wise device technology to measure adherence to hydroxyurea therapy in youth with sickle cell disease. J Pediatr Hematol Oncol 2021 Jan;43(1):e19-e25. [doi: 10.1097/MPH.0000000000001997] [Medline: 33235145]
70. Levenstein S, Prantera C, Varvo V, Scribano ML, Berto E, Luzi C, et al. Development of the Perceived Stress Questionnaire: a new tool for psychosomatic research. J Psychosom Res 1993 Jan;37(1):19-32. [doi: 10.1016/0022-3999(93)90120-5] [Medline: 8421257]
71. Clay OJ, Telfair J. Evaluation of a disease-specific self-efficacy instrument in adolescents with sickle cell disease and its relationship to adjustment. Child Neuropsychol 2007 Mar;13(2):188-203. [doi: 10.1080/09297040600770746] [Medline: 17364574]
72. Van Buuren S. Flexible Imputation of Missing Data. 2nd edition. Boca Raton, FL, USA: CRC Press; 2018.

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73. Bakshi N, Smith ME, Ross D, Krishnamurti L. Novel metrics in the longitudinal evaluation of pain data in sickle cell disease. Clin J Pain 2017 Jun;33(6):517-527. [doi: 10.1097/AJP.0000000000000431] [Medline: 27584817]
74. Jonassaint CR, Shah N, Jonassaint J, De Castro L. Usability and feasibility of an mHealth intervention for monitoring and managing pain symptoms in sickle cell disease: the sickle cell disease mobile application to record symptoms via technology (SMART). Hemoglobin 2015;39(3):162-168. [doi: 10.3109/03630269.2015.1025141] [Medline: 25831427]
75. McClellan CB, Schatz JC, Puffer E, Sanchez CE, Stancil MT, Roberts CW. Use of handheld wireless technology for a home-based sickle cell pain management protocol. J Pediatr Psychol 2009 Jun;34(5):564-573. [doi: 10.1093/jpepsy/jsn121] [Medline: 19029141]
76. Creary SE, Gladwin MT, Byrne M, Hildesheim M, Krishnamurti L. A pilot study of electronic directly observed therapy to improve hydroxyurea adherence in pediatric patients with sickle-cell disease. Pediatr Blood Cancer 2014 Jun;61(6):1068-1073. [doi: 10.1002/pbc.24931] [Medline: 24436121]
77. Estepp JH, Winter B, Johnson M, Smeltzer MP, Howard SC, Hankins JS. Improved hydroxyurea effect with the use of text messaging in children with sickle cell anemia. Pediatr Blood Cancer 2014 Nov;61(11):2031-2036. [doi: 10.1002/pbc.25177] [Medline: 25132074]
78. Inoue S, Kodjebacheva G, Scherrer T, Rice G, Grigorian M, Blankenship J, et al. Adherence to hydroxyurea medication by children with sickle cell disease (SCD) using an electronic device: a feasibility study. Int J Hematol 2016 Aug;104(2):200-207. [doi: 10.1007/s12185-016-2027-x] [Medline: 27225236]
79. Pernell BM, DeBaun MR, Becker K, Rodeghier M, Bryant V, Cronin RM. Improving medication adherence with two-way short message service reminders in sickle cell disease and asthma. A feasibility randomized controlled trial. Appl Clin Inform 2017 May 24;8(2):541-559 [FREE Full text] [doi: 10.4338/ACI-2016-12-RA-0203] [Medline: 28536723]
80. Gallo AM, Wilkie DJ, Wang E, Labotka RJ, Molokie RE, Stahl C, et al. Evaluation of the SCKnowIQ tool and reproductive CHOICES intervention among young adults with sickle cell disease or sickle cell trait. Clin Nurs Res 2014 Aug;23(4):421-441 [FREE Full text] [doi: 10.1177/1054773813479377] [Medline: 23572406]
81. Wilkie DJ, Gallo AM, Yao Y, Molokie RE, Stahl C, Hershberger PE, et al. Reproductive health choices for young adults with sickle cell disease or trait: randomized controlled trial immediate posttest effects. Nurs Res 2013;62(5):352-361 [FREE Full text] [doi: 10.1097/NNR.0b013e3182a0316b] [Medline: 23995469]

Abbreviations

ED: emergency department
IRB: institutional review board
mHealth: mobile health
OME: oral morphine equivalence
PI: principal investigator
PSQ: Perceived Stress Questionnaire
RCT: randomized controlled trial
RDE: relaxation and distraction exercise
RS: research specialist
SCD: sickle cell disease
UF: University of Florida
YCWS: You Cope, We Support

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Protocol

Examining the International Palliative Care Systems in Rural Areas: Protocol for a Comparative Case Study

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Abstract

Background: The aging population in the Global North is associated with an increased prevalence of multiple chronic diseases that would benefit from integrated palliative care. In this context, it is vital to consider the effectiveness of health care systems' response to the needs of the older population residing in rural areas, including access to palliative care services. Understanding palliative care program availability and palliative care system characteristics is important in creating useful health interventions in rural areas.

Objective: This study aims to provide an international view on palliative care in rural areas. A study exploring palliative care services offered in Southern Minnesota will be carried out, building on a previous study conducted in Osona, Spain. Findings from both studies will be compared, providing insights into the strengths of each system and identifying areas for growth.

Methods: This study will be performed using qualitative case study methodology. Using a similar methodology to the one used in the Spanish study, palliative care services will be explored in a similarly sized rural area in Southern Minnesota. This will be accomplished by (1) reviewing available literature related to the Southern Minnesota palliative care system and (2) identifying key providers in this US palliative care system who will be invited to participate in semistructured interviews. The study participants will be asked about the gaps between ideal integrated palliative care system services and the existing complementary palliative care services, and the ethical issues and dilemmas that evolved during the COVID-19 pandemic.

Results: Following ethical approval for this protocol, data collection is anticipated to begin in spring or summer 2022 and is expected to take 6 months. Data collection will be followed by data analysis in fall 2022. Finally, the researchers plan to disseminate the findings in spring 2023.

Conclusions: Comparing 2 similarly sized but culturally different rural palliative care systems in Minnesota and Osona will provide insights into how integrated palliative care systems impact the older population and those with chronic illnesses. Study findings will contribute to enhanced patient care, organizational improvements, policy change, and an understanding of the impact of different health care system models.

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KEYWORDS

palliative care; palliative care systems; integrated palliative care; global health comparison; hospice; rural health; ethical dilemmas; COVID-19; coronavirus; complementary therapy

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Introduction

An aging population in the Global North is associated with an increased prevalence of chronic diseases that will ultimately contribute to their death [1]. Due to the population's increasing life span and resultant aging, it is essential to consider how effectively health care systems, especially palliative care services, respond to patients with chronic illnesses [2-4].

The World Health Organization states that palliative care aims to improve quality of life for those patients living with life-limiting diseases, by reducing pain and proactively managing and treating symptoms associated with their disease processes [5]. Historically, palliative care was limited to patients with cancer [6] and was described as care for individuals with a life-threatening disease [1]. With an aging population, palliative care systems evolved and are no longer limited to oncological or life-threatening diseases [7]. Palliative care currently includes patients with multiple morbidities [8] and individuals in need of quality-of-life–focused care due to frailty, advanced age [9], or disabling conditions [10,11]. Thus, palliative care services are justified based on individual patients' needs rather than specific diagnostic codes. The target patient for palliative care is an individual with a "palliative cluster" of symptoms or factors, including a life-threatening or life-limiting, chronic, or terminal condition, necessitating multidimensional needs.

Past health care models focused on disease-directed care in which the recognition of the terminal nature of a patient's condition occurs late, resulting in delayed hospice and end-of-life care [12]. However, the changes in managing chronic and life-limiting conditions to enhance the quality of life have resulted in a new model in which palliative care service is initiated at the time of diagnosis. In this model, the focus shifts toward symptom management rather than cure, and a transition to hospice care when a patient's life expectancy is 6 months or less; during this time, the primary purpose of care is maximizing the patient's quality of life [13].

A challenge for health care systems is how to provide integrated care for patients with increasingly complex chronic conditions [14]. Integrated care is a combination of multiple disciplines at different levels of care, focused on improving the quality of health care services [3]. It also facilitates connections and cooperation between funding sources, organizations, and clinical services, with the purpose of offering efficient and high-quality care. As a result, integrated palliative care (IPC) provides coordinated services of care [15].

For patients in Southern Minnesota, access to palliative and hospice care services can differ based on the type of insurance the patient has. For example, the national insurance for the older population, Medicare Part A, covers inpatient hospital stays, short-term stays at nursing facilities, and home care [16]. Reimbursement for palliative care is not standardized as it is for hospice care [17,18]. In contrast, the Spanish health care system provides universal access to all residents. Instituto Nacional de la Salud (the government's public health organization) provides health care services to all communities in the country [19], and these services include palliative care for patients with chronic illnesses and terminal diseases.

In both countries, with aging populations, the main challenge for health care systems is to provide integrated care for patients with increasingly complex chronic conditions [14]. IPC is an approach to improve services for patients with chronic illnesses and terminal diseases.

The COVID-19 pandemic can be a distinguishing marker between the period considered "normal" and the pandemic era, which brought many changes to society and health care delivery [20,21]. The pandemic also impacted health care providers who were faced with ethical dilemmas such as determining resource allocation and the prioritization of patient care [22], as well as end-of-life care decisions [23]. Additional ethical concerns encountered by palliative care providers were autonomy in the patient and family decision-making processes [24], the discontinuation of treatments and therapies [23], and communicating with families and patients in a society that required social distancing and limiting factors such as face masks [22].

When taking care of patients with chronic conditions, integrative and complementary care is often experienced as beneficial [25]. The integrative health approach provides patients in need of palliative care with nonpharmacological strategies to manage pain and other nausea, depression, and anxiety symptoms [26]. Examples include aromatherapy, acupuncture, massage, homeopathic practices, and cultural practices [27]. In addition, palliative care in conjunction with complementary care can offer patients comfort during this phase of life [26].

One way to see how care is being delivered to people with complex chronic conditions is through the analysis of reality; therefore, this study aims to first describe the Southern Minnesota palliative care system in the United States and then compare it to the palliative care system in Spain. To be able to carry out the general objective of the study, the following specific objectives will be developed:

1. Describing the palliative care system in Southern Minnesota
2. Comprehending the ethical dilemmas health care providers encounter while providing care in the Southern Minnesota palliative care system
3. Identifying specific impacts resulting from the COVID-19 pandemic
4. Assessing the complementary services offered by palliative care service providers in Southern Minnesota
5. Identifying and comparing the commonalities and differences between this study in Southern Minnesota and the results found in a previous study from Osona, Spain

Methods

Design and Methods

This research will follow the same design and methods used in the study conducted in Osona, Spain (M Mondejar-Pont, PhD, unpublished data, November 2020). This study will use a qualitative methodology with a prospective, multiple embedded case study design as described by Yin [28]. This design allows

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us to explore the embedded subunits of multiple cases to understand more about the case itself.

This study will describe the Southern Minnesota palliative care service and its essential integrated palliative care system elements, identify the ethical dilemmas experienced, and identify the complementary therapies offered. The results found in this study will then be compared to the results found in the initial study conducted in Osona, Spain. This comparison will aim to identify similarities, differences, and informative aspects that may benefit each system, while taking into consideration the contextual and cultural differences between the two.

Case Selection

Blue Earth, Nicollet, and Brown counties in Southern Minnesota were selected for this study based on similarities between these areas and the region in Spain that is the population of comparison. In addition, Blue Earth, Nicollet, and Brown Counties include the Mankato metropolitan area and the surrounding rural areas [29] that have significantly smaller populations and less access to health care services. These counties will be referred to as Southern Minnesota for ease of readability.

These 2 regions were selected since they have similar populations: Osona county has a population of 163,702 [30], and Southern Minnesota has a population of 125,912 [31]. In these regions, the older population is represented with a similar proportion: 18% in Osona [32] and 24% in Southern Minnesota [33]. With a significant proportion of rural populations aging in place, access to palliative care service is imperative yet more challenging outside of larger urban areas [34]. By comparing and contrasting two similarly sized regions with different health care systems and reimbursement models, this research will ultimately provide information that the palliative care systems in both regions can use to improve their practices.

Participants

Consistent with the study completed in Osona, Spain, this study will use a purposive sampling strategy including the following 2 types of participants who will be invited to take part in the study: (1) those who hold decision-making positions in organizations providing palliative care, including managers, coordinators, or lead administrators; and (2) professionals involved in the provision of palliative care, such as nurses, social workers, and physicians.

We anticipate interviewing up to 25 participants, similar to the study completed in Spain, representing a wide variety of roles within palliative care systems. Interviews will be analyzed using the direct content analysis approach explained further below, and the analysis will conclude once the research team determines that data saturation has been reached. The research team will determine that data saturation has been reached when no new additional information, new codes, or categories are possible to obtain. If data saturation is not reached after 25 interviews, interviews will continue until saturation is reached.

Initially, professionals in leadership positions will be interviewed about the palliative care system. The interviews with individuals in leadership positions aim to gain a holistic sense of the organization, communication, and coordination efforts at the macro level. These professionals, following a snowball strategy, will provide contact information of direct care providers. Direct care providers can give more detailed insights about the palliative care system at the micro level.

Data Collection

The study will be divided into the following 2 phases to respond to the study's main goals:

- Phase 1 aims to identify a description of the palliative care system in Southern Minnesota through a search in the available documents and literature review.
- In Phase 2, the aim is to identify the integrated elements of palliative care systems; the ethical dilemmas encountered prior to, during, and in the current phase of the COVID-19 pandemic; and the complementary care offered. During this phase, key personnel and direct health care professionals will be interviewed individually by members of the research team. These semistructured interviews will take place via teleconferencing or phone. All interviews will be audio recorded (Multimedia Appendix 1 includes the survey questions) to be later transcribed and analyzed. Finally, the results from this study of the Southern Minnesota palliative care system will be compared with the results found in the research completed in Osona, Spain.

Data Management and Analysis

Anonymous participant data will be stored in a protected database such as Microsoft Teams with a login function. The master database will be kept in a password-protected, university-issued computer.

Interviews will be audio recorded and transcribed verbatim. Transcriptions will be analyzed using deductive content analysis supported by the qualitative data analysis software NVivo (version 12; QSR International).

The deductive or directed content analysis approach uses previous research findings to examine the studies' new data to identify similarities and differences and compare the same categories at different times and in other locations. Deductive content analysis has 3 main processes: data preparation, organization, and reporting. In the data preparation phase, a matrix of categories from existing theories is created and then compared to the emerging categories from the study's data [35]. In the organization phase, documents and interviews will be analyzed using deductive content analysis, and prior theoretical propositions will guide the initial coding process and formation of first categories. Then, new categories emerging from the data will be generated, and finally, links between initial and newly generated categories will be established and reported as results.

The research team members will individually review study findings, identifying themes, concepts, and case components; the research team will then meet to discuss results until consensus and data saturation are reached. Once themes, concepts, and case components have been identified for the Southern Minnesota palliative care system, they will be compared to those in Osona's palliative care system. Similarities

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and differences will be used to identify system strengths and areas for growth.

Ethical Review

Informed consent will be obtained to assure voluntary participation. Participants may withdraw at any time at their discretion. Therefore, we believe that the potential for risk in this study is minimal.

To minimize the burden of data collection on busy professionals, interviews will be limited to a maximum of 60 minutes. Interviews will be conducted by experienced researchers.

An application for ethical approval has been submitted to the Institutional Review Board of Minnesota State University, Mankato and is awaiting approval (1877595).

Results

This study was initiated in August 2021, when the research team met and established its organization and the project goals. The Institutional Review Board application was submitted in April 2022, and further project planning has been undertaken during spring 2022. Results are pending ethical review and data collection, which will take place in spring and summer 2022, followed by data analysis in fall 2022. Dissemination of results and development of various study reports will be anticipated after data analysis is completed in 2023.

Anticipated results for this study are expected to be consistent with those found in the foundational study completed in Osona, Spain. In that study, major themes included a need for improved collaboration, continuity of care, and sustainable funding. Ethical dilemmas identified included the decision to continue nonbeneficial treatment, life-sustaining and life-prolonging therapies, and palliative sedation.

Discussion

Anticipated outcomes for this study on IPC in Southern Minnesota will include suggestions to enhance patient care, improve organizational structures, and change policy, as indicated by the study findings. Understanding ethical dilemmas encountered by palliative care service providers and the complementary therapies used will identify new patient-centered care strategies.

There is currently an increased interest in IPC, an optimal approach to provide care for patients with chronic conditions and terminal illnesses [36]. However, the literature indicates that there is no agreement on the definition of IPC's essential components, and thus, there is the need to define its integral elements [37,38]. Consequently, IPC implementation varies across settings, and understanding its application is complicated. Describing and comparing different IPC systems such as the ones in Southern Minnesota and Osona offers greater insights into the implementation of IPC systems in 2 different countries.

The COVID-19 pandemic offers an opportunity for reflection and a new interpretation of health issues, especially in the ethical domain [20], such as resource provision and care prioritization [22]. In addition, the pandemic has exposed unique health-related ethical dilemmas [39], resulting in more complex decision-making processes [23]. This study will reveal the ethical dilemmas Southern Minnesota palliative care providers have encountered during the COVID-19 pandemic and compare them to those confronted by health care professionals in Osona's palliative care system.

In summary, further research on the implementation and evaluation of IPC systems is needed. Describing the essential elements, ethical dilemmas, and complementary therapies of the Southern Minnesota palliative care system will bring a greater understanding of their implementation within the IPC systems. Additionally, comparing 2 IPC systems that are similar in population and rural setting will provide a richer understanding of the impact of IPC systems on people with chronic illnesses. Study findings will contribute to enhanced patient care, organizational improvements, policy change, and a better understanding of the impact of different health care system models.

Acknowledgments

The research team would like to express their appreciation to Glen Taylor Nursing Institute for Family and Society for facilitating and supporting this collaboration.

Conflicts of Interest

None declared.

Multimedia Appendix 1
Interview script.
[DOCX File , 22 KB - resprot_v11i7e36037_app1.docx]

References

1. Siouta N, van Beek K, Preston N, Hasselaar J, Hughes S, Payne S, et al. Towards integration of palliative care in patients with chronic heart failure and chronic obstructive pulmonary disease: a systematic literature review of European guidelines and pathways. BMC Palliat Care 2016 Feb 13;15(1):1-12 [FREE Full text] [doi: 10.1186/s12904-016-0089-4] [Medline: 26872741]

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2. Ewert B, Hodiamont F, van Wijngaarden J, Payne S, Groot M, Hasselaar J, et al. Building a taxonomy of integrated palliative care initiatives: results from a focus group. BMJ Support Palliat Care 2016 Mar 08;6(1):14-20 [FREE Full text] [doi: 10.1136/bmjspcare-2014-000841] [Medline: 26647043]
3. Lyngsø AM, Godtfredsen NS, Høst D, Frølich A. Instruments to assess integrated care: a systematic review. Int J Integr Care 2014 Sep 25;14(3):1-15. [doi: 10.5334/ijic.1184]
4. Garralda E, Hasselaar J, Carrasco JM, Van Beek K, Siouta N, Csikos A, et al. Integrated palliative care in the Spanish context: a systematic review of the literature. BMC Palliat Care 2016 May 13;15(1):49 [FREE Full text] [doi: 10.1186/s12904-016-0120-9] [Medline: 27177608]
5. Palliative care. World Health Organization. 2018. URL: https://www.who.int/news-room/fact-sheets/detail/palliative-care [accessed 2019-01-30]
6. Gómez-Batiste X, Martínez-Muñoz M, Blay C, Amblàs J, Vila L, Costa X, et al. Identifying patients with chronic conditions in need of palliative care in the general population: development of the NECPAL tool and preliminary prevalence rates in Catalonia. BMJ Support Palliat Care 2012;3(3):300-308. [doi: 10.1136/bmjspcare-2012-000211] [Medline: 24644748]
7. den Herder-van der Eerden M, Ewert B, Hodiamont F, Hesse M, Hasselaar J, Radbruch L. Towards accessible integrated palliative care. JICA 2017 Jul 03;25(3):222-232. [doi: 10.1108/jica-03-2017-0006]
8. Kamal AH, Currow DC, Ritchie CS, Bull J, Abernethy AP. Community-based palliative care: the natural evolution for palliative care delivery in the U.S. J Pain Symptom Manage 2013;46(2):254-264 [FREE Full text] [doi: 10.1016/j.jpainsymman.2012.07.018] [Medline: 23159685]
9. Kallen MA, Yang D, Haas N. A technical solution to improving palliative and hospice care. Support Care Cancer 2012 Jan 16;20(1):167-174. [doi: 10.1007/s00520-011-1086-z] [Medline: 21240650]
10. Engel PA, Spencer J, Paul T, Boardman JB. The geriatrics in primary care demonstration: integrating comprehensive geriatric care into the medical home: preliminary data. J Am Geriatr Soc 2016 Apr 21;64(4):875-879. [doi: 10.1111/jgs.14026] [Medline: 27100583]
11. Building integrated palliative care programs and services. Càtedra de Cures Palliatives. Vic, Catalonia; 2017. URL: http://www.thewhpca.org/resources/category/building-integrated-palliative-care-programs-and-services [accessed 2021-06-03]
12. Buss MK, Rock LK, McCarthy EP. Understanding palliative care and hospice: a review for primary care providers. Mayo Clin Proc 2017;92(2):280-286. [doi: 10.1016/j.mayocp.2016.11.007] [Medline: 28160875]
13. Boucher NA, Bull JH, Cross SH, Kirby C, Davis JK, Taylor DH. Patient, caregiver, and taxpayer knowledge of palliative care and views on a model of community-based palliative care. J Pain Symptom Manage 2018 Dec;56(6):951-956 [FREE Full text] [doi: 10.1016/j.jpainsymman.2018.08.007] [Medline: 30149059]
14. Singer SJ, Burgers J, Friedberg M, Rosenthal MB, Leape L, Schneider E. Defining and measuring integrated patient care: promoting the next frontier in health care delivery. Med Care Res Rev 2011;68(1):112-127. [doi: 10.1177/1077558710371485] [Medline: 20555018]
15. Mondejar-Pont M, Ramon-Aribau A, Gómez-Batiste X. Integrated palliative care definition and constitutive elements: scoping review. JICA 2019 Oct 10;27(4):285-304. [doi: 10.1108/jica-11-2018-0069]
16. Sherrell Z. Medicare and palliative care: what to know. Medical News Today. 2020 Nov 13. URL: https://www.medicalnewstoday.com/articles/does-medicare-cover-palliative-care [accessed 2021-08-10]
17. How does medicare help with serious illness care? CaringInfo. 2021. URL: https://www.caringinfo.org/planning/financial-matters/medicare/ [accessed 2021-08-10]
18. Hospice care Coverage. Medicare. 2021. URL: https://www.medicare.gov/coverage/hospice-care [accessed 2021-08-10]
19. Centeno C, Arnillas P, Hernansanz S, Flores LA, Gómez M, López-Lara F. The reality of palliative care in Spain. Palliat Med 2000 Sep 01;14(5):387-394. [doi: 10.1191/026921600701536219] [Medline: 11064785]
20. Doldi M, Moscatelli A, Ravelli A, Spiazzi R, Petralia P. Medicine and humanism in the time of COVID-19. Ethical choices. Acta Biomed 2020 Nov 10;91(4):1-10 [FREE Full text] [doi: 10.23750/abm.v91i4.10569] [Medline: 33525224]
21. Blot F, Dumont SN, Vigouret-Viant L, Verotte N, Rossignol J, Rieutord A, et al. Ethical issues related to the COVID-19 pandemic in patients with cancer: experience and organisations in a French comprehensive cancer centre. BMJ Support Palliat Care 2020 Aug 27:1-8. [doi: 10.1136/bmjspcare-2020-002504] [Medline: 32855231]
22. Bolt SR, van der Steen JT, Mujezinović I, Janssen DJ, Schols JM, Zwakhalen SM, et al. Practical nursing recommendations for palliative care for people with dementia living in long-term care facilities during the COVID-19 pandemic: A rapid scoping review. Int J Nurs Stud 2021 Jan;113:103781 [FREE Full text] [doi: 10.1016/j.ijnurstu.2020.103781] [Medline: 33080475]
23. Han JJ, Luc JG, Pak E. Ethical dilemmas associated with the COVID-19 pandemic: dealing with the unknowns and unanswerables during training. J Am Coll Cardiol 2020 Sep 08;76(10):1266-1269 [FREE Full text] [doi: 10.1016/j.jacc.2020.07.041] [Medline: 32883420]
24. Robert R, Kentish-Barnes N, Boyer A, Laurent A, Azoulay E, Reignier J. Ethical dilemmas due to the Covid-19 pandemic. Ann Intensive Care 2020 Jun 17;10(1):84 [FREE Full text] [doi: 10.1186/s13613-020-00702-7] [Medline: 32556826]
25. Dahlin CM. National consensus project for quality palliative care: assuring quality palliative care through clinical practice guidelines. In: Oxford Textbook of Palliative Nursing (5th ed). Oxford: Oxford University Press; 2018.

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26. Adler SR, Marchand LR, Heap N. Integrative palliative care: enhancing the natural synergy between integrative health and palliative medicine. J Altern Complement Med 2019;25(3):257-259. [doi: 10.1089/acm.2019.29063.sra] [Medline: 30864844]
27. Zeng YS, Wang C, Ward KE, Hume AL. Complementary and alternative medicine in hospice and palliative care: a systematic review. J Pain Symptom Manage 2018;56(5):781-794 [FREE Full text] [doi: 10.1016/j.jpainsymman.2018.07.016] [Medline: 30076965]
28. Yin RK. Case Study Research: Design and Method (second edition). New York: Sage; 1994.
29. Defining rural population. US Health Resources and Services Administration. Defining Rural Populations. 2021. URL: https://www.hrsa.gov/rural-health/about-us/definition/index.html [accessed 2021-08-10]
30. Official statistics of Catalunya. Gencat. 2020. URL: https://www.idescat.cat/?lang=en [accessed 2021-07-15]
31. Minnesota Counties by population. Minnesota Demographics. Census redistricting data. 2020. URL: https://www.minnesota-demographics.com/counties_by_population [accessed 2021-01-09]
32. Servei Català de la Salut. Mòduls de seguiment d'indicadors de qualitat. https://msiq.catsalut.cat/index.html [accessed 2019-07-23].
33. It's time to face aging, Minnesota. FaceAging MN. 2021. URL: https://faceagingmn.org/minnesota-population-aging-map/ [accessed 2021-12-28]
34. Symens Smith A, Trevelyan E. Older population in rural America. United States Census Bureau. 2019 Oct 22. URL: https://www.census.gov/library/stories/2019/10/older-population-in-rural-america.html [accessed 2021-08-10]
35. Assarroudi A, Heshmati Nabavi F, Armat MR, Ebadi A, Vaismoradi M. Directed qualitative content analysis: the description and elaboration of its underpinning methods and data analysis process. J Res Nurs 2018 Feb 10;23(1):42-55 [FREE Full text] [doi: 10.1177/1744987117741667] [Medline: 34394406]
36. Bainbridge D, Brazil K, Krueger P, Ploeg J, Taniguchi A, Darnay J. Evaluating program integration and the rise in collaboration: case study of a palliative care network. J Palliat Care 2018 Dec 19;27(4):270-278.
37. van der Eerden M, Csikos A, Busa C, Hughes S, Radbruch L, Menten J, et al. Experiences of patients, family and professional caregivers with Integrated Palliative Care in Europe: protocol for an international, multicenter, prospective, mixed method study. BMC Palliat Care 2014 Nov 21;13(1):1-9. [doi: 10.1186/1472-684x-13-52]
38. Tan WS, Lee A, Yang SY, Chan S, Wu HY, Ng CWL, et al. Integrating palliative care across settings: a retrospective cohort study of a hospice home care programme for cancer patients. Palliat Med 2016 Jul 11;30(7):634-641. [doi: 10.1177/0269216315622126] [Medline: 26867937]
39. Chamsi-Pasha H, Chamsi-Pasha M, Albar M. Ethical dilemmas in the era of COVID-19. Avicenna J Med 2020;10(3):102-105 [FREE Full text] [doi: 10.4103/ajm.ajm_119_20] [Medline: 32832425]

Abbreviations

IPC: integrated palliative care

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Protocol

The Role of Mealtimes in Fostering Language Development and Aligning Home and School Learning: Protocol for a Multi-Method Study of Preschool Children in Rural Kenya and Zambia

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Abstract

Background: The association between school and home is fundamental to sustainable education: parents' understanding of the school's priorities and teachers' understanding of their pupils' home environment are both vital for children to remain in school and succeed academically. The relationship between parents and teachers is closest in preschool settings, providing a valuable opportunity to build bridges between home and school. In this protocol paper, we outline our planned methods for identifying beneficial home and school behaviors.

Objective: Our project aims to identify culture-specific structures and behaviors in home and school settings, which influence the quantity and quality of child-directed speech and identify positive experiences that can help improve children's linguistic development and nutrition.

Methods: Using a mixed methods approach and focusing on early language learning, nutrition, and responsive caregiving, we will video-record and analyze mealtime language and eating behaviors at home and in school, targeting 80 preschool children and their families in rural Kenya and Zambia. In addition, we will assess children's language skills through audio recordings and use questionnaire-based interviews to collect extensive sociodemographic and dietary data.

Results: Between the start of our project in January 2020 and the end of December 2021, we had collected complete sets of sociodemographic, observational, and food recall data for 40 children in Kenya and 16 children in Zambia. By the end of May 2022, we had started data collection for an additional 24 children in Zambia and transcribed and coded approximately 85% of the data. By the end of September, 2022, we plan to complete data collection, transcription, and coding for the entire sample of 80 children across both countries. From September 2022 onwards, we will focus on analyzing our language data, and we hope to have results ready for publication in early 2023. By relating children's language outcomes and nutritional intake to the observed mealtime behaviors, we hope to identify practices that increase the quantity and quality of child-directed speech and improve children's nutritional intake.

Conclusions: Good nutrition and the promotion of language learning are key issues in early childhood development. By using a cross-cultural approach, combining a variety of methods, and working closely with stakeholders and policy makers throughout the project, we hope to find and share best practices for improving children's linguistic outcomes and nutrition and lay the foundation for the development of practitioner networks and parent outreach programs.

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KEYWORDS

language development; nutrition; preschool education; school; education; home; environment; academic; children; student; language learning; language; caregiving; responsive caregiving; speech; child-directed speech; nutritional level

Introduction

Sustainable education builds on a strong connection between school and home settings. In order for children to remain in school and succeed academically, it is important to have not only teachers who understand their home environment but also parents who are familiar with their children's educational settings [1]. However, home and school remain largely separated in many African countries [2]. At home, children start out by learning about all aspects of life in an integrated way, which is quite different from the typical school setting with a strict separation of disciplines [3,4]. As a result, children are likely to find it difficult to adapt to the school environment and the required focus on different areas. Indeed, many African children do not meet expected school standards for their age; in Kenya 6-to-13–year-old primary school children are roughly 2 years behind the expected academic levels for numeracy and literacy skills by international standards [5], and this gap is even more pronounced in rural areas of low socioeconomic status [6]. Thus, there is significant potential to raise educational standards by better aligning school with home as part of focused early-year interventions across rural sub-Saharan Africa.

Two key drivers of children's educational success that are determined both by home and school are good nutrition [7,8] and a responsive caregiving environment that supports rich linguistic interactions [9-11]. Mealtimes provide an ideal context to evaluate both of these factors as one can detail not only regular dietary intake but also exposure to potentially sophisticated language for a meaningful duration of time each day [12,13]. Studies to date suggest that children's diets and the structure of home mealtimes vary considerably both between and within African countries [14]. In this study, we propose to measure this variation in families based in Kenya and Zambia and relate this to later cognitive outcomes in order to identify potential bridges between home and school settings, which could support their development.

Regarding dietary variation, we will make use of the mealtime settings to explore children's nutritional intakes and identify best practices for providing equally healthy and nutritious diets for all children at home. While children's nutritional status has improved throughout the last decade, food insecurity and malnutrition still affect millions in Kenya and Zambia. In 2014, it was reported that 26% of Kenyan children were stunted, 11% were underweight, and 4% were wasted. In Zambia numbers were even higher, with 40% of children stunted, 15% underweight, and 6% wasted [15].

Stunting is strongly related to parental education and income and is more common in children of mothers who have not completed primary school or are in the lowest wealth quintile [16,17]. In addition, children in rural Kenya often have deficiencies in iron, calcium, and zinc [18], all of which are thought to influence children's cognitive development [19].

Concerning linguistic variation, substantial differences can arise from the context in which families share meals. While children in rural areas often eat alone or with their mothers, parents who have spent more time in school might prefer family meals where everyone eats together. As a result, children's communicative experiences vary in many ways. Families in higher-socioeconomic status settings are more likely to have homes with electricity and a TV set in the sitting room, which might interfere with mealtime interactions and lead to delayed language development [20]. Although these factors suggest a counterintuitive pattern where children in low–socioeconomic status families may have greater exposure to family communication during mealtimes, the benefits gained largely depend on the quality of these communicative interactions. Previous work has shown that the semantic and pragmatic content of caregiver-child interactions varies enormously between social settings [21] and cultures [22]. An important aspect of our project is thus to identify culture-specific structures and behaviors that influence the quantity and quality of child-directed speech in potentially language-rich settings.

Our research addresses 3 major challenges for early development in low-income communities: improving children's nutrition, improving children's linguistic development, and aligning school education with children's everyday experience [23,24].

By observing children's and caregivers' behavior and language use in home and school settings, we aim to identify positive experiences that teachers can build on in the classroom and that parents can use at home. Ultimately, we hope to initiate a collaborative network that involves teachers from Early Child Development and Education (ECDE) centers along with families to improve 3 domains of nurturing care (nutrition, early learning, and responsive caregiving) for children in their charge. Figure 1 illustrates the overarching goals of our project [25].

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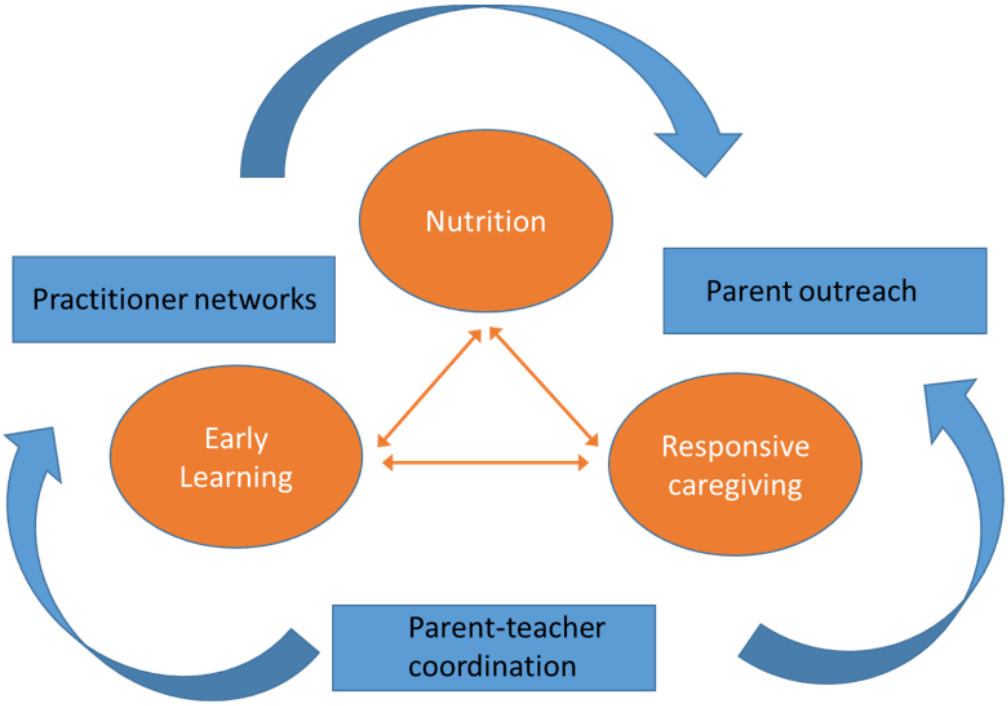
Figure 1. Priorities for targeting key domains of early childhood education and care and aligning preschool and home settings. Developed from Black et al [25].



The specific goals of this protocol provide the first steps toward our overarching aim. Specifically, our aims were as follows:

1. To observe child language exposure and child language outcomes across a 2-year time span: (1) measure the quantity and quality of child-directed and child-accessible speech within home and school mealtime language and identify mealtime practices associated with individual differences in language exposure; and (2) examine whether individual differences in language exposure are related to developments in the target child's language proficiency;
2. To observe mealtime behaviors at home and collect dietary data to identify practices that support healthy child nutrition; and
3. To identify best practices that can cross-inform home and school settings about supporting early cognitive development to foster educational success.

Methods

Ethics Approval

The project has been reviewed by the ethics review unit at Baraton University of Eastern Africa (B22972019), by the University of Zambia ethics committee (2020-Nov-111) as well as by the Aston University research ethics committee (#1547), and we have obtained permission to conduct this research from the relevant authorities in Kenya and Zambia.

Setting and Participant Selection

Our participants are 4-to-7–year-old children, their caregivers, siblings, peers, and others who live and eat with our target children.

In Kenya, we are recruiting 40 children from 2 rural primary schools in Laikipia County, and in Zambia, we are recruiting the same number of individuals from a total of 4 rural primary schools, amounting to a total of 80 children across the 2 countries. Our Kenyan participants are predominantly Kikuyu, and our Zambian participants are from Tonga and Lozi communities.

From each participating school, we are also recruiting one preschool teacher to become part of our research team. Throughout the project, our teacher-researchers will help establish contacts with local families and assist with data collection.

Data Collection

Mealtime Observations

We will observe each child for a total of 4 mealtimes within a period of 3 months: twice at home and twice in school. In addition, we will have one pre–data collection observation per family and 2 per school to familiarize all participants with the recording situation. We know that a high level of meal-to-meal variability across different eating episodes is likely [26], and we will attempt to minimize this by observing lunchtime meals for all participants and having multiple observations for each child. In all cases, the research team will attempt to record "typical" mealtime interactions (defined by parents and teachers), using digital recording equipment placed covertly from the child's view. For each observation, we will ask adult participants whether the mealtime was unusual or normal, rating it on a scale from 1 (very different from usual) to 5 (completely normal).

Child Language Outcomes

In order to test for associations between mealtime language and behaviors with language outcomes, we will measure children's linguistic skills 1 year after our initial baseline observations.

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We will provide children with a wordless picture book, and following a short period of familiarization, we will ask them to recount the story to an assistant over the phone. In addition, we will ask children to provide a free narrative of recent events or experiences. In both cases, we will measure the quantity of word types and tokens produced by the child.

Dietary Recall

In addition to our observations, we will use a 24-hour dietary recall to assess children's food and beverage intake in more detail. Caregivers will be asked to recall a list of all food and drinks consumed in the last 24 hours—quantity, preparation methods, and meal times—for a total of 3 days (2 weekdays and 1 Sunday). Photographs of the foods and drinks described in the recalls will be collected by the caregiver using a smartphone to assist with validation and portion size estimation. The dietary recall procedure will follow the multi-pass method that has been adapted to local standards in line with recommendations from the GloboDiet-Africa team [27] and extensively piloted with local preschool teachers and research assistants.

Background Information

In order to put our findings into perspective, we will measure covariates that tend to be associated with child language and educational attainment [5], including household income, parental education, child gender, and child age [5,28]. To that end, we have developed a comprehensive sociodemographic questionnaire, which will be administered to our participating families on the first day of our visit. In order to minimize the burden on our participants and ensure that they do not have to be literate, local research assistants will read the questions in local languages and record the answers. We will also measure the number of adults and siblings living in participating family homes as this is likely to influence language exposure.

In addition, we will collect data about children's reading opportunities and practices at home. To complement our dietary data, we will also measure children's weight and height. Child height and weight will be collected in schools by a team of teachers or research assistants trained in using measuring materials. All measures will be taken by one team member and confirmed by a second member of the team. Children will be weighed and measured in their school uniforms with shoes removed.

Data Management

The study will be conducted in accordance with data sharing agreements established prior to data collection, which are aligned with each university's policies, standard operating procedures, and regulatory requirements for data protection, storage and security, and secure data sharing across sites at Aston University, Kisii University, and the University of Zambia. Each participant will be assigned a unique registration number. A master list linking each participant's registration number to identifying details will be stored separately from the deidentified data. Data will be securely stored on paper (inside a locked filing cabinet) and electronically (in password-protected folders) at each site. In addition, electronic data will be stored on a secure server at Aston University.

Protocol Adaptation Owing to the COVID-19 Pandemic

Prior to the COVID-19 outbreak, we had successfully recruited 16 families in Kenya and had begun collecting initial home and school mealtime observations. As soon as COVID-19 restrictions were introduced at each site (March 2020), we suspended all the observations we had planned and stopped all in-person contact between the research team and community members in order to avoid potential transmission of the virus. Using already established links between participating families and research assistants, we were, however, able to continue collecting food recall data over the phone. Once schools were reopened, we continued our recruitment activities with eligible families through local ECDE teachers.

Additionally, as a result of the pandemic, we also decided to collect language outcome data using phone story book retell activities with children in order to minimize direct contact. We worked with teachers and local assistants from our participating communities to select an appropriate story book that the children would find relatable, which was also likely to elicit rich language. In order to further minimize contact, we distributed the story books via participating ECDE teachers during normal everyday interactions with participating families in the community. To ensure that none of the children had previous experience with the book, we handed them out in sealed envelopes and asked parents to open them only at the time of the recording. Teachers familiarized parents with the planned procedures when distributing books and also used this opportunity to hand out masks and sanitizers and sensitize participants about health-related behaviors during the pandemic.

Data Coding Plan

Linguistic Measures Taken From Mealtime Language Observation Data

Participants are likely to be multilingual and speak in their native languages (Kikuyu and Tonga or Lozi at the Kenyan and Zambian sites, respectively) as well as use official languages (Kiswahili or English in Kenya and English in Zambia). Since the use of native languages is encouraged in the preschool setting, we expect to find a similar mix of languages in both settings. We will transcribe 20 minutes of conversation from each video recording, starting from when the target child has received his or her meal. All transcriptions will be performed by local research assistants who are fluent in the expected languages, using ELAN software [29]. In addition, the transcribers will provide an English translation of the conversation in order to enable the entire research team to understand the content. Coding and analyses will, however, be based on the original languages used and will be carried out by research assistants who are fluent in the local languages. We will code for utterance direction and accessibility, as well as communicative function of utterances. In addition, we will measure (1) word types and tokens produced by the child, (2) adult word types and tokens within overheard speech segments, (3) adult word types and tokens within child-directed segments [30], and (4) word types and tokens spoken by other children, within segments directed at our target child (see Multimedia Appendix 1 for the language coding scheme).

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Behavioral Measures Taken From Mealtime Observation Data

In order to code behavioral variables from our recordings, we have developed a culturally appropriate coding scheme for family mealtimes, using an adapted version of a coding scheme developed by Mutoro et al [31] for children living in low-income areas in Nairobi. Mutoro's original scheme was developed for younger children; hence, our coding scheme was adapted to suit the behaviors and interactions of older children. The new scheme codes for the mealtime setup and seating arrangements (including who is eating with the child and whether bowls are shared), the location of the child (eg, sitting on the floor or at the table), and the presence of any distractions (such as the radio, TV, or animals). The scheme codes for behaviors include caregivers' encouragement to eat, prompting to eat, negativity or use of force, as well as child behaviors such as interest in food, interactions with other children, mood, distractibility, and any challenging behaviors during the meal. The scheme also codes for the overall tone of the mealtime and considers how much the child eats from among the foods offered. The scheme was codeveloped by academic experts (including native experts) in eating behavior, parenting, child development, and observational methodologies, alongside local teachers and local research assistants who were able to advise on culturally specific meanings of specific behaviors, which were used to adapt the scheme and to appropriately reflect the nature of the interactions (see Multimedia Appendix 2 for the full behavioral coding scheme).

Nutritional Assessment

From the recall data for each child, we will calculate the amount of food in grams per day and then use the Food Composition Tables from Kenya [32] to calculate mean daily nutrient intakes. These will then be compared to nutrient intake recommendations as outlined in the joint Food and Agriculture Organization of the United Nations (FAO) and World Health Organization (WHO) 2002 report [33] to calculate nutrient adequacy ratios. The joint FAO/WHO 2004 report on energy requirements [34] will be used to determine adequate or inadequate energy (in kcal) intakes based on age, sex, and weight. Child height and weight will be converted to weight-for-height for age Z scores (WHZs) and height-for-age (HAZ) Z scores, using the WHO AnthroPlus software version 1.0.4 [35]. Children will be classified as being underweight if their WHZs are ≤−2 SD. Having overweight or obesity will be defined as WHZ>2 SD and >3 SD, respectively. Stunting will be defined as HAZ≤− 2 SD.

Data Analysis Plan

Language and Behavioral Analysis

For language and behavioral analysis, we shall carry out the following:

- Compare scores from the mealtime coding scheme to identify whether there are significant differences between home and school settings for each of the potential predictors (eg, caregiver sensitivity and distractors) and examine the nature of mealtime structure (ie, number of people and seating arrangement) to highlight key differences;
- Examine variability in mealtime language measures within and across school or home settings and, if appropriate, merge data within a setting. We will then examine which of our predictors and covariates are significantly associated with our mealtime child language measures and our child-language outcomes;
- Conduct a series of hierarchical regressions (controlling for significant covariates) to examine which behavioral factors are predictive of each of our mealtime language and child-language outcome variables.

Dietary Analysis

For the dietary analysis, we will carry out the following:

- Compute average daily nutrient intake estimates and explore adequacy ratios of key vitamins and minerals. These include energy, calcium, iron, magnesium, zinc, selenium, vitamin A (retinol equivalents), thiamin, riboflavin, niacin, folate, vitamin B12, and vitamin C. In addition, we will calculate dietary diversity and food variety scores and assess levels of stunting and wasting;
- Assess whether the rich observational data validates parentally reported dietary intake for the children. As for most children, a 24-hour recall was completed the day following home mealtime observations we can compare foods consumed during the mealtime with those reported in the 24-hour recall;
- Explore whether children's diets and mealtime experience are related to social and background variables (eg, number of people and seating arrangement), as well as behavioral variables that have previously been associated with food intake (eg, caregiver responsiveness, prompting, and use of distractions);
- Compare home and school observations to see how interactions differ depending on the context and explore what behaviors support better nutrition and language development for children;
- Explore the role of siblings and other children who are more involved in mealtime interactions in rural Africa compared to Western countries, and assess whether the quality and quantity of interactions with other children is beneficial for child nutritional adequacy and language outcomes.

Results

Our study started in February 2020, which coincided with the onset of the COVID-19 pandemic in Kenya. Despite the resulting challenges, we managed to continue our work owing to our close relationships with the communities and by adapting our aforementioned methods. As of May 2022, we had collected complete sets of sociodemographic, observational, and food recall data for all 40 children in Kenya, and we will have transcribed and coded the data by the end of August 2022. In addition, we have collected and transcribed language outcome data for 14 Kenyan children and intend to collect and transcribe those data for the remaining 26 children by September 2022. The nutritional data for a subset of our Kenyan participants, which had been collected during the onset of the COVID-19 pandemic, has already resulted in a published paper [36]. Our results show that reduced access to marketplaces, financial

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restrictions, and limited availability of products led to changes in the types and quantities of food that parents were able to provide during the pandemic.

In Zambia, we had collected and transcribed sociodemographic and observational data for 16 children by the end of December 2021 and added food recall and language outcome data from them by the end of May 2022. In addition, we recruited another 24 children in March-April 2022 and hope to complete data collection for the entire sample by the end of August 2022.

From September 2022 onward, we will focus on analyzing our language data, and we hope to have results ready for publication in early 2023.

Discussion

Principal Findings

Key to the success of early childhood development programs is good nutrition and the promotion of language learning through responsive caregiving [37]. This project is novel in its focus on both language development and nutrition. These two aspects of child development have tended to be studied separately in previous research, thus neglecting the potential for each area to shape the other. Our research findings will advance theories about how early developmental experiences during mealtimes influence language development and nutrition. Some factors we identify will likely be universal across cultures (eg, the importance of quality and quantity of child-directed speech on children's language outcomes) and other factors will likely vary across cultures (eg, the effect of men and women eating together on child-directed speech). The extent to which these factors are common across Kenya and Zambia will indicate the generalizability of our findings to other rural communities in Africa and worldwide. Outputs will include the following: (1) identification of culturally relevant caregiver behaviors (including those of siblings and peers) that enhance the quantity and quality of child-directed speech during mealtimes and, in turn, promote child language; (2) assessment of the influence of caregiving practices and mealtime structures on children's nutrition; and (3) identification of best practices at home and in school, which can cross-inform the 2 settings.

Comparison With Prior Work

Nutrition in the early years of life is crucial to children's health, growth, and cognitive development. Previous research with children in sub-Saharan Africa suggests that diets are mainly cereal-based and have low levels of dietary diversity [38]. In many cases, children also have inadequate energy intakes and do not consume enough fat or micronutrients such as calcium, zinc, riboflavin, or vitamins A and B_{12} [38,39]. Identifying best practices for raising children's nutritional levels in low-income, rural settings, which can easily be adapted for use across similar communities, can have a lasting positive impact on children's lives.

A focus on young children's exposure to and use of language during mealtimes is also valuable for 2 reasons: (1) mealtimes provide a rich source of social interaction, and (2) the focus on eating is likely to be perceived as a natural setting for communication. We know that from early childhood, the quantity and quality of child-directed speech is important for language learning, and that naturalistic measures of type and token frequency are a valuable way of measuring linguistic experience and proficiency across different cultures and languages [40], provided all speakers who engage with the child are counted. There is strong empirical evidence that siblings play a more important role in language socialization in rural African families than in Western societies [41,42]. Serpell [43] notes that preadolescent children are often left in charge of their younger siblings in multi-age play groups; hence, including older siblings in our observations will greatly increase the scope of existing work.

Strengths and Limitations

While we have attempted our best to collect naturalistic data, video observations can always create slightly artificial situations. We have attempted to alleviate this problem by adding dummy recordings and carefully preparing participants in prerecording interviews, but it is still possible that we have not captured the most natural behaviors. In addition, we decided to focus on lunch times in order to not interfere too much with our participants' private lives; nonetheless, suppers might have provided a more typical setting for family mealtimes. Lastly, the number of both participants and observations was restricted by time and available funding for our project. Extending both would certainly lead to a richer and more powerful data set.

Future Directions

Our project is thus only a small step toward understanding how children's social environment shapes their developmental outcomes. A longitudinal setup following children's development from their first year of life throughout preschool would provide much deeper and more comprehensive insights. In addition, adding participants from different socioeconomic, cultural, and linguistic backgrounds would allow us to draw much wider conclusions. In terms of interventions, it would be interesting to focus on peer-to-peer interactions and identify situations and ways in which children in mixed age groups can support each other's learning, thus further bridging the home and school environments.

Dissemination Plan

We hope to publish at least 3 additional papers toward the end of our project in early 2023: one focusing on children's linguistic outcomes, one targeting children's nutritional status, and one qualitative paper describing and comparing children's home and school environments across sites.

In addition, we will share our results with colleagues and stakeholders through meetings, conferences, and social media. Using a bottom-up approach, we will discuss our results with parents and teachers from our local communities and share their feedback with policy makers at local, national, and international levels. To that end, we have built a close network of collaborators including school representatives, educationalists, language and community experts, and relevant government officials in Kenya and Zambia.

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Acknowledgments

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Data Availability

The data that support the findings of this study will be openly available in the UK Data Archive [44].

Conflicts of Interest

None declared.

Multimedia Appendix 1
Language coding scheme.
[DOCX File , 36 KB - resprot_v11i7e36925_app1.docx]

Multimedia Appendix 2
Behavioral coding scheme.
[DOCX File , 42 KB - resprot_v11i7e36925_app2.docx]

References

1. Muigai J. Parental Involvement in Primary Schools in Kenya as a major strategy for academic success. Eur J Educ 2018:19. [doi: 10.46827/ejes.v0i0.2011]
2. Lemmer E. Parent involvement in teacher education in South Africa. Int J About Parents Educ 2007;1:218-229 [FREE Full text]
3. Akinsola E. Omoluwabis approach to educating the African child. In: Handbook of African Educational Theories and Practices: A Generative Teacher Education Curriculum. Bamenda: Human Development Resource Centre; 2012:221-244.
4. Gwanfogbe MB. Africas triple education heritages a historical comparison. In: Handbook of African Educational Theories and Practices: A Generative Teacher Education Curriculum. Bamenda: Human Development Resource Centre; 2012:39-66.
5. Munene II. Providing basic education for all in Africa: what we have learned. Africa Education Review 2015 Jul 27;12(1):1-6. [doi: 10.1080/18146627.2015.1036538]
6. Jones S, Schipper Y. Does family background matter for learning in East Africa? Africa Education Review 2015 Jul 27;12(1):7-27. [doi: 10.1080/18146627.2015.1036540]
7. Grantham-McGregor S. A review of studies of the effect of severe malnutrition on mental development. J Nutr 1995 Aug;125(8 Suppl):2233S-2238S. [doi: 10.1093/jn/125.suppl_8.2233S] [Medline: 7542705]
8. Gansaonré RJ, Moore L, Bleau L, Kobiané JF, Haddad S. Stunting, age at school entry and academic performance in developing countries: A systematic review and meta-analysis. Acta Paediatr 2022 Jun 12. [doi: 10.1111/apa.16449] [Medline: 35691004]
9. Roulstone S, Law J, Rush R, Clegg J, Peters T. Investigating the role of language in children's early educational outcomes. Department for Education. URL: https://eresearch.qmu.ac.uk/bitstream/handle/20.500.12289/2484/DFE-RR134.pdf?sequence=1&isAllowed=y [accessed 2022-06-14]
10. Duff FJ, Reen G, Plunkett K, Nation K. Do infant vocabulary skills predict school-age language and literacy outcomes? J Child Psychol Psychiatry 2015 Aug 04;56(8):848-856. [doi: 10.1111/jcpp.12378] [Medline: 25557322]
11. Hulme C, Snowling MJ, West G, Lervåg A, Melby-Lervåg M. Children's language skills can be improved: lessons from psychological science for educational policy. Curr Dir Psychol Sci 2020 Jul 08;29(4):372-377. [doi: 10.1177/0963721420923684]
12. Snow CE, Beals DE. Mealtime talk that supports literacy development. New Dir Child Adolesc Dev 2006;Spring(111):51-66. [doi: 10.1002/cd.155] [Medline: 16646499]
13. Weizman ZO, Snow CE. Lexical input as related to children's vocabulary acquisition: effects of sophisticated exposure and support for meaning. Dev Psychol 2001 Mar;37(2):265-279. [doi: 10.1037/0012-1649.37.2.265] [Medline: 11269394]

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14. Stewart CP, Iannotti L, Dewey KG, Michaelsen KF, Onyango AW. Contextualising complementary feeding in a broader framework for stunting prevention. Matern Child Nutr 2013 Sep 18;9 Suppl 2:27-45. [doi: 10.1111/mcn.12088] [Medline: 24074316]
15. Jonah CMP, Sambu WC, May JD. A comparative analysis of socioeconomic inequities in stunting: a case of three middle-income African countries. Arch Public Health 2018 Dec 10;76(1):77 [FREE Full text] [doi: 10.1186/s13690-018-0320-2] [Medline: 30555694]
16. Demographic and Health Survey. 2014. URL: https://dhsprogram.com/pubs/pdf/fr308/fr308.pdf [accessed 2022-06-14]
17. Marinda PA. Child-mother nutrition and health status in rural Kenya: the role of intra-household resource allocation and education. Int J Cons Stud 2006 Jul;30(4):327-336. [doi: 10.1111/j.1470-6431.2006.00518.x]
18. Ferguson E, Chege P, Kimiywe J, Wiesmann D, Hotz C. Zinc, iron and calcium are major limiting nutrients in the complementary diets of rural Kenyan children. Matern Child Nutr 2015 Dec 17;11 Suppl 3:6-20. [doi: 10.1111/mcn.12243] [Medline: 26778799]
19. Black M. Micronutrient deficiencies and cognitive functioning. J Nutr 2003 Nov;133(11 Suppl 2):3927S-3931S. [doi: 10.1093/jn/133.11.3927S] [Medline: 14672291]
20. Chonchaiya W, Pruksananonda C. Television viewing associates with delayed language development. Acta Paediatr 2008 Jul;97(7):977-982. [doi: 10.1111/j.1651-2227.2008.00831.x] [Medline: 18460044]
21. Heath SB, Heath SB. Ways with Words: Language, Life and Work in Communities and Classrooms. Cambridge: Cambridge University Press; 1983.
22. Gauvain M, Munroe RL, Beebe H. Children's questions in cross-cultural perspective. J Cross-Cult Psychol 2013 Apr 23;44(7):1148-1165. [doi: 10.1177/0022022113485430]
23. Ng'asike JT. African early childhood development curriculum and pedagogy for Turkana nomadic pastoralist communities of Kenya. New Dir Child Adolesc Dev 2014 Dec 15;2014(146):43-60. [doi: 10.1002/cad.20072] [Medline: 25512045]
24. Kerubo IP. African Indigenous Education As Practiced By The Maasai Of Kenya. University of Nairobi. 2016. URL: http://erepository.uonbi.ac.ke/handle/11295/99982 [accessed 2022-06-14]
25. Black M, Gove A, Merseth K. Platforms to reach children in early childhood. Disease Control Priorities Nov 20 2017:8. [doi: 10.1596/978-1-4648-0423-6_ch19] [Medline: 30212126]
26. Young B, Drewett R. Eating behaviour and its variability in 1-year-old children. Appetite 2000 Oct;35(2):171-177. [doi: 10.1006/appe.2000.0346] [Medline: 10986110]
27. Aglago EK, Landais E, Nicolas G, Margetts B, Leclercq C, Allemand P, et al. Evaluation of the international standardized 24-h dietary recall methodology (GloboDiet) for potential application in research and surveillance within African settings. Global Health 2017 Jun 19;13(1):35 [FREE Full text] [doi: 10.1186/s12992-017-0260-6] [Medline: 28629424]
28. Wakiuru MM. Influence of parents' socio-economic status on their participation in children's pre-school education in Kayole, Nairobi County, Kenya. Kenyatta University. 2016. URL: https://ir-library.ku.ac.ke/bitstream/handle/123456789/17577/Influence%20of%20parents%E2%80%99%20socio-economic%20status.pdf?sequence=1&isAllowed=y [accessed 2022-06-14]
29. ELAN. The Language Archive. URL: https://archive.mpi.nl/tla/elan [accessed 2022-06-14]
30. Weisleder A, Fernald A. Talking to children matters: early language experience strengthens processing and builds vocabulary. Psychol Sci 2013 Nov 01;24(11):2143-2152. [doi: 10.1177/0956797613488145] [Medline: 24022649]
31. Mutoro AN, Garcia AL, Wright CM. What can meal observations tell us about eating behavior in malnourished children? Int J Environ Res Public Health 2019 Jun 21;16(12):2197 [FREE Full text] [doi: 10.3390/ijerph16122197] [Medline: 31234377]
32. FAO/Government OK. FAO Myanmar Newsletter. Food and Agriculture Organization of the United Nations. 2018. URL: http://www.fao.org/3/I9120EN/i9120en.pdf [accessed 2022-06-14]
33. Akré J. World Health Organization. In: Encyclopedia of Human Nutrition (Second Edition). Amsterdam: Elsevier; 2005:437-445.
34. Food and Agriculture Organization of the United Naitons, United Nations University, World Health Organization. Human Energy Requirements: Report of a Joint FAO/WHO/UNU Expert Consultation: Rome, 17-24 October 2001. Rome: Food and Agriculture Organization; 2004.
35. Growth reference data for 5-19 years. World Health Organization. URL: https://www.who.int/tools/growth-reference-data-for-5to19-years/application-tools [accessed 2021-08-05]
36. Jarman M, Zeidler H, Shapiro L, Clarke R, Mooya H, Simatende B, et al. Qualitative accounts of school-aged children's diets during the COVID-19 pandemic in rural, central, Kenya. Nutrients 2021 Oct 09;13(10):3543 [FREE Full text] [doi: 10.3390/nu13103543] [Medline: 34684544]
37. Advancing Early Childhood Development: from Science to Scale. The Lancet. 2016. URL: https://www.thelancet.com/series/ECD2016 [accessed 2022-06-14]
38. Neumann C, Bwibo N, Murphy S, Sigman M, Whaley S, Allen L, et al. Animal source foods improve dietary quality, micronutrient status, growth and cognitive function in Kenyan school children: background, study design and baseline findings. J Nutr 2003 Nov;133(11 Suppl 2):3941S-3949S. [doi: 10.1093/jn/133.11.3941S] [Medline: 14672294]

XSL•FO
RenderX

39. Ndungu ZW, Chege PM. Dietary diversity and micronutrients adequacy of diets consumed by school aged children in Nairobi City County, Kenya. Nutr Food Technol Open Access 2019;5(1). [doi: 10.16966/2470-6086.156]
40. Hart B, Risley TR. Meaningful Differences in the Everyday Experience of Young American Children. Baltimore, MD: P.H. Brookes; 1995.
41. Sperry DE, Sperry LL, Miller PJ. Reexamining the verbal environments of children from different socioeconomic backgrounds. Child Dev 2019 Jul 30;90(4):1303-1318. [doi: 10.1111/cdev.13072] [Medline: 29707767]
42. Schieffelin BB, Ochs E. Language socialization. Annu Rev Anthropol 1986 Oct;15(1):163-191. [doi: 10.1146/annurev.an.15.100186.001115]
43. Serpell R. Literacy and child development in a contemporary African society. Child Dev Perspect 2020 May 07;14(2):90-96. [doi: 10.1111/cdep.12363]
44. UK Data Service: ReShare. URL: http://reshare.ukdataservice.ac.uk [accessed 2022-06-17]

Abbreviations

ECDE: Early Childhood Development and Education
FAO: Food and Agriculture Organization of the United Nations
HAZ: height-for-age Z score
WHO: World Health Organization
WHZ: weight-for-height for age Z score

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Protocol

An Intervention to Increase Outdoor Play in Early Childhood Education Centers (PROmoting Early Childhood Outside): Protocol for a Pilot Wait-list Control Cluster Randomized Trial

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Abstract

Background: Participation in outdoor play has been extensively documented as beneficial for the health, well-being, and development of children. Canadian early childhood education centers (ECECs) are important settings in young children's lives and provide opportunities to participate in outdoor play. However, there are barriers to the provision of outdoor play opportunities at ECECs, such as adverse weather conditions, poorly designed outdoor spaces, outdoor time policies, and early childhood educator comfort levels.

Objective: The PROmoting Early Childhood Outside (PRO-ECO) study is a wait-list control cluster randomized trial that evaluates the impact of the PRO-ECO intervention, an innovative outdoor play intervention, on children's outdoor play behavior. The purpose of this paper was to provide a detailed overview of the pilot study protocol and the methods that will be used to develop, implement, and evaluate the PRO-ECO intervention.

Methods: A total of 8 ECECs delivering licensed care to children aged 2.5 to 6 years in the Greater Vancouver region of British Columbia, Canada, and operated by the YMCA of Greater Vancouver (YMCA GV) are included in this study. Using a wait-list control cluster randomized trial design, we randomly allocated ECECs to either the PRO-ECO intervention arm (n=4) or the wait-list control arm (n=4). The primary outcome measures include changes in the proportion and diversity of observed outdoor play behavior during dedicated outdoor times at the ECECs as measured through observational behavior mapping. Secondary outcome measures include changes in educator attitudes; quality of ECECs' outdoor play space; and children's psychosocial

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strengths, physical activity levels, and social behaviors. A process evaluation of the acceptability of the PRO-ECO intervention in the 8 YMCA GV ECECs will also be assessed. Outcome data will be collected at baseline, 6-month follow-up, and 12-month follow-up. Mixed effect models will test the effect of the PRO-ECO intervention on quantitative outcomes. Baseline and postintervention data will be included in the analysis, controlling for the cluster design. Qualitative data will support quantitative findings and provide evidence for the acceptability of implementation.

Results: Participant recruitment for this study began in August 2021, and baseline data collection was completed at all 8 ECECs in November 2021. As of April 2022, a total of 130 children have been recruited to participate in this study.

Conclusions: The PRO-ECO pilot study will develop, implement, and evaluate the PRO-ECO intervention within 8 YMCA GV ECECs in the Vancouver region of British Columbia, Canada. The findings of this study will be useful for early childhood educators, ECEC providers, and policy makers to consider means for enhancing outdoor play provision and assessing the sustainability of the intervention in ECEC settings.

Trial Registration: ClinicalTrials.gov NCT05075580; https://clinicaltrials.gov/ct2/show/NCT05073380

International Registered Report Identifier (IRRID): DERR1-10.2196/38365

(JMIR Res Protoc 2022;11(7):e38365) doi:10.2196/38365

KEYWORDS

early childhood education and care; preschool; randomized controlled trial; RCT; intervention studies; outdoor play; built environment; pedagogy; behavior mapping

Introduction

Background

Outdoor play is "a form of play that takes place outdoors, where the outdoors is defined as any open-air, wild, natural, or human-made space" [1]. The value of outdoor play for children's health, well-being, and development has been extensively documented [2-8]. Significant evidence outlines the importance of outdoor play in children's cognitive, physical, emotional, and social development; health; and overall well-being [9-16]. In addition, spending time outdoors can boost children's vitamin D levels, spatial awareness, and motor skills while offering opportunities to stimulate physical activity [5,6,17]. Despite these benefits, children in North America are spending less time outdoors because of the changing landscape of neighborhoods, increased time spent on technology, and shifting family lifestyles [8,18-21]. Many children have limited access to outdoor environments or face barriers to accessing opportunities for outdoor play [19].

To address declines in children's opportunities for outdoor play, it is important to develop strategies and interventions that target the early years (0-6 years). Exposure to unstructured outdoor play experiences at an early age promotes positive self-esteem, attention skills, autonomy, and confidence [5,22], and supports lifelong healthier lifestyles [5]. Early childhood education centers (ECECs) are fundamental environments for the early years in Canada, with approximately 60% of children aged 0 to 5 years attending some form of childcare [23]. ECECs provide children with opportunities for outdoor play in environments that they may not otherwise experience in their homes or communities [24]. The provision of opportunities for outdoor play in ECECs depends on the built environment; early childhood educators' (ECEs) pedagogical approaches, knowledge, and self-efficacy; the policies that guide the delivery of early childhood education (government and program-specific); and the attitudes of parents and communities. Although outdoor play is an essential component of the pedagogy and facility design in ECEC settings in Canada, there is vast diversity in its provision and practice across programs. Many ECECs struggle to provide high-quality and stimulating outdoor play time and can encounter multiple actual and perceived barriers that span individual, interpersonal, organizational, and societal factors such as limited training in supporting outdoor play, excessive fears related to child safety, and deficiencies in the size of and affordances in the outdoor space [25-27].

The early childhood education landscape in British Columbia (BC) is governed by federal, provincial, and municipal policies. ECECs in BC must adhere to provincial Child Care Licensing Regulations, which are regulated by local health authorities across BC [28]. These regulations enforce a minimum of 6 m^2 of outdoor play area for each child and a minimum of 60 minutes of outdoor active play per day [28,29]. Outside of these requirements, it is up to the individual ECEC to determine the design and use of their outdoor space within the constraints of other licensing regulations.

Ecological models of health behaviors and child development demonstrate that ECEs' and children's behaviors are influenced by individual-level factors (eg, ECE knowledge and children's attitudes), social factors (coworker support and parent knowledge and attitudes), organizational factors (center policy and support), environmental factors (outdoor space and environmental features), and policy factors (licensing and governing policies) [30-32]. Increasing the capacity of ECECs to support high-quality outdoor play experiences for children requires a complex intervention with multiple components addressing the barriers and challenges of the ECECs' socioecological environment [33]. A complex intervention contains multiple interacting components, requires intervention participants (in this case, ECEs) to engage in several challenging behaviors, targets multiple organizational levels, requires collecting a range of measures to evaluate the intervention's diverse effects and potential unintended consequences, and

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allows for flexibility in tailoring the intervention to local circumstances [34].

Previous studies have evaluated play-based interventions to increase children's physical activity in ECECs [35,36]. However, there is minimal evidence of appropriate interventions that support children's participation in outdoor play in ECECs. The PROmoting Early Childhood Outside (PRO-ECO) wait-list control cluster randomized trial aims to evaluate the PRO-ECO pilot intervention, a comprehensive outdoor play intervention for children in ECECs. The aim of this paper was to describe the design and protocol of the PRO-ECO study. To our knowledge, this is the first cluster randomized controlled trial to evaluate a comprehensive outdoor play intervention in Canadian ECECs.

Study Objectives

The PRO-ECO study is guided by the following objectives: (1) to develop and implement the pilot PRO-ECO intervention with overarching components common to all ECEC intervention sites as well as customizable components that are responsive to the needs of each ECEC, (2) to assess the efficacy of the PRO-ECO intervention in increasing and diversifying outdoor play behavior in children aged 2.5 to 6 years, and (3) to assess the acceptability of the PRO-ECO intervention.

Methods

The methods outlined in this study are informed by the CONSORT (Consolidated Standards of Reporting Trials) statement for cluster randomized controlled trials [37] and the SPIRIT (Standard Protocol Items: Recommendations for Intervention Trials) statement for clinical trial protocols [38] and based on guidance on the development of complex interventions from the evaluation framework of the Medical Research Council [34].

Study Design

This study is a pilot wait-list control cluster randomized trial (trial registration NCT05075580) with an intervention arm and a wait-list control arm (Figure 1). A mixed methods approach will be used to collect qualitative and quantitative data designed to meet the study objectives. Quantitative outcomes support the evaluation of the primary outcome variables, and qualitative data assess the acceptability of the implementation of the intervention. Qualitative data will be collected concurrently with quantitative data and allow researchers to explore how the participants experience the intervention.

The study will be conducted in 8 ECECs operated by the YMCA of Greater Vancouver (YMCA GV) from September 2021 to November 2022. Individual ECECs served as the unit of randomization, with 50% (4/8) intervention sites and 50% (4/8) wait-list control sites composing the final sample. Intervention sites received the intervention immediately following baseline data collection, whereas wait-list control sites will receive the intervention 6 months later. Data on outcome measures will be collected at 3 time points: baseline (time 1), 6-month follow-up (time 2), and 12-month follow-up (time 3). Thus, outcome data will assess short- and longer-term outcomes within the intervention group and short-term outcomes within the wait-list control group. Baseline and postintervention data collection will occur during the fall and spring to ensure similar weather patterns at all time points.

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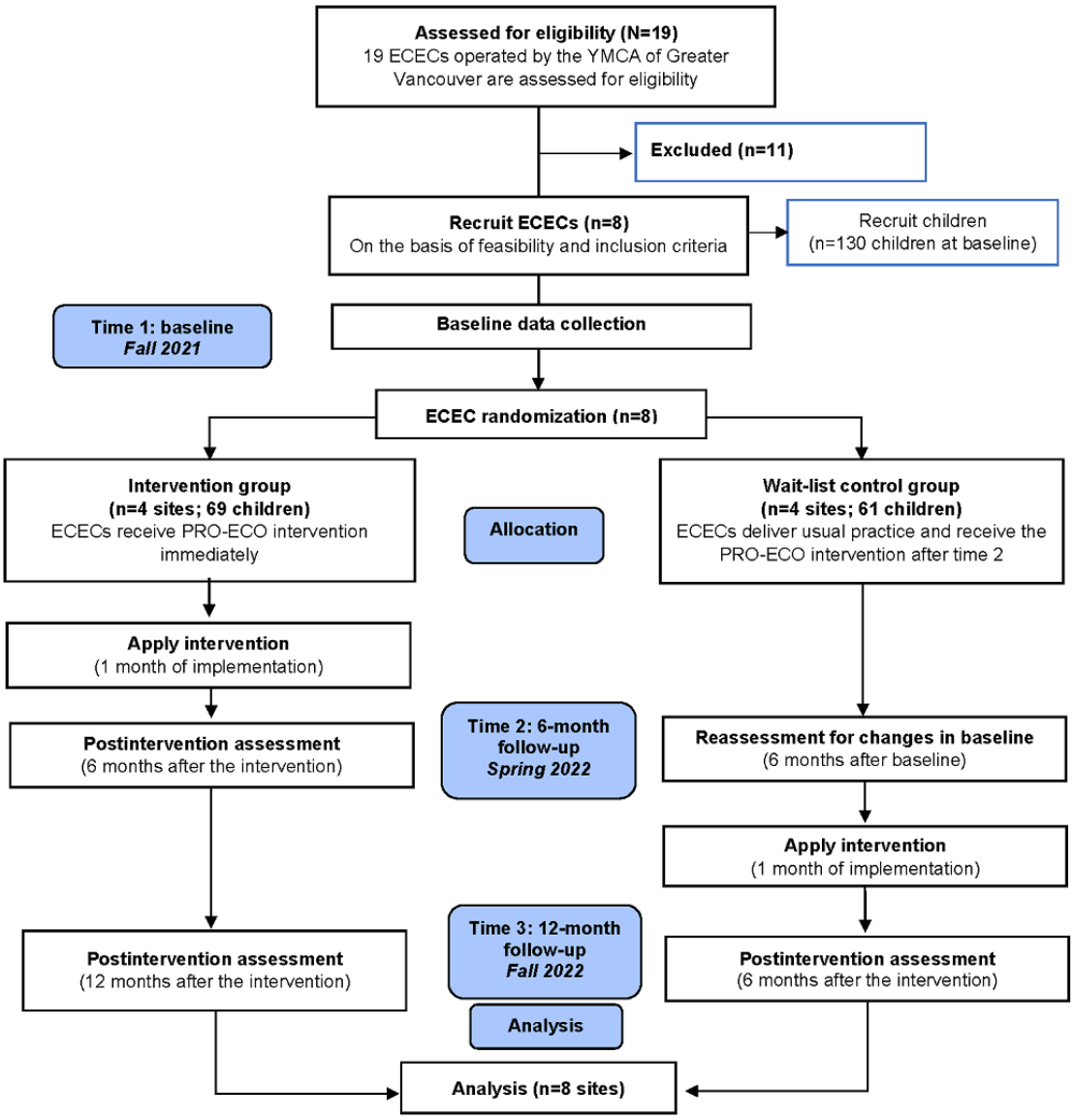
Figure 1. Wait-list control cluster randomized trial flow diagram: PROmoting Early Childhood Outside (PRO-ECO) pilot study. ECEC: early childhood education center.



Participant Eligibility and Recruitment

ECEC Recruitment

The PRO-ECO intervention will be piloted in 3 cities within the Greater Vancouver region in BC, Canada: Burnaby, Richmond, and Vancouver. The YMCA is one of the largest child care providers in BC, delivering early childhood education services across the province through their local chapters [39]. All 19 ECECs operated by the YMCA GV that provide care for children aged 2.5 to 6 years opt into the Affordable Child Care Benefit, helping ensure they are inclusive of all families. Of these 19 ECECs, 8 (42%) were selected based on their proximity to researchers at the University of British Columbia and their readiness to participate in the study as assessed through informal interviews with YMCA GV staff. Following site selection, each ECEC appointed a staff research lead (*champion*) to liaise between the research team, ECE staff, and parents. In addition, the YMCA GV selected 4 managers to work closely with the research team on all phases of the study. ECEs and ECEC supervisors and managers were also included in this study.

Children and Parents

Children were included in this study if they were aged between 2.5 and 6 years, were attending a participating ECEC between September 2021 and November 2021, and had parental consent. Recruitment of children and parents occurred through the champion at each ECEC, who distributed letters and emails and initiated face-to-face conversations. Over the course of the study, participating children may leave their ECEC, and newly enrolled children will be recruited as the study progresses.

Sample Size

This study will produce preliminary data for the calculation of a sample size for future studies [40]. Therefore, the sample size for this study is based on the feasibility of the pilot study. Recruitment for this study occurred during the COVID-19 pandemic, and many ECECs were operating with reduced enrollment. A total of 157 children were enrolled in participating ECECs and invited to participate, of whom 82 (52.2%) participated in the intervention arm and 75 (47.8%) participated in the wait-list control arm. Across all 8 ECECs, 82.8%

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(130/157) of children consented to participate in baseline data collection.

Randomization, Stratification, and Blinding

Before baseline data collection, we completed a stratified randomization of ECECs based on 2 stratification variables: *percentage of families enrolled in the BC Affordable Child Care Benefit* (<100% or 100%) and *type of facility* (above-grade or at-grade). Information on the type of facility and the percentage of families enrolled in the BC Affordable Child Care Benefit was collected from each ECEC site before randomization. Within each stratum, block randomization was applied to assign each center to the intervention group or the wait-list control group using Research Randomizer [41]. The research trial coordinator (RR) was not blinded to the randomization of each site; however, the research assistants were blinded at baseline data collection. Furthermore, the research staff member performing the data analysis will be blinded to randomization at the data analysis stage.

PRO-ECO Intervention

Intervention Development

Social cognitive theory provides the theoretical base for the PRO-ECO intervention. Furthermore, we are following the intervention mapping approach outlined by Bartholomew et al [42] to ensure that the intervention is grounded in theory, evidence, and the socioecological context and needs of the relevant population. Detailed information on the development of the PRO-ECO intervention can be found in Multimedia Appendix 1 [42-44].

Intervention Components

The PRO-ECO intervention is tailored to individual sites. Through the collection of focus group and baseline data, the intervention will be further refined to provide site-specific adjustments, such as specific materials in the built environment design modification or targeted follow-up training and mentorship. The PRO-ECO intervention involves 4 primary components designed to address the complexities and realities of outdoor play participation (Table 1). Funding for the built environment components of the PRO-ECO intervention at each site was provided by the YMCA GV, and the BC Cancer Agency provided monetary funds for the shade-related interventions. In addition to the 4 key intervention components, the study team secured donated rain gear items for children that were distributed to the ECEC if requested.

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Table 1. PROmoting Early Childhood Outside intervention components.

Intervention component	Intervention activity	Universal vs tailored to ECEC[a]	Socioecological level	Target population
YMCA GV[b] outdoor play policy	• Implementation of organizational "Outdoor Play Policy" across all YMCA GV ECECs that outlines enhanced outdoor play requirements and procedures. A parent handbook outlining outdoor play expectations will also be developed.	Universal	Organization	YMCA GV, ECECs, and ECEs[c]

ECE training	• A series of training sessions and opportunities for YMCA ECEs, including:
	  • 1-day training that includes content on the importance of outdoor risky play, methods for risk-benefit assessment, and encouragement of the use of loose parts
	  • Web-based supplemental training on pedagogical narration
	  • ECE outdoor play web-based training tool [45]
		Universal	Individual and center	ECE

ECE training	• Ongoing monthly and as-needed supportive training and mentorship provided by YMCA senior managers and research team	Tailored	Individual and center	ECE

ECEC outdoor space modification	• Each ECEC site will undergo an outdoor space modification as follows:
	  • Design plans for each center will be based on the Seven Cs and developed by 14 University of British Columbia School of Architecture and Landscape Architecture graduate students in a design studio.
	  • Graduate students will co-design modifications to the built environment with ECECs.
	  • Graduate students will implement modifications.
	  • A budget of CAD $4000 (US $3181.36) for general expenses and CAD $2000 (US $1590.68) for shade-related interventions is available for each site.
		Tailored	Center	ECEC, children, and ECEs

Parent engagement	• Parent engagement events will be provided to increase knowledge of the importance of outdoor play and encourage parent involvement in implementing the outdoor space modification. • Pedagogical narration of children's outdoor play experiences and learning will be posted by ECEs on the internal YMCA mobile app for access by parents.	Tailored	Center	Parents and community

[a]ECEC: early childhood education center.

[b]YMCA GV: YMCA of Greater Vancouver.

[c]ECE: early childhood educator.

Delivery of the Intervention

The intervention is split into 2 phases: the introduction phase and the maintenance phase. The introduction phase includes the implementation of the PRO-ECO intervention at the 4 intervention sites and takes up to 1 month. The maintenance phase is in place for 11 months after the PRO-ECO intervention is completely implemented in the intervention group and for 5 months for the wait-list control group. It involves maintaining the components of the intervention throughout the course of the study. The maintenance phase ends once the postintervention data are collected at time 3 (fall 2022).

Intervention Group

ECECs randomly assigned to the intervention group received the PRO-ECO intervention immediately following completion of time 1 baseline data collection. At time 2 in spring 2022, 6-month postintervention data will be collected. At time 3 in fall 2022, 12-month postintervention data will be collected.

Wait-list Control Group

ECECs randomly assigned to the wait-list control group continued with their normal daily practice, including standard curriculum and outdoor play time after time 1 baseline data collection. At time 2 in spring 2022, additional baseline data will be collected. The 4 wait-list control ECECs will receive the PRO-ECO intervention after time 2 data collection has occurred. Time 3 postintervention data collection will be completed 6 months after receiving the intervention, in fall 2022.

Data Collection and Measures

Primary Outcomes

The primary trial outcome is the occurrence of outdoor play behavior at ECECs during designated outdoor play times. Play behavior is coded using the expanded version of the Tool for Observing Play Outdoors (TOPO) developed by Loebach and Cox [46] and captured using a systematic observational mapping

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protocol. The TOPO measures children's play behavior through validated categories of 8 play types and 1 nonplay type along with their corresponding subtypes (Table 2). For this study, we will code play behavior and nonplay behavior at the subtype level at each ECEC, with all play types being categorized as *Play* and all nonplay types being categorized as *Nonplay* for the analysis of our primary outcome. In addition, diversity of children's outdoor play behavior will be examined using proportions of different play types.

The TOPO is implemented using a place-based observational behavior mapping (OBM) protocol. OBM strives to understand how an environment supports movement and use behaviors by mapping, recording, organizing, displaying, and analyzing geographically located data [47,48]. Base maps are used to provide an overview of the given environment, and predetermined observable data variables are collected. Each ECEC outdoor play space was divided into 2 measurement zones. In total, 2 researchers (one in each zone) will conduct observations at each ECEC as children participate in designated outdoor play time as determined by the ECEC. Researchers will scan each zone in a counterclockwise direction selecting the first child to enter the viewpoint. The researchers will then capture a 15-second video of the child's outdoor play and assign play behavior data to the primary activity performed during the video. A total of 200 fifteen-second play events will be compiled and coded for each ECEC site at each data collection time point (time 1, time 2, and time 3). The observational data will be collected using a place-centered approach that captures play behaviors of a range of children across the *space* of the ECEC rather than a person-centered approach that focuses on individual children. During each observation period, if there is no child in a given observational zone, a note will be made to indicate that no child was playing in that zone at that time. Additional variables will be collected through OBM and are outlined in Textbox 1.

The reliability of the OBM method is defined by the degree of interrater reliability and agreement, which will be assessed using weighted κ and intraclass correlation coefficients [49,50]. All researchers will participate in training sessions on the OBM methodology, and interrater reliability and agreement will be assessed at this time. In addition, a 10% sample of data at each time point will be recorded to assess the interrater reliability and agreement. A κ value of ≥0.70 will be used as commonly accepted as adequate for scientific research [49].

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Table 2. Tool for Observing Play Outdoors developed by Loebach and Cox [46].

Play type and subtype	Description
Physical play	
Gross motor	Using large muscles, whole body movement, large muscle activities that require hand-eye coordination
Fine motor	Smaller muscle movements and hand-eye coordination, picking up or manipulating small objects
Vestibular	Activities that test and improve sense of balance or reinforce their relationship to the earth, movement of the head or quick movements in multiple directions
Rough and tumble	Engagement in playful or mock fighting or wrestling or more broadly playful physical contact
Exploratory play	
Sensory	Primarily passive (ie, nonmanipulative) exploration of an object or environment, focused sensory attention
Active	Active manipulation of an object or the environment
Constructive	Physically building or constructing something or thoughtful destruction or taking apart of something
Imaginative play	
Symbolic	Using an object, action, or idea as a symbol for something else with no evidence of sociodramatic or fantasy
Sociodramatic	Pretending typical social, domestic, or interpersonal experiences or roles they may experience as adults
Fantasy	Enacting something that is unlikely to occur in real life
Play with rules	
Organic	2 or more kids agree to play or challenge each other in a certain way where they develop, negotiate, or change the rules as they go
Conventional	2 or more kids play games that have common, universal, or well-known rules that the players understand
Bio play	
Plants	Observes, discusses, or interacts with a living plant or parts of the plant (flowers or seed pods)
Wildlife	Observes, discusses, or interacts with wildlife (that is not a domestic pet)
Care	Acts in a way that demonstrates care or stewardship for the environment or an appreciation of nature
Expressive play	
Performance	Intentionally performing for others in some way
Artistic	Manipulating the environment specifically for an artistic, creative, or esthetic outcome
Language	Activities involving the playful use or testing of sound, words, or language
Conversation	Primary interaction is social conversation with children or adults
Restorative play	
Resting	Taking a mental break or rest
Retreat	Remove themselves to a small, controlled space, may watch others
Reading	Reading or writing for pleasure or listening to others or music
Onlooking	Child deliberately steps back from nearby play for a period of observation
Digital play	
Device	Playing with or on a digital device with no interaction with the environment
Augmented	Using a digital device to augment their interaction with the physical world
Embedded	Interacting with digital prompts or devices embedded in the environment without a personal digital device
Nonplay	
Self-care	Taking care of themselves or their appearance, can include helping another with these activities
Nutrition	When a child is taking a break to eat or drink
Distress	When a child is disengaged from play and exhibiting signs of distress
Aggression	Refers to nonplayful, antagonistic interactions with another child or adult
Transition	Nonplayful movement from one space to another, no active engagement or exploration of the environment
Other	Other types of observed “nonplay” activities, can include “chores” or cleanup work

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Textbox 1. Collected variables within the observational behavior mapping protocol.

Variables and levels

- Sex: male, female, and unknown
- Play type (see Table 2 for subtypes): physical, imaginative, bio, restorative, exploratory, play with rules, expressive, digital, and nonplay
- Risk-taking behavior: risk avoidance, exploratory risk appraisal, low or no risk, low-risk positive, low-risk negative, moderate-risk negative, moderate-risk positive, high-risk negative, and high-risk positive
- Play communication: play, environment, peer-social, adult-social, cowabunga!, self-talk, could not hear, ask for help, none, and other
- Adult interaction: no adult present, observing, participating, directing, restricting, and other
- Physical activity intensity: stationary or motionless, stationary with limb or trunk movements, slow or easy movement, moderate movement, and fast movement
- Peer interaction: solitary, parallel, cooperative, onlooking, unoccupied, and conflict
- Group size: open text
- Environmental interaction: fixed manufactured, fixed natural, loose manufactured, loose natural, and narrative text
- Interacted with coder: yes and no
- Adult says *Be careful*: yes and no
- Open coding: open text

Additional Outcome Measures

Attitudes Toward Outdoor Risky Play

The effect of the intervention on ECEs' tolerance of risk in play will be assessed using the Teacher Tolerance of Risk in Play Scale [51]. The Teacher Tolerance of Risk in Play Scale is a 25-item instrument that has been validated for use as a measure of intervention effects aimed at increasing children's access to risky play (a fundamental component of outdoor play) [51]. This measure will be administered to all ECEs at the 8 study sites during all data collection phases (times 1, 2, and 3).

Quality of ECEC Outdoor Spaces

The Seven Cs framework will form the basis for the assessment of outdoor space quality at all ECEC sites and the reassessment of the environment at ECEC sites after implementation of the PRO-ECO intervention and will guide the development of the plan for modification of the outdoor environment [52]. The Seven Cs framework was designed to provide guidance in the design of outdoor play spaces for children in early childhood settings based on 7 criteria: character, context, connectivity, change, chance, clarity, and challenge [52]. The Seven Cs assessment tool for ECECs will be used for baseline and postintervention measurement [53].

Acceptability of the PRO-ECO Intervention

As this study pilots an outdoor play intervention that can be replicated at other ECECs, it is imperative to assess the process of intervention implementation and acceptability (from the perspective of ECEs, parents, and YMCA GV managers). In this study, acceptability relates to the willingness of individuals (ECEs, parents, and children) and the organization (YMCA GV) to participate in the intervention, inform future recommendations, and apply the intervention for future use. Qualitative data will be collected before and after the intervention to understand the acceptability of the PRO-ECO intervention by the target populations at each site. Focus groups and individual key informant interviews will be organized with ECEs and ECEC administrators, who can provide critical and reflective information about the acceptability of the intervention. To understand parents' perceptions of the acceptability of the PRO-ECO intervention, a purposive sample of parents will be engaged to participate in intercept interviews. The intercept interview method provides a convenient way of interviewing the target population at the time and location most relevant and convenient in the context of the study [54]. In our study, it will be at the time of child drop-off or pick-up at their ECEC. Intercept interviews will be approximately 10 minutes long to accommodate parents' busy schedules.

Semistructured interview guides have been developed for the focus groups, key informant interviews, and intercept interviews with parents. These interview guides were developed by theorizing the constructs of acceptability in our study [55], such as perceived change in children's outdoor play because of the intervention, feasibility for broad implementation, and the cost-benefit of the intervention. Focus groups will be administered to discuss children's outdoor play, the challenges they are experiencing, and their suggestions for change, including modifications to the outdoor space. Qualitative methods will be administered at time 1 (baseline) for all sites, at time 2 for intervention ECECs, and at time 3 for wait-list control ECECs.

Economic Evaluation of the PRO-ECO Intervention

An economic evaluation will examine the costs of implementation of the intervention and the cost versus benefits of the PRO-ECO intervention. YMCA GV administrative data that can be monetized will be collected to consider the monetary benefits of the PRO-ECO intervention in comparison with the capital costs of intervention administration. Information will be collected throughout the study (Textbox 2) to compile a comprehensive economic evaluation guided by the framework by Levin and Schwartz [56].

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An additional economic analysis will also consider the resources and costs associated with expanding the PRO-ECO intervention to future ECEC sites.

Textbox 2. Information collected throughout the study to compile a comprehensive economic evaluation.

Information for economic evaluation

- Ongoing administrative costs specific to the PROmoting Early Childhood Outside (PRO-ECO) intervention in both the introduction and maintenance phases (ie, beyond usual early childhood education center [ECEC] programming costs):
  - Capital costs of using, maintaining, and staffing ECECs
  - Out-of-pocket ECEC expenses
  - Early childhood educator (ECE) and manager time commitment
  - ECE sick days
  - ECEC staff turnovers
  - Children's attendance rates
  - Reported incidents of challenging child behaviors
  - Reported incidents of child injuries
  - Benefits of the PRO-ECO intervention (outdoor play proportion)
- Implementation costs of the PRO-ECO intervention components:
  - ECE training (eg, total hours spent training and average hourly pay of trainers)
  - Built environment modifications (eg, supply costs, total hours spent purchasing supplies, total hours spent designing built environment modifications, total hours spent modifying the built environment, and average hourly pay of all parties involved)
  - Parent engagement (eg, total hours spent engaging with parents and average hourly pay of trainers)
  - Additional outdoor gear for children and ECEs (eg, jackets, boots, and rain ponchos)

Child Health, Development, and Well-being

The psychosocial strengths of children will be assessed using the Strengths and Difficulties Questionnaire, teacher version [57], which includes 25 items across 5 scales measuring emotional symptoms, conduct problems, hyperactivity or inattention, peer relationship problems, and prosocial behavior. When combining the subscales without the prosocial scale, a total difficulty score is provided to outline psychosocial challenges and strengths [58]. In addition, ECEs' perceptions of children's confidence, motivation, knowledge, and understanding of outdoor play participation will be captured through ECEs' pedagogical narratives, focus groups, and interviews. Children's physical activity intensity will be measured using the Children's Activity Rating Scale (CARS) as part of the OBM protocol [59]. Injury incidents will be measured through the abstraction of data from ECEC incident report forms. The Preschool Social Behavior Scale-Teacher Form [60] will be used to measure child development and behavior outcomes, including 19 items measuring relational aggression, overt aggression, prosocial behavior, and depressed affect. Child health, development, and well-being outcomes will be assessed at baseline (time 1), 6-month follow-up (time 2), and 12-month follow-up (time 3).

Study Covariates

Covariates for this study will include demographic information of children, including sex, age, first language spoken at home, family composition, average household income, and the highest level of education completed by a household member. The demographic information of the children will be collected using parent-reported questionnaires. In addition, the child's length of time at the ECEC and other forms of formal care, as well as the type of care (full-time or part-time), will be collected. At the time of data collection, data on the weather, temperature, and time of day will be recorded. The study covariates will be collected at each data collection time point (time 1, time 2, and time 3).

The following information related to recruitment, retention, and attendance will be collected throughout the intervention period (1 year) for both the intervention and control sites: (1) number of eligible children that were approached to participate in the study; (2) number of children who consented to participate, did not consent to participate, or did not respond; (3) number of children who withdrew from the study; (4) number of children who enrolled in the ECECs after initiation of the intervention; (5) number of children who left the ECEC after initiation of the intervention; and (6) individual and center-wide attendance rates at each ECEC. An overview of outcome variables measured as part of the PRO-ECO study is shown in Table 3.

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Table 3. Outcome variables and measures for the PROmoting Early Childhood Outside (PRO-ECO) study[a].

Outcome, subcategory, and variable	Measure	Informant			
		Child	ECE[b]	ECEC[c]	Parent
Primary outcomes—children					
Occurrence of outdoor play	TOPO[d]—play type	✓			
Diversity of outdoor play behavior	TOPO—play type	✓			
Additional outcomes					
ECEC					
Quality of ECECs' outdoor play space	Seven Cs ECEC assessment score			✓	
ECEs' attitudes toward risky play	T-TRiPS[e]		✓		
Acceptability of PRO-ECO intervention	Interviews and focus groups with ECEs and administrators; intercept interviews with parents		✓		✓
Economic analysis of PRO-ECO intervention	ECE and child attendance, ECE staff turnover, incidents of children's challenging behaviors, institution and intervention costs, and nonfinancial outcomes (outdoor play)		✓	✓	
Child health, development, and well-being					
Psychosocial	SDQ[f]	✓			
Injury	Reported incidents			✓	
Physical activity intensity	OBM[g] (CARS[h])	✓			
Development and behavior outcomes	PSBS-T[i]		✓		

[a]All variables will be collected at each time point (time 1, time 2, and time 3).

[b]ECE: early childhood educator.

[c]ECEC: early childhood education center.

[d]TOPO: Tool for Observing Play Outdoors.

[e]T-TRiPS: Teacher Tolerance of Risk in Play Scale.

[f]SDQ: Strengths and Difficulties Questionnaire.

[g]OBM: observational behavior mapping.

[h]CARS: Children's Activity Rating Scale.

[i]PSBS-T: Preschool Social Behavior Scale-Teacher Form.

Analysis

Primary Outcome Analysis

The proportion of play occurrence in comparison with nonplay occurrence across ECECs at baseline will be summarized by intervention group using frequency and percentages. This follows a similar analysis completed by van Dijk-Wesselius et al [61], who used a comparison of children's play and nonplay behavior before and after the intervention as an effective and significant measurement outcome of children's outdoor play occurrences. The frequencies and percentages of all play types will also be summarized by treatment group to provide a descriptive overview of diversity of play. This follows previous descriptive analyses completed by Loebach et al [48,62], who used OBM data to examine the frequency and diversity of play types. Baseline demographic and ECEC characteristics will be summarized by group using mean and SD and median and IQR for continuous variables, and frequencies and percentages for categorical characteristics. Bivariable relationships between children's demographic characteristics and outdoor play occurrence, as well as by intervention group, will be explored to assess for potential confounding at an individual level given that randomization is at the cluster level. Mixed effect models will be used to assess differences in quantitative outcome measures between the intervention and wait-list control groups as well as within-group comparisons of pre- and postintervention measures.

Cost-benefit Analysis

Cost-benefit analyses aim to estimate the costs and benefits of a particular policy or program and determine whether the societal impacts are worth the investment. For both short- and long-term cost-benefit analyses, we will (1) estimate the economic values of the costs and benefits for the a priori variables of interest (capital costs and changes in occurrence of outdoor play) and (2) apply an investment criterion to the estimated values of costs and benefits [63]. Our analysis framework will be based on decades of published methods from economists evaluating the Perry Preschool project [64-67], a

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longitudinal study that followed preschool-aged children from disadvantaged backgrounds through adult life [63,68]. To assess societal effects, we will use a net present value criterion to account for benefits and costs that vary over time [63]. For the cost-effectiveness analysis, we will examine differences in outdoor play occurrences per dollar spent on the PRO-ECO intervention versus traditional outdoor play delivery [69].

Qualitative Analysis

Qualitative interview data from ECE focus groups, individual key informant interviews, and intercept interviews with parents will be analyzed using the qualitative content analysis method [70]. Theorized constructs of acceptability, which inform our interview guides, will also be used as the analytical framework to understand and categorize participant narratives. Given that the primary aim of the qualitative interviews is to describe participants' acceptability of the intervention, this deductive analytical approach will serve well in providing focus and content for different constructs of our interest. New concepts will also be constructed that are not fully captured or described by the existing analytical framework, and concepts that are deemed necessary for further exploration will be analyzed anew using the thematic analysis method [71]. More specifically, we will follow 6 phases of reflexive thematic analysis—*familiarization, generating initial codes, searching for themes, reviewing themes, defining and naming themes, and producing the reports*—to go beyond descriptive reports and yield a more complex and nuanced account of a phenomenon or experience.

Ethics Approval

Ethics certification was received from the University of British Columbia and the Children's and Women's Health Centre of British Columbia Research Ethics Board (H20-03912).

Results

This study was developed to implement and evaluate the PRO-ECO intervention. Funding to conduct this study was confirmed in January 2021. Ethics approval through the University of British Columbia and the Children's and Women's Health Centre of British Columbia Research Ethics Board was received in March 2021, and participants were recruited beginning in August 2021. Baseline data were collected from October 2021 to November 2021, and the intervention ECEC sites received the PRO-ECO intervention in December 2021. As of April 2022, a total of 130 children have been recruited to participate in this study.

Discussion

Overview

This study is novel in building and evaluating a comprehensive intervention to enhance outdoor play in Canadian ECECs. The PRO-ECO intervention addresses ECECs' socioecological context, including the ECEs' individual knowledge, attitudes, and behaviors; parents' knowledge and attitudes toward outdoor play; the quality of the outdoor play space; and the policies governing the facility. The intervention is underpinned by social cognitive theory using evidence-based behavior change techniques to foster change. It includes aspects that can be universally applied but also the flexibility to tailor to local needs and context. Using a mixed methods, wait-list control cluster randomized trial design, the implementation and efficacy of the PRO-ECO intervention can be assessed.

The results and lessons learned through this study will inform the feasibility of a full-scale randomized trial that continues to assess the effectiveness of the intervention as well as help develop guidelines for the implementation of the PRO-ECO intervention in other ECECs. Furthermore, the health economic analyses will generate data to inform the sustainability of future academic and health policies in ECECs.

Strengths and Limitations

A strength of this study and the development of the PRO-ECO intervention is that an interdisciplinary stakeholder committee has been gathered to inform best practices and the primary components of this intervention. The process has included extensive partnership and consultation with YMCA GV management; ECEs; licensing officers; and multidisciplinary experts in early childhood education, landscape architecture, public health, outdoor play, and child development.

The PRO-ECO study will provide evidence-based information on the curriculum, policies, outdoor environments, and professional development training that support outdoor play opportunities among children in ECECs. The results of this study may be applied broadly through the expansion of the intervention to other YMCA ECECs and potentially other child care programs across Canada. This study will also provide insightful alignment with ongoing international research on outdoor play in ECECs, such as a recent study published in Norway [27] and research in Washington on their newly licensed outdoor ECEC programs [72].

In designing the PRO-ECO study, the research team identified common challenges when implementing an outdoor play intervention in ECECs and aimed to address them in the study design. However, because of the complexity of this study design, there are limitations that are anticipated throughout this study. First, the PRO-ECO intervention is a pilot study and, therefore, the sample size is based on feasibility while retaining optimal statistical power. To understand if the PRO-ECO intervention can be administered and assessed in a larger sample size, a sample of 8 ECECs is included in this study. This sample size could limit the identification of our estimated effect size between the intervention and control groups. The site inclusion criteria consider the readiness of the site to participate and the geographic area where the site is located. In addition, stratified randomization strives to create an intervention and control group that are similar while also ensuring there is a diverse representation of child care sites in the Greater Vancouver region. However, although considerations were made to create a diverse and representative sample of child care sites, we cannot account or stratify for all site characteristics.

Although this study strives to measure change in the occurrence of outdoor play before and after the intervention in comparison with nonplay, there is a possibility that the amount of *nonplay*

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at baseline is already low and would be difficult to reduce further. In this case, it may not be possible to detect a significant increase in the occurrence of outdoor play after the implementation of the intervention. Examining diversity of play as an additional primary outcome measure will provide more information to understand changes in outdoor play frequencies before and after the intervention and inform play measures for future studies. The CARS is a direct observation method used to measure physical activity levels among children and was selected based on the financial resources available for this study. In comparison with the use of indirect calorimetry, accelerometry, and heart rate monitoring to measure children's physical activity levels, the CARS may be subject to measurement error. However, all researchers collecting these data were extensively trained on the use of this tool, and previous studies have validated the use of direct observation methods, including the CARS, to assess children's physical activity [73].

Postintervention data collection will occur 1 year after baseline. It is expected that some children will be lost to follow-up as a result of leaving the ECEC or withdrawing consent. As indicated earlier, primary variable data will be collected at the center level, allowing us to study ECECs rather than individual children. Although the children participating in this study may change, we will engage additional children for postintervention data collection as needed. We anticipate study contamination between sites as ECEs can be moved between sites to accommodate staffing shortages. Furthermore, the champions at each site attend a weekly PRO-ECO project meeting where logistics are discussed and would be aware of the general activities involved in implementing the PRO-ECO intervention.

In addition, the design of this study commenced in 2019, before the COVID-19 global pandemic. Although ECECs continue to function and provide essential care to many families, we recognize that this has caused changes in the delivery of education and care across Canada. Disruption related to enrollment rates, staffing, or outdoor play practices at ECECs may cause limitations to participation and data collection in our study.

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Authors' Contributions

MB conceived the study. RR wrote the first full draft of this manuscript. Led by MB, all coauthors assisted in refining the study and intervention. JL and AC provided training on observational behavior mapping and the Tool for Observing Play Outdoors. SH led the development of the outdoor space modification. All authors read and approved the final manuscript.

Conflicts of Interest

None declared.

Multimedia Appendix 1
PROmoting Early Childhood Outside intervention development.
[DOCX File , 429 KB - resprot_v11i7e38365_app1.docx]

References

1. Outdoor play glossary of terms. Outdoor Play Canada. 2022. URL: https://www.outdoorplaycanada.ca/portfolio_page/outdoor-play-glossary-of-terms/ [accessed 2022-03-20]
2. Pellegrini AD, Dupuis D, Smith PK. Play in evolution and development. Develop Rev 2007 Jun;27(2):261-276. [doi: 10.1016/j.dr.2006.09.001]
3. Pellegrini AD, Smith PK. The development of play during childhood: forms and possible functions. Child Psychol Psychiatr Rev 1998 May 01;3(2):51-57. [doi: 10.1017/s1360641798001476]
4. Ginsburg K, American Academy of Pediatrics Committee on Communications, American Academy of Pediatrics Committee on Psychosocial Aspects of Child and Family Health. The importance of play in promoting healthy child development and maintaining strong parent-child bonds. Pediatrics 2007 Jan;119(1):182-191. [doi: 10.1542/peds.2006-2697] [Medline: 17200287]
5. Bento G, Dias G. The importance of outdoor play for young children's healthy development. Porto Biomed J 2017;2(5):157-160 [FREE Full text] [doi: 10.1016/j.pbj.2017.03.003] [Medline: 32258612]
6. Tremblay M, Gray C, Babcock S, Barnes J, Bradstreet C, Carr D, et al. Position statement on active outdoor play. Int J Environ Res Public Health 2015 Jun 08;12(6):6475-6505 [FREE Full text] [doi: 10.3390/ijerph120606475] [Medline: 26062040]

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7. Brussoni M, Gibbons R, Gray C, Ishikawa T, Sandseter E, Bienenstock A, et al. What is the relationship between risky outdoor play and health in children? A systematic review. Int J Environ Res Public Health 2015 Jun 08;12(6):6423-6454 [FREE Full text] [doi: 10.3390/ijerph120606423] [Medline: 26062038]
8. Kemple KM, Oh J, Kenney E, Smith-Bonahue T. The power of outdoor play and play in natural environments. Childhood Educ 2016 Oct 27;92(6):446-454. [doi: 10.1080/00094056.2016.1251793]
9. Thomas F, Harding S. The role of play: play outdoors as the medium and mechanism for well-being, learning and development. In: Outdoor Provision in the Early Years. Thousand Oaks, California: SAGE Publications; 2011.
10. Kellert S. Experiencing nature: affective, cognitive, and evaluative development in children. In: Children and Nature: Psychological, Sociocultural, and Evolutionary Investigations. Cambridge, Massachusetts: The MIT Press; 2002.
11. Little H, Wyver S. Outdoor play: does avoiding the risks reduce the benefits? Australasian J Early Childhood 2008 Jun 01;33(2):33-40. [doi: 10.1177/183693910803300206]
12. Wells NM, Evans GW. Nearby nature: a buffer of life stress among rural children. Environ Behav 2016 Jul 26;35(3):311-330. [doi: 10.1177/0013916503035003001]
13. Baldwin D, Rudge S. The role of serotonin in depression and anxiety. Int Clin Psychopharmacol 1995 Jan;9 Suppl 4:41-45. [doi: 10.1097/00004850-199501004-00006] [Medline: 7622823]
14. Levandovski R, Pfaffenseller B, Carissimi A, Gama CS, Hidalgo MP. The effect of sunlight exposure on interleukin-6 levels in depressive and non-depressive subjects. BMC Psychiatry 2013 Mar 05;13(1):75. [doi: 10.1186/1471-244x-13-75]
15. Santer J, Griffiths C, Goodall D. Free Play in Early Childhood A Literature Review. London: National Children's Bureau; 2007.
16. Fyfe-Johnson A, Hazlehurst M, Perrins S, Bratman G, Thomas R, Garrett K, et al. Nature and children's health: a systematic review. Pediatrics 2021 Oct;148(4):e2020049155. [doi: 10.1542/peds.2020-049155] [Medline: 34588297]
17. Absoud M, Cummins C, Lim MJ, Wassmer E, Shaw N. Prevalence and predictors of vitamin D insufficiency in children: a Great Britain population based study. PLoS One 2011 Jul 22;6(7):e22179 [FREE Full text] [doi: 10.1371/journal.pone.0022179] [Medline: 21799790]
18. Lester S, Russell W. Children's right to play. In: The SAGE Handbook of Play and Learning in Early Childhood. London: SAGE Publications; 2014.
19. Clements R. An investigation of the status of outdoor play. Contemporary Issues Early Childhood 2016 Jul 20;5(1):68-80. [doi: 10.2304/ciec.2004.5.1.10]
20. Charles C, Louv R, Bodner L, Guns B. Children and Nature 2008: a Report on the Movement to Reconnect. Children & Nature Network. 2008 Jan. URL: https://www.childrenandnature.org/wp-content/uploads/CNMovement.pdf [accessed 2022-06-22]
21. Rivkin M. “Happy Play in Grassy Places”: the importance of the outdoor environment in Dewey's educational ideal. Early Child Educ J 1998;25:199-202. [doi: 10.1023/A:1025613413109]
22. Ulset V, Vitaro F, Brendgen M, Bekkhus M, Borge AI. Time spent outdoors during preschool: links with children's cognitive and behavioral development. J Environ Psychol 2017 Oct;52:69-80. [doi: 10.1016/j.jenvp.2017.05.007]
23. Zhang S, Garner R, Heidinger L, Findlay L. Parents’ use of child care services and differences in use by mothers’ employment status. Statistics Canada. URL: https://www150.statcan.gc.ca/n1/pub/75-006-x/2021001/article/00007-eng.htm [accessed 2021-11-28]
24. Copeland KA, Khoury JC, Kalkwarf HJ. Child care center characteristics associated with preschoolers' physical activity. Am J Prev Med 2016 Apr;50(4):470-479 [FREE Full text] [doi: 10.1016/j.amepre.2015.08.028] [Medline: 26585052]
25. Dietze B, Kashin D. Perceptions that early learning teachers have about outdoor play and nature. Learn Landscape 2019 May 31;12(1):91-105. [doi: 10.36510/learnland.v12i1.981]
26. Wagner SL, Forer B, Cepeda IL, Goelman H, Maggi S, D’Angiulli A, et al. Perceived stress and Canadian early childcare educators. Child Youth Care Forum 2012 Sep 25;42(1):53-70. [doi: 10.1007/s10566-012-9187-5]
27. Sandseter EB, Cordovil R, Hagen TL, Lopes F. Barriers for outdoor play in early childhood education and care (ECEC) institutions: perception of risk in children’s play among European parents and ECEC practitioners. Child Care Pract 2019 Nov 22;26(2):111-129. [doi: 10.1080/13575279.2019.1685461]
28. Community care and assisted living act CHILD CARE LICENSING REGULATION. Government of British Columbia. URL: https://www.bclaws.gov.bc.ca/civix/document/id/complete/statreg/332_2007 [accessed 2022-03-20]
29. Director of licensing standards of practice safe play space. Government of British Columbia. 2007. URL: https://www2.gov.bc.ca/assets/gov/health/about-bc-s-health-care-system/child-day-care/safe_play_space.pdf [accessed 2022-03-20]
30. Sallis JF, Cervero RB, Ascher W, Henderson KA, Kraft MK, Kerr J. An ecological approach to creating active living communities. Annu Rev Public Health 2006 Apr 01;27(1):297-322. [doi: 10.1146/annurev.publhealth.27.021405.102100] [Medline: 16533119]
31. Sugiyama T, Okely AD, Masters JM, Moore GT. Attributes of child care centers and outdoor play areas associated with preschoolers’ physical activity and sedentary behavior. Environ Behav 2010 Dec 17;44(3):334-349. [doi: 10.1177/0013916510393276]

XSL•FO
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32. Cheng T, Brussoni M, Han C, Munday F, Zeni M. Perceived challenges of early childhood educators in promoting unstructured outdoor play: an ecological systems perspective. Early Years 2022 Feb 26:1-17. [doi: 10.1080/09575146.2022.2034140]
33. Messing S, Rütten A, Abu-Omar K, Ungerer-Röhrich U, Goodwin L, Burlacu I, et al. How can physical activity be promoted among children and adolescents? A systematic review of reviews across settings. Front Public Health 2019 Mar 19;7:55 [FREE Full text] [doi: 10.3389/fpubh.2019.00055] [Medline: 30941342]
34. Craig P, Dieppe P, Macintyre S, Michie S, Nazareth I, Petticrew M. Developing and evaluating complex interventions: the new Medical Research Council guidance. Int J Nurs Stud 2013 May;50(5):587-592. [doi: 10.1016/j.ijnurstu.2012.09.010] [Medline: 23159157]
35. Stone MR, Houser NE, Cawley J, Kolen AM, Rainham D, Rehman L, et al. Accelerometry-measured physical activity and sedentary behaviour of preschoolers in Nova Scotia, Canada. Appl Physiol Nutr Metab 2019 Sep;44(9):1005-1011 [FREE Full text] [doi: 10.1139/apnm-2018-0683] [Medline: 30730761]
36. Tucker P, Vanderloo LM, Johnson AM, Burke SM, Irwin JD, Gaston A, et al. Impact of the Supporting Physical Activity in the Childcare Environment (SPACE) intervention on preschoolers' physical activity levels and sedentary time: a single-blind cluster randomized controlled trial. Int J Behav Nutr Phys Act 2017 Sep 07;14(1):120 [FREE Full text] [doi: 10.1186/s12966-017-0579-7] [Medline: 28882152]
37. Campbell MK, Piaggio G, Elbourne DR, Altman DG, CONSORT Group. Consort 2010 statement: extension to cluster randomised trials. BMJ 2012 Sep 04;345(1):e5661. [doi: 10.1136/bmj.e5661] [Medline: 22951546]
38. Chan A, Tetzlaff JM, Altman DG, Dickersin K, Moher D. SPIRIT 2013: new guidance for content of clinical trial protocols. Lancet 2013 Jan 12;381(9861):91-92. [doi: 10.1016/S0140-6736(12)62160-6] [Medline: 23305999]
39. YMCA Member Associations. YMCA Canada. 2021. URL: https://www.ymca.ca/who-we-are/about-us/find-your-ymca [accessed 2021-05-05]
40. In J. Introduction of a pilot study. Korean J Anesthesiol 2017 Dec;70(6):601-605 [FREE Full text] [doi: 10.4097/kjae.2017.70.6.601] [Medline: 29225742]
41. Research Randomizer.: Social Psychology Network URL: https://www.randomizer.org/ [accessed 2021-08-30]
42. Bartholomew L, Markham C, Ruiter R, Fernandez M, Kok G, Parcel G. Planning Health Promotion Programs: An Intervention Mapping Approach, 4th Edition. Hoboken, New Jersey, United States: John Wiley & Sons; 2016.
43. Bandura A. Social cognitive theory: an agentic perspective. Annu Rev Psychol 2001;52:1-26. [doi: 10.1146/annurev.psych.52.1.1] [Medline: 11148297]
44. Brussoni M, Han CS, Jacob J, Munday F, Zeni M, Walters M, et al. A web-based risk-reframing intervention to influence early childhood educators' attitudes and supportive behaviors toward outdoor play: protocol for the OutsidePlay study randomized controlled trial. JMIR Res Protoc 2021 Nov 18;10(11):e31041 [FREE Full text] [doi: 10.2196/31041] [Medline: 34792479]
45. Brussoni M, Han C, Jacob J. OutsidePlay. What is outdoor play?. URL: https://outsideplay.ca/ [accessed 2021-11-18]
46. Loebach J, Cox A. Tool for observing play outdoors (TOPO): a new typology for capturing children's play behaviors in outdoor environments. Int J Environ Res Public Health 2020 Aug 04;17(15):5611 [FREE Full text] [doi: 10.3390/ijerph17155611] [Medline: 32759703]
47. Using behaviour mapping to investigate healthy outdoor environments for children and families: conceptual framework, procedures and applications. In: Innovative Approaches to Researching Landscape and Health. Milton Park, Abingdon-on-Thames, Oxfordshire, England, UK: Routledge; 2010.
48. Cox A, Loebach J, Little S. Understanding the nature play milieu: using behavior mapping to investigate children's activities in outdoor play spaces. Child Youth Environ 2018;28(2):232. [doi: 10.7721/chilyoutenvi.28.2.0232]
49. Cronbach LJ. Coefficient alpha and the internal structure of tests. Psychometrika 1951 Sep;16(3):297-334. [doi: 10.1007/BF02310555]
50. Shrout PE, Fleiss JL. Intraclass correlations: uses in assessing rater reliability. Psychol Bull 1979;86(2):420-428. [doi: 10.1037//0033-2909.86.2.420]
51. Teacher tolerance of risk in play scale (T-TRiPS): evaluating the psychometric properties of a new measure. Colorado State University. 2021. URL: https://mountainscholar.org/handle/10217/232469 [accessed 2021-11-29]
52. Herrington S, Lesmeister C. The design of landscapes at child-care centres: seven Cs. Landscape Res 2006 Jan;31(1):63-82. [doi: 10.1080/01426390500448575]
53. Brussoni M, Ishikawa T, Brunelle S, Herrington S. Landscapes for play: effects of an intervention to promote nature-based risky play in early childhood centres. J Environ Psychol 2017 Dec;54:139-150. [doi: 10.1016/j.jenvp.2017.11.001]
54. Ayala G, Elder J. Qualitative methods to ensure acceptability of behavioral and social interventions to the target population. J Public Health Dent 2011;71 Suppl 1:S69-S79 [FREE Full text] [doi: 10.1111/j.1752-7325.2011.00241.x] [Medline: 21656958]
55. Sekhon M, Cartwright M, Francis JJ. Acceptability of healthcare interventions: an overview of reviews and development of a theoretical framework. BMC Health Serv Res 2017 Jan 26;17(1):88 [FREE Full text] [doi: 10.1186/s12913-017-2031-8] [Medline: 28126032]

XSL•FO
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56. Levin H, Schwartz H. What is the cost of a preschool program? University of Pennsylvania. 2007 Mar 23. URL: https://repository.upenn.edu/cbcse/18/ [accessed 2022-03-20]
57. Goodman R. Psychometric properties of the strengths and difficulties questionnaire. J Am Acad Child Adolesc Psychiatry 2001 Nov;40(11):1337-1345. [doi: 10.1097/00004583-200111000-00015] [Medline: 11699809]
58. Stone LL, Otten R, Engels RC, Vermulst AA, Janssens JM. Psychometric properties of the parent and teacher versions of the strengths and difficulties questionnaire for 4- to 12-year-olds: a review. Clin Child Fam Psychol Rev 2010 Sep;13(3):254-274 [FREE Full text] [doi: 10.1007/s10567-010-0071-2] [Medline: 20589428]
59. Puhl J, Greaves K, Hoyt M, Baranowski T. Children's Activity Rating Scale (CARS): description and calibration. Res Q Exerc Sport 1990 Mar;61(1):26-36. [doi: 10.1080/02701367.1990.10607475] [Medline: 2091164]
60. Crick NR, Casas JF, Mosher M. Relational and overt aggression in preschool. Develop Psychol 1997;33(4):579-588. [doi: 10.1037/0012-1649.33.4.579]
61. van Dijk-Wesselius JE, Maas J, van Vugt M, van den Berg AE. A comparison of children's play and non-play behavior before and after schoolyard greening monitored by video observations. J Environ Psychol 2022 Apr;80:101760. [doi: 10.1016/j.jenvp.2022.101760]
62. Loebach J, Cox A, Little S. Behavior mapping to support the development of youth-friendly public outdoor spaces. In: The Routledge Handbook of Designing Public Spaces for Young People. New York: Routledge; 2020.
63. Barnett W. The Perry Preschool Program and Its Long-Term Effects: A Benefit-Cost Analysis. High/Scope Early Childhood Policy Papers, No. 2. Ypsilanti: High/Scope Educational Research Foundation; 1985.
64. Barnett S. Lives in the Balance: Age-27 Benefit-Cost Analysis of the High/Scope Perry Preschool Program. Monographs of the High/Scope Educational Research Foundation, Number Eleven. Ypsilanti: High/Scope Educational Research Foundation; 1996.
65. Belfield C, Nores M, Barnett WS, Schweinhart L. The High/Scope Perry preschool program: cost-benefit analysis using data from the age-40 followup. J Human Resources 2006;41(1):162-190 [FREE Full text] [doi: 10.3368/jhr.xli.1.162]
66. Muennig P, Schweinhart L, Montie J, Neidell M. Effects of a prekindergarten educational intervention on adult health: 37-year follow-up results of a randomized controlled trial. Am J Public Health 2009 Aug;99(8):1431-1437. [doi: 10.2105/ajph.2008.148353]
67. Schweinhart LJ. The value of high-quality full-day preschool. JAMA 2014 Nov 26;312(20):2101-2102. [doi: 10.1001/jama.2014.15124] [Medline: 25423218]
68. Heckman JJ, Moon SH, Pinto R, Savelyev PA, Yavitz A. The rate of return to the high/scope perry preschool program. J Public Econ 2010 Feb 01;94(1-2):114-128 [FREE Full text] [doi: 10.1016/j.jpubeco.2009.11.001] [Medline: 21804653]
69. Gortmaker SL, Long MW, Resch SC, Ward ZJ, Cradock AL, Barrett JL, et al. Cost effectiveness of childhood obesity interventions: evidence and methods for CHOICES. Am J Prev Med 2015 Jul;49(1):102-111. [doi: 10.1016/j.amepre.2015.03.032] [Medline: 26094231]
70. Elo S, Kyngäs H. The qualitative content analysis process. J Adv Nurs 2008 Apr;62(1):107-115. [doi: 10.1111/j.1365-2648.2007.04569.x] [Medline: 18352969]
71. Braun V, Clarke V, Hayfield N, Terry G. Thematic analysis. In: Handbook of Research Methods in Health Social Sciences. Singapore: Springer; 2019.
72. Washington becomes first in the nation to license outdoor, nature-based child care. Washington State Department of Children Youth and Families. URL: https://www.dcyf.wa.gov/news/washington-becomes-first-nation-license-outdoor-nature-based-child-care [accessed 2022-03-20]
73. McKenzie T. Use of direct observation to assess physical activity. In: Physical Activity Assessments for Health-related Research. Champaign, IL: Human Kinetics; 2002.

Abbreviations

BC: British Columbia
CARS: Children's Activity Rating Scale
CONSORT: Consolidated Standards of Reporting Trials
ECE: early childhood educator
ECEC: early childhood education center
OBM: observational behavior mapping
PRO-ECO: PROmoting Early Childhood Outside
SPIRIT: Standard Protocol Items: Recommendations for Intervention Trials
TOPO: Tool for Observing Play Outdoors
YMCA GV: YMCA of Greater Vancouver

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Protocol

The Impact of an Evidence-Informed Spinal Cord Injury Activities of Daily Living Education Manual (SADL-eM): Protocol for a Randomized Controlled Trial

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Abstract

Background: Spinal cord injury (SCI) is a catastrophic injury associated with functional loss and life-threatening complications. Many people with SCI in the Gaza Strip of Palestine are discharged from inpatient rehabilitation to the community while still lacking many daily life skills. This randomized controlled trial (RCT) seeks to test the impact of the Spinal Cord Injury Activities of Daily Living Education Manual (SADL-eM)—an evidence-based occupational therapy patient educational intervention—on rehabilitation outcomes.

Objective: The proposed trial aims to evaluate the SADL-eM intervention compared with standard treatment among people with SCI.

Methods: This is a parallel RCT with two study arms: intervention and control. A total of 90 patients treated in inpatient rehabilitation settings will be randomly allocated to two study groups. Both groups will receive standard care. The intervention group will also use the SADL-eM with their treating occupational therapist during rehabilitation. The SADL-eM is a comprehensive activities of daily living (ADL) educational tool that was codeveloped with people with SCI and stakeholders across Gaza. The self-report version of the Spinal Cord Independence Measure will be used on admission (ie, baseline measure) and after 6 weeks as the primary outcome measure. Secondary outcomes include the third version of the Spinal Cord Independence Measure, the Private Religiousness Practices Scale, the Organizational Religiousness Short-Form, additional ADL domains covered by the education manual, and adherence to the intervention. The effect of the intervention will be determined using repeated-measures analysis of variance.

Results: This study will be conducted from April 2021 through December 2022, with results expected to be available in January 2023.

Conclusions: If the SADL-eM is demonstrated as clinically effective, this will have significant implications for occupational therapy interventions in low- and middle-income countries.

Trial Registration: ClinicalTrials.gov NCT04735887; https://clinicaltrials.gov/ct2/show/NCT04735887

(JMIR Res Protoc 2022;11(7):e30611) doi:10.2196/30611

KEYWORDS

occupational therapy; educational intervention; activities of daily living; spinal cord injury; clinical trials

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Introduction

Background

Spinal cord injury (SCI) describes the damage to the spinal cord resulting from trauma (eg, stab wound), disease (eg, transverse myelitis), or degeneration (eg, due to a tumor or infection, such as tuberculosis). An SCI can result in paralysis of the extremities and trunk below the level of lesion that determines residual motor and sensory dysfunction [1]. All people with SCI have the right to participate in activities and occupations that are meaningful and purposeful, and that enable them to reach their desired potentials. However, many people with SCI in low- and middle-income countries (LMIC) are discharged from inpatient rehabilitation to the community while still dependent during many activities of daily living (ADLs). These ADLs include basic self-care activities, such as bathing, dressing, toileting, eating, and mobility [2]. Limited access to community-based rehabilitation services means that inpatient rehabilitation services need to be as effective as possible before discharge. In addition, patients need access to relevant information when they return home and continue their recovery journey. This paper describes a randomized controlled trial (RCT) study protocol that seeks to test the impact of the Spinal Cord Injury Activities of Daily Living Education Manual (SADL-eM), a contextually relevant education tool for people with SCI living in the Gaza Strip of Palestine.

Patient Education Following Spinal Cord Injury

People with SCI have many information needs after injury. Patient education is one affordable and accessible strategy that may enhance the effectiveness of rehabilitation for people with SCI in LMIC. Health professionals, such as occupational therapists, are a preferred source of information for health education seekers about SCI [3,4]. Education for patients with SCI aims to develop knowledge, skills, attitudes, and behaviors to maintain health and well-being, prevent secondary complications, and enhance active life participation after SCI [5]. Caregivers of people with SCI reported that health education is associated with less burden of disability. The most common topics covered include general health-related issues, home adaptation, assistive devices, and financial aspects [4]. Letts and colleagues [6] suggested that body anatomy and functioning topics should be presented early in the admission phase, while other topics like community integration can be presented at later phases of rehabilitation, so that people with SCI become progressively more independent.

Effective SCI education should be accessible and motivating in terms of information and how it is presented [3]. Educational interventions should provide support, for example, access to online support groups, consultations with rehabilitation professionals, and opportunities to ask questions. SCI educational interventions should also be cost-effective and up to date, and should meet the needs of the diversity of people accessing rehabilitation services [6]. It is also important that SCI education for adults promote autonomy and is guided by adult learning theory to facilitate the active roles of people with SCI [7]. Continuing postdischarge care and linking to community resources and the health care system are critical components of SCI education. Staff availability and patient readiness are also two important concerns for effective patient education. Time allocated for patient education can be inadequate due to patient treatment workload and staffing shortages. Decreased motivation and interest on the part of the patient during rehabilitation are other barriers to patient education [8].

Despite widespread guidance on education for patients with SCI, little research has been conducted on the effectiveness of education focused on ADLs for people with SCI [3,9]. A recent systematic review of clinical trials of ADL educational interventions identified only three interventions in four publications [10]. None of these significantly improved participation, although a meta-analysis showed that two of the interventions had a positive effect on the performance of ADLs, mobility (ie, wheelchair ambulation and transfers), and prevention of secondary complications, and resulted in a decrease in doctors' visits. In addition, all three interventions were delivered in high-income countries.

The first intervention included in that systematic review was the clinical practice guidelines for Preservation of Upper Limb Function Following Spinal Cord Injury, an ADL educational program focused on wheelchair ambulation and transfers. It involved two separate and specific forms: one for the therapist and one for the patient. The patient form was designed to be accessible, appropriate for novice adults without a previous medical background, and organized into modules. The therapist form was more complex regarding the level of information and was suitable for health professionals with a medical educational background [11]. To meet different learners' styles and preferences, different educational formats were used, including interactive discussions, printed handouts, pictures, and videos illustrating wheelchair propulsion and transfer skills to take home after discharge [11].

In the second intervention, the Peer Mentoring Programme, people with SCI acted as mentors and educators to people with newly acquired injuries. The peer mentors saw their mentees in person or communicated with them by phone during daily life scenarios within the first week of admission to active inpatient rehabilitation. The mentors then monitored the health status of their mentees using the Medical Complications Tracking Form; provided education relevant to ADL, prevention of complications, and incontinence issues; and initiated referrals to health care professionals if needed [12].

The third intervention, the Needs Assessment and Goal Planning Programme (NAGPP), is a comprehensive rehabilitation tool for everyday clinical use that was used as an ADL educational program. The Needs Assessment Checklist (NAC) is a part of the NAGPP and is used to evaluate and compare rehabilitation needs and outcomes. Therefore, the NAC reflects the patient's perception of his or her needs, choices, and priorities. The NAC was administered twice by a key worker who had the responsibility of coordinating the Rehabilitation and Goal Planning Programme: the first after beginning the active rehabilitation program and the second on admission to the predischarge rehabilitation ward. The key worker had the responsibility of coordinating the goal planning system with

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other members of the multidisciplinary team, and the patient was responsible for establishing and identifying needs, clarifying goals, and specifying targets [13].

More recently, Ziba and colleagues [14] evaluated the effect of a self-care educational program on the quality of life for people with SCI. Their study demonstrated that self-care program training was effective in improving the quality of life of people with SCI. Furthermore, Zarei and colleagues [15] investigated the positive effect of the education of patients with SCI and its contribution to satisfaction with marital sex life in men with SCI. These two clinical trials demonstrated the association between self-care education and satisfaction gained by improved levels of functionality and performance of ADLs. In their scoping review of health education by peers for people with SCI, Chaffey and Bigby [16] addressed another aspect of quality of life and satisfaction in their finding that people with SCI perceived their participation in peer education programs as supportive. In addition, education that includes peers helps people with SCI explore their potential, promotes self-confidence, and improves health outcomes.

Context of This Study

Palestine is characterized as one of the LMIC [17]. In 2016, Palestine registered 504 new cases of SCI, while the total cases with SCI in Palestine were 21,989. The incidence of SCI in Palestine was 90 cases per million people, while the prevalence was 6130 cases per million people; these data are relevant to Palestine. People with SCI in the Gaza Strip are predominantly young men, Muslim, living in family homes, and unemployed [18]. People with SCI requiring inpatient rehabilitation in the Gaza Strip complete their medical management in a secondary health care facility. Once medically stable, they are referred and admitted to an inpatient rehabilitation setting. Inpatient medical rehabilitation is provided in three clinical settings, which provide a short stay of 6 to 8 weeks. Rehabilitation focuses on preventing secondary complications and optimizing function. SCI rehabilitation aims to promote the participation of people with SCI in meaningful occupations of choice [19].

Similar to people with SCI in other LMIC, people with SCI in Gaza are frequently discharged prematurely from inpatient rehabilitation to the community, while lacking essential self-care skills, such as toileting and safe transfers [1]. This places them at higher risk of life-threatening complications. Community-based rehabilitation is not widely available. Assistive technology is often required by people with SCI to facilitate occupational participation. However, only 5% to 15% of people with SCI in LMIC have access to assistive technology [17].

Barriers to effective rehabilitation for people with SCI in Gaza include timely admission to a suitable rehabilitation setting, inadequate stays in inpatient rehabilitation, insufficient learning of daily life skills during inpatient rehabilitation, and lack of access to proper assistive technology. Moreover, many patients are added to the waiting list before admission. These barriers drive the need to develop evidence-based interventions during inpatient care that will improve rehabilitation outcomes, such as performance of ADLs [10].

There is little information about preferred educational formats on the part of people with SCI due to limited research targeting this topic. Some authors regard the internet as the best option, due to low cost and wide reach [20]. This is not always the case. Most people with SCI in LMIC are unemployed young men who have financial limitations and, therefore, cannot afford to pay for the internet and advanced technology, such as cell phones and iPads. We believe that a low-cost, paper-based manual format will enable improved access to information during inpatient rehabilitation, as well as when patients return to their community.

In 2018 we began a project to develop and evaluate the effectiveness of patient education for rehabilitation services in Gaza. We used participatory action research methods to develop an ADL education manual—the SADL-eM—that could promote occupational therapy education for people with SCI in the Gaza Strip, Palestine [21]. The aim of this study is to evaluate the impact of using the SADL-eM as an information tool during occupational therapy with people with SCI who are undergoing inpatient rehabilitation for an SCI in the Gaza Strip, Palestine. By improving patient education, this study may improve rehabilitation outcomes and patients' involvement in their treatment during their short stay in one of three inpatient rehabilitation settings available in the Gaza Strip. An effective educational intervention may also enhance the quality of care and reduce the cost of health care services in the long term.

Research Question

The research question for this study is as follows: Does the implementation of the SADL-eM delivered to patients with SCI in an inpatient rehabilitation setting in the Gaza Strip improve independence in ADL and participation over 6 weeks?

Primary Objectives

The primary objectives for this study are as follows:

1. To compare the effect of the education manual, relative to usual care, on self-reported changes in ADL from admission to 6 weeks postadmission, using the self-report version of the Spinal Cord Independence Measure (SCIM-SR) patient-rated measure.
2. To compare the effect of the education manual, relative to usual care, on observed changes in ADL from admission to 6 weeks postadmission, using the third version of the Spinal Cord Independence Measure (SCIM-III) clinician-rated measure.
3. To compare the effect of the education manual, relative to usual care, on religious practice, using the Private Religiousness Practices Scale and Organizational Religiousness Short-Form.
4. To compare the effect of the education manual, relative to usual care, on the domains of ADL covered by the education manual, including driving and community mobility, personal device care, health management and maintenance, ablution, and Islamic prayer, using questions developed for this research.

Secondary Objectives

The secondary objectives for this study are as follows:

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1. To determine the significance of biographical variables (ie, address zone, age, gender, highest level of education, marital status, employment status, monthly income, level of SCI, and type of SCI: complete or incomplete), the American Spinal Injury Association Impairment Scale score, and dysfunction on changes in ADL performance.
2. To measure adherence to the intervention using the therapist-report questionnaire regarding SADL-eM adherence, which will be developed for this purpose.

Research Hypotheses

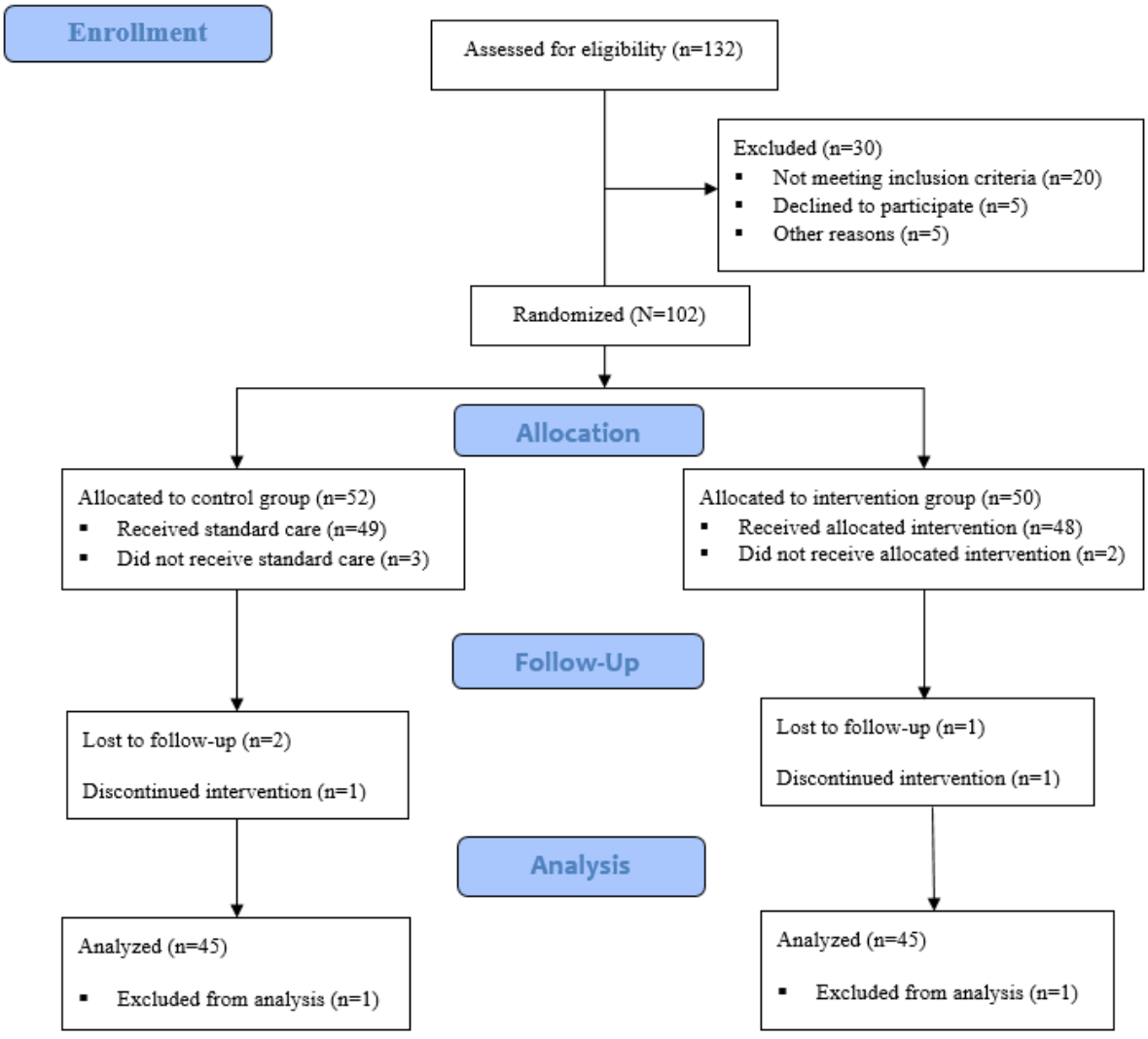
The null hypothesis for this study is as follows: there is no ADL outcome difference between the SADL-eM and the standard care delivered to inpatients with SCI in a rehabilitation setting. The alternative hypothesis for this study is as follows: the implementation of the SADL-eM delivered to inpatients with SCI in a rehabilitation setting has a significant impact on their ADL.

Methods

Study Design

Figure 1 shows the study flow diagram. This is a parallel RCT with a pretest and a posttest to evaluate a hypothesis of a cause-and-effect relationship. This study uses the CONSORT (Consolidated Standards of Reporting Trials) statement as the proposed standard for the reporting of parallel-group RCTs [22].

Figure 1. Study flow diagram according to the CONSORT (Consolidated Standards of Reporting Trials) statement.



Participants and Recruitment

Participants in the study will be inpatients with SCI from the Gaza Strip, of both genders, with any cause or type of SCI, and aged 18 to 65 years. They will be recruited from the group of admitted inpatients in one of the three rehabilitation settings in the Gaza Strip, Palestine: Hamad Rehabilitation Hospital, El-Wafa Rehabilitation Hospital, and Al-Amal Rehabilitation Hospital. Readmitted patients will be included in the study if they are eligible. Over the first 3 days of admission of each person with SCI in any of the three rehabilitation facilities, a clinical research supervisor will recruit study participants based on the study eligibility criteria. Inclusion and exclusion criteria are listed in Textbox 1.

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Textbox 1. Inclusion and exclusion criteria.

Inclusion criteria

- Confirmed spinal cord injury (SCI) diagnosis by computed tomography or magnetic resonance imaging report
- The American Spinal Injury Association Impairment Scale (ASIA): categories A, B, and C
- Aged between 18 and 65 years old
- Stable medical condition
- Time elapsed after SCI is not more than 6 months
- Minimum time of stay in inpatient rehabilitation unit is 6 weeks
- Active involvement in rehabilitation program
- Sufficient comprehension (ie, reading and writing) of the Arabic language

Exclusion criteria

- Unconfirmed diagnosis
- Patients who have communication or cognitive disorders, such as global aphasia and memory deficit
- Patients with a disturbed level of awareness, such as being in a coma or experiencing lethargy
- Time elapsed since SCI is more than 6 months
- ASIA: categories D and E
- Unstable medical condition
- Patients who have other causes of disability in addition to SCI, such as stroke or amputation
- Aged less than 18 years old or more than 65 years old
- Time of stay in inpatient rehabilitation unit is less than 6 weeks
- Inactive involvement in rehabilitation program
- Patients with a progressive disease or a psychiatric condition that would interfere with active participation in the rehabilitation program
- Patients with cardiovascular contraindications
- Persons who become ambulatory during the inpatient period
- Persons with complete tetraplegia caused by an SCI at the C4 level or above
- Persons on mechanical ventilation

Informed Consent

Each eligible participant who agrees to participate in the study will sign a written consent form before being included any of the study procedures or interventions. This consent form will be kept in a locked filing cabinet that will only be accessible by the research team.

Sample Size Calculation

We aim to recruit 90 participants to demonstrate a small effect caused by the intervention, with a postintervention mean difference of 15% between the intervention and control groups. The mean scores of the SCIM-III and the SCIM-SR at enrollment are expected to be 30% for both groups; at postintervention, these are expected to be 65% for the intervention group and 50% for the control group. A sample size of 90 participants, with 45 in each group, is sufficient for 80% power, a 5% margin of error, a CI of 95%, and an SD of 20%.

Blinding

This study uses an assessor-blinded data collection method. The study process conceals the intervention group identity from outcome assessors after participants' treatment assignment through randomization to minimize possible bias on the part of the outcome assessors, which could influence the reliability of study results. Moreover, therapists involved in the study and participants in the intervention group will be informed to refrain from sharing any part of the manual or included information with other patients or staff.

Randomization

The study sample of 90 SCI individuals will be randomized into two groups using a simple randomization approach, where an allocation list will be generated using the Random Number Generator online program. The two groups are as follows: conventional therapy group (n=45) and intervention (ie, SADL-eM) plus conventional therapy group (n=45). Eligible participants will be assigned to one study group according to the generated list.

Study Setting

Hamad Rehabilitation Hospital, El-Wafa Rehabilitation Hospital, and Al-Amal Rehabilitation Hospital are three inpatient rehabilitation settings that are part of the private health sector

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in the Gaza Strip of Palestine and provide comprehensive rehabilitation services. Their rehabilitation teams include physical rehabilitation doctors, rehabilitation nurses, physiotherapists, occupational therapists, speech therapists, clinical dietitians, psychologists, social workers, orthoptists, and community-based rehabilitation workers.

Feasibility Study

Feasibility studies are preliminary studies with small samples that investigate whether the main study can be conducted under the given conditions. RCTs usually use the feasibility study design to improve the trial's feasibility and avoid crucial barriers [23]. A total of 15 participants with SCI of any cause and type, aged 18 to 65 years old, and with a previous inpatient rehabilitation experience will participate in the feasibility study. They will be selected from the 2019-2020 inpatient list from the Hamad Rehabilitation Hospital. They will complete the SCIM-SR. A well-trained research assistant who is an occupational therapist will administer the biographical data collection tool, the SCIM-III, the Private Religiousness Practices Scale, the Organizational Religiousness Short-Form, and data collection regarding the domains of ADL covered by the education manual, including driving and community mobility, personal device care, health management and maintenance, ablution, and Islamic prayer. The patients and the research assistant will comment on the tools employed and point out any problems with the tests' instructions, instances where items are not clear, and formatting and other typographical errors and issues. Each question that measures performance of and participation in ADL will be analyzed using Cronbach α to test and improve reliability.

Activities of Daily Living Education Manual for People With SCI: The SADL-eM

Both study groups will receive usual care. In addition, each participant in the intervention group will receive a copy of the SADL-eM. The SADL-eM was developed by the authors following a systematic review and user-led development project. A team of 54 subject matter experts collaborated in a participatory action research project to develop the manual. To our knowledge, the SADL-eM is the first comprehensive SCI ADL educational tool available in Arabic [21].

The SADL-eM includes three elements essential to the intervention: knowledge, skills, and advice. The manual is made up of six detailed sections, including an introduction and the following five chapters: (1) Rehabilitation Team, (2) ADL, (3) Assistive Devices, (4) Home Environment Adaptation, and (5) Knowledge Guide. The SADL-eM uses text and illustrative pictures that were carefully selected for contextual relevance. The manual is simple and easy to use, and is suitable for people with a nonmedical background. However, good Arabic-language comprehension and the ability to read and write is mandatory for users. The purpose of the SADL-eM is to serve as a treatment tool during inpatient rehabilitation [21].

A clinical research supervisor will provide each participant in the intervention group with a hard copy of the SADL-eM and will explain the purpose of the manual and how to use it. The manual will be reviewed by the treating occupational therapist who received training on the use of the SADL-eM (ie, a 6-hour training on the minimum standards of the use of the SADL-eM for SCI education) and by the person with SCI during their treatment sessions. During occupational therapy sessions, the therapist will refer to the relevant chapter of the manual and answer the participant's queries regarding the content of the manual. The therapist will also indicate to the participants which parts of the manual are not relevant to them, based on their gender, driving status, or level of SCI.

According to the minimum standards of SADL-eM use for SCI education, the therapist will include the manual in as many SADL-eM educational sessions as required, but not less than three 15-minute sessions per week. The minimum level of clinical experience required of each treating occupational therapist will be 2 years. Good Arabic-language comprehension and the ability to read and write is mandatory for both therapists and patients. Commitment and adherence to the SADL-eM minimum standards are prerequisites and will be assured during the consenting of participants.

The participants will keep the manual to review after sessions and after discharge from the inpatient rehabilitation setting. The research assistant who performs data collection, the clinical research supervisor, and the occupational therapy team will be invited for an informational session prior to data collection in each of the participating settings. The informational session will focus on the study purpose, recruitment, eligibility criteria, use of the SADL-eM, roles, bias reduction, and blinding. The use of data collection tools will take place in a separate session with the research assistant. The principal researcher will answer all questions from the research team during informational sessions and during the research study.

For the purpose of this study, the SADL-eM will be provided during face-to-face individual occupational therapy sessions without any constraints regarding the treatment area. The face-to-face delivery of the SADL-eM does not require any infrastructure or special equipment.

The number of sessions, time allocated, and frequency of sessions will be determined by each therapist and participant to ensure that the treatment is person centered, given that the minimum standards of the SADL-eM implementation are met. Determinants may include a participant's capabilities, potential, and progress during treatment as well as the scope of the service, such as time allocated for each patient, therapist-to-patient ratio, and frequency of inpatient sessions. The therapist and the participant will continue to use the manual during treatment sessions until they decide there is no need for further use of the manual or the participant is discharged. The treating occupational therapists will retain records of any change or modification of the SADL-eM administration. The researchers will conduct a pilot study in a similar sample of 15 people with SCI to improve the use of the intervention and data collection tools.

Nonadherence to medical treatment in clinical trials of medical efficacy may obscure the data that are collected and disrupt the findings that are obtained [24]. The steps to ensure adherence to the intervention during the study include clearly defining the intervention, measuring adherence, and then comprehensively

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reporting adherence to the intervention. Attendance records collected by the therapist (ie, time, duration, and intensity of treatment and elements covered by the manual) and the therapist-report questionnaire regarding SADL-eM adherence will be used to measure and report adherence to the SADL-eM intervention.

Data Collection

Table 1 outlines the schedule of the enrollment tasks, interventions, and assessments that occurred at the study time points.

Table 1. The schedule of enrollment tasks, interventions, and assessments.

Study tasks	Study time point					
	Enrollment: Apr 2021	Allocation: Day 0	Postallocation			
			Day 1	Day 42 (week 6)	Day 43	Day 44
Enrollment tasks						
Eligibility screen	✓[a]					
Informed consent	✓					
Admission to study		✓				
Interventions						
Intervention A[b]			✓	✓		
Intervention B[c]			✓	✓		
Assessments						
Baseline variables						
Patient education		✓				
ADL[d]		✓				
Outcome variables						
SCIM-SR[e]		✓			✓	
SCIM-III[f]		✓			✓	
Other data variables						
The Private Religiousness Practices Scale		✓			✓	
Organizational Religiousness Short-Form		✓			✓	
SADL-eM[g] adherence therapist-report questionnaire						✓

[a]A checkmark indicates that the task, intervention, or assessment was performed at the indicated time point.

[b]Inpatient rehabilitation with standard care.

[c]Health education using the SADL-eM.

[d]ADL: activities of daily living.

[e]SCIM-SR: self-report version of the Spinal Cord Independence Measure.

[f]SCIM-III: third version of the Spinal Cord Independence Measure.

[g]SADL-eM: Spinal Cord Injury Activities of Daily Living Education Manual.

Participants' recruitment and admission to the study will continue until the desired sample size is reached. The allocation sequence will be concealed from patients, therapists, and assessors. The data regarding exposure to the educational intervention will be collected by a separate research assistant (ie, the research coordinator) by phone and will be concealed from the assessors. Each occupational therapy department will assign four therapists to follow up the trial cases: two for the intervention group and two for the control group. All the staff in the occupational therapy department, the participants, and the assessors will be asked to refrain from discussing the trial and intervention material between them. The importance of concealing any information until the end of the study will be explained. Study participants will not be allowed to switch between occupational therapists or study arms. They will be asked not to participate in other educational interventions, peer or external, related to their rehabilitation or seek treatment outside their trial. The head of the occupational therapy department within each rehabilitation setting will supervise participants and the assigned occupational therapists in both study arms to reduce contamination bias, such as sharing intervention content with the control group, sharing similar time

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and space of occupational therapy sessions, and exchange of therapists.

Contamination bias due to already-existing background or receipt of additional educational interventions will be measured within each arm of the study using the chi-square test to compare the progress means. However, no case will be eliminated from statistical analysis due to contamination bias.

The study will adopt approaches to prevent the loss of participants to follow-up by making questionnaires as easy to complete as possible, providing incentives in the form of a free copy of the education manual for the control group after completing the study, and explaining the importance of the study [25].

The researchers will use the same outcome measures throughout the study and within both study arms. Biographical data will be collected by a research assistant once on admission of the participant and after they have provided consent to participate. ADL data collection from each participant in the study will take place in a face-to-face interview at two time points: once on admission before being provided with the education manual and again 6 weeks later. This data will be collected using the following: (1) the patient-administered SCIM-SR and (2) the research assistant–administered SCIM-III, Private Religiousness Practices Scale, Organizational Religiousness Short-Form, and domains of ADL covered by the education manual, including driving and community mobility, personal device care, health management and maintenance, ablution, and Islamic prayer. The data will be used to answer the research question and test the study hypothesis.

The validity of the experimental study can be threatened by history, selection, and maturation [26]. The validity of this study's findings will be enhanced by concealing the intervention group using a blinded assessor throughout the study. Sampling and contamination bias will be minimized through randomization and assuring the freedom of participation and anonymity of participants.

Objective data collected in clinical settings using valid and reliable tools are essential for evaluating the impact of an intervention [27]. The validity and reliability of the data collected and the results of the study will be improved using standardized measurement tools, such as the SCIM-SR and the SCIM-III (Table 2 [27-31]).

Table 2. Summary of data collection tools.

Data collection tool	Items, n	Score range; interpretation	Scale	Language version	Administration	Psychometric properties
Biographical data collection tool	24	N/A[a]	Nominal, ordinal, and interval	English	Assessor reported	Developed by the researchers to be used in this study
SCIM-SR[b] [27]	17	0-100; a higher score indicates better function	Ordinal	English; will be translated into Arabic	Patient reported	Good reliability: Pearson correlation coefficients and ICCs[c] of the total and subscale scores are above 0.7
SCIM-III[d] [27,28]	17	0-100; a higher score indicates better function	Ordinal	English	Assessor reported	Good reliability: Cronbach α=.70-.78; κ coefficient=0.64-0.84; Pearson correlation coefficients and ICCs of the total and subscale scores are 0.84-0.94
The Private Religiousness Practices Scale [29]	4	4-27; a lower score is better	Ordinal	English	Assessor or patient reported	Acceptable reliability: Cronbach α=.70
The Organizational Religiousness Short-Form [29,30]	2	2-18; a higher score is better	Ordinal	English	Assessor or patient reported	Acceptable reliability: Cronbach α=.70-.76
The SADL-eM[e] adherence therapist-report questionnaire [31]	8	N/A	Nominal and interval	English	Occupational therapist reported	Developed by the researchers to be used in this study

[a]N/A: not applicable; this measure does not give scores as outcomes.

[b]SCIM-SR: self-report version of the Spinal Cord Independence Measure.

[c]ICC: intraclass correlation coefficient.

[d]SCIM-III: third version of the Spinal Cord Independence Measure.

[e]SADL-eM: Spinal Cord Injury Activities of Daily Living Education Manual.

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Primary Outcome Tool

The SCIM-SR evaluates the ability of a person with SCI to perform specified activities independently, with assistance or with assistive devices, from the perspective of the people with SCI. Research supports the criterion validity of SCIM-SR [27]. The tool is not available in Arabic so the first author will translate the SCIM-SR to Arabic by forward-backward translation and test the usability of the Arabic version in the feasibility study.

Secondary Outcome Tools

The biographical data collection tool captures demographic and socioeconomic data, including age, gender, marital status, level of education, employment, monthly income, accommodation, diagnosis, and cause and type of SCI.

The SCIM-III evaluates the ability of a person with SCI to perform specified activities independently, with assistance or with assistive devices, from the perspective of the health care provider. It requires 30 to 45 minutes to complete the assessment by observation and about 20 minutes by interview [27]. The SCIM-III has been evaluated in multiple countries, including in the Middle East, and it appears to be resistant to cross-cultural differences [32]. The tool is not available in Arabic so the English version will be used [28].

The Private Religiousness Practices Scale measures the frequency of an individual's involvement in religious behaviors: prayer, religious attendance (ie, attending a church or mosque), reading the Bible or Quran, and watching religious programs on television [29]. The tool is not available in Arabic so the English version will be used [30].

The Organizational Religiousness Short-Form measures the involvement of the individual with a formal public religious institution, such as a church or mosque [29]. The tool is not available in Arabic so the English version will be used [30].

The SADL-eM adherence therapist-report questionnaire is based on the Morisky Medication Adherence Scale. This tool measures any change to the supplied SADL-eM in terms of the content of the intervention, topics, described techniques, mode, format, and degree of individualization of the intervention [31]. The tool keeps a record of educational sessions by day, duration, intensity, and elements covered. This English version of this tool will be used.

Ethical Considerations

Ethical approval was obtained from the Stellenbosch University Human Research Ethics Committee (HREC project ID: 1635) and the Helsinki Committee for Ethical Approval (PHRC/HC/689/20). This trial was registered at ClinicalTrials.gov (NCT04735887). At recruitment, participants will be provided with comprehensive information to explain the trial and their participation. Patients' questions will be answered by the researcher honestly and as fully as possible. Participants' consent to be included in the study will be recorded in writing. All the data and the signed consent forms will be securely stored during and after study completion in a locked cabinet on hospital premises, up to 5 years after publication. Participants will be free to withdraw at any time. Participant anonymity and confidentiality of information collected for the research will be assured in the consent form and sustained throughout the study. The study is unlikely to result in any harm, risk, or discomfort to participants. The participants in the control group will receive a copy of the SADL-eM at the end of the study.

COVID-19 Considerations

The treating occupational therapists and research assistant will follow the required COVID-19 precautions published by the World Health Organization and applied by each facility [33]. This includes the use of medical disposable gowns, disposable latex gloves, face shields, surgical masks, and hand hygiene using 70% alcohol or alcohol gel. These supplies will be provided by each facility as requirements of usual treatment.

Data Analysis Plan

Captured data will be coded and reviewed by the authors for clarity and completion. A spreadsheet will be prepared by and then loaded into SPSS software (version 21; IBM Corp) for analysis. To ensure study reliability, the first author will perform data entry, the research assistant will check the data entry using the original forms, and the clinical research supervisor will check the data for missing data and entry errors. During analysis, missing data will be replaced by the means, for continuous or discrete variables, or modes, for ordinal or nominal variables.

To describe participants' characteristics (eg, age, gender, level of injury, and completeness of injury), descriptive statistics, such as frequency, percentage, and mean and SD, will be used for normally distributed data. Median and IQR will be used for continuous variables that are not normally distributed. The Shapiro-Wilk test will be used to test data distribution normality [34].

We will then use the repeated-measures ANOVA and linear mixed models to compare the mean scores of the primary outcome tool (ie, SCIM-SR) and the secondary outcome tools (ie, the SCIM-III, the Private Religiousness Practices Scale, and the Organizational Religiousness Short-Form) to test the research hypothesis. Linear mixed models have an advantage in dealing with missing values and provide fixed and random effects [25]. Repeated-measures ANOVA assumptions will be tested using the Mauchly test of sphericity [34]. If this test is nonsignificant (P>.05), we will assume that the data meet the assumption of sphericity, similar to the homogeneity of variance for between-group ANOVA. Violation of the sphericity assumption will require correction using either the Greenhouse-Geiger correction (ε<.75) or the Huynh-Feldt correction (ε>.75). The effect size will be calculated using Cohen d [35]. Corallo et al [36] provided accepted benchmarks for SCIM-III outcomes for clinicians and researchers: 12% for tetraplegia and 43.3% for paraplegia. Table 3 summarizes the statistical analysis tests intended to be used in this study.

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Table 3. Summary of statistical analysis plan.

Study objective	Analysis plan
To compare the effect of the education manual, relative to usual care, on self-reported changes in ADL[a] from admission to 6 weeks postadmission, using the SCIM-SR[b] patient-rated measure	Repeated-measures ANOVA and linear mixed models to assess differences between intervention and control groups using the ADL data
To compare the effect of the education manual, relative to usual care, on observed changes in ADL from admission to 6 weeks postadmission, using the SCIM-III[c] clinician-rated measure	Repeated-measures ANOVA and linear mixed models to assess differences between intervention and control groups using the ADL data
To compare the effect of the education manual, relative to usual care, on religious practice using the Private Religiousness Practices Scale and the Organizational Religiousness Short-Form	Repeated-measures ANOVA and linear mixed models to assess differences between intervention and control groups using the ADL data
To compare the effect of the education manual, relative to usual care, on the domains of ADL covered by the education manual, including driving and community mobility, personal device care, health management and maintenance, ablution, and Islamic prayer, using questions developed for this research	Repeated-measures ANOVA and linear mixed models to assess differences between intervention and control groups using the ADL data
To determine the significance of biographical variables (ie, address zone, age, gender, highest level of education, marital status, employment status, monthly income, level of SCI[d], and type of SCI: complete or incomplete), the ASIA[e] score, and dysfunction on changes in ADL performance	McNemar and chi-square tests for nominal variables; *t* tests and Mann-Whitney *U* tests for interval variables
To measure the adherence to the intervention using the SADL-eM[f] adherence therapist-report questionnaire, which will be developed for this purpose	Descriptive statistics, such as frequency and percentage

[a]ADL: activities of daily living.

[b]SCIM-SR: self-report version of the Spinal Cord Independence Measure.

[c]SCIM-III: third version of the Spinal Cord Independence Measure.

[d]SCI: spinal cord injury.

[e]ASIA: American Spinal Injury Association Impairment Scale.

[f]SADL-eM: Spinal Cord Injury Activities of Daily Living Education Manual.

This is an RCT that will be conducted in clinical settings (ie, rehabilitation hospitals) where contamination bias is evident. Therefore, we followed the intention-to-treat (ITT) principle to assess outcomes based on the treatment group and not based on the intervention. By using the ITT principle, we aim to avoid potential bias due to exclusion of ineligible cases and prevent attrition bias when evaluating the intervention [26].

Protocol Amendments

The authors will request approval for important protocol modifications, such as changes to eligibility criteria, outcomes, and analyses, from the HREC of Stellenbosch University under the regulations of the Declaration of Helsinki. Deviations from this protocol will be reported when publishing or presenting the trial outcomes.

Results

This is an approved RCT that was registered in 2020. Data collection for the internal pilot study started in April 2021. Between April 2021 and March 2022, 32 cases were eligible and included in the study. The majority were males (n=23, 72%), and the rest were females (n=9, 28%). Each of the intervention and control groups included 16 cases. Trial data collection is expected to continue until December 2022. Results are expected to be available in January 2023.

Discussion

Overview

The anticipated main finding of this study is that the use of a codeveloped, contextualized ADL education manual during inpatient occupational therapy rehabilitation will improve performance of ADL for people with SCI living in Gaza, Palestine, in comparison to usual care. The study findings will provide us with important information about the performance of ADL among people with SCI, based on widely used data collection tools (ie, the SCIM-SR and the SCIM-III), as well as participation in other important aspects of religious life (ie, the Private Religiousness Practices Scale and the Organizational Religiousness Short-Form) and community life (ie, driving and community mobility, personal device care, and health management and maintenance). The findings will also illustrate adherence on the part of people with SCI and health professionals to the educational intervention.

Providing occupational therapy patient education that meets the needs of people with SCI aims to improve their ADL performance and optimize their rehabilitation outcomes [10]. The SADL-eM is an evidence-informed codeveloped manual that supports a client-centered approach and aims to teach people with SCI how to handle their ADL after injury, during the inpatient rehabilitation phase, and when living at home. We hope that the SADL-eM will promote occupational participation, health and well-being, quality of life, and community inclusion

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among people with SCI in LMIC, where medical interventions are evaluated based on their outcomes and cost-efficacy [37].

Inpatient SCI education is designed to promote participation [10]. A systematic review identified three health and participation educational interventions. Although many ADL domains were not addressed in these interventions, there is evidence that SCI education that is focused on ADL optimizes rehabilitation outcomes [10]. More recent studies indicated increased demand for health education, addressed wider ADL domains, used new educational interventions, and highlighted the importance of previous interventions. People with SCI have also demonstrated their interest in topics such as community resources, home modifications, assistive devices, and driving rehabilitation [38].

A specific educational mobile app was evaluated among men with SCI and showed positive results in the marital sex life of men with SCI [39]. Mortenson et al [40] evaluated stakeholders' perspectives on the development of a functional mobile app to facilitate self-management skills needed to prevent secondary complications following recent SCI during inpatient rehabilitation. Stakeholders focused on individualized tools, targeting goals, and increasing participation.

Self-care and peer education are basic interventions in health and participation education. A self-care educational program was found to be significant in inpatient rehabilitation and improved the quality of life of people with SCI [16]. Peer education has been used for more than two decades in people with SCI and it is gaining more interest. People with SCI perceived peer education as a means of "opening closed doors" and "going back to life." This viewpoint was attributed to the support and experience that the peer educators provided to people with SCI [16]. Recently, Carney et al [41] initiated a large project to develop the International Spinal Cord Injury/Dysfunction Education Basic Data Set. This database is accessible by service developers and researchers, service providers, and service users.

The use of a randomized controlled study design is a strength of this study. High-quality and well-controlled clinical trials are essential to developing effective interventions for people with SCI [10,11]. An additional strength is the involvement of people with SCI and a wide range of health professionals involved in rehabilitation following SCI, from all three rehabilitation services in Gaza, in the development of the education manual. Co-construction with service users and service providers means that the voices of important stakeholders are represented. Consequently, the educational intervention is culturally relevant to people with SCI living in Gaza. In particular, the manual addresses the unique participation needs of Muslim people with SCI. Furthermore, the intervention advocates for the right to health information as well as participation in a wide range of activities and occupations that are meaningful to people with SCI in Gaza.

If the SADL-eM is demonstrated to be clinically effective, it will have significant implications for occupational therapy research and practice in LMIC, where limited resources are allocated for SCI rehabilitation, community-based rehabilitation, and assistive devices. Furthermore, people with SCI experience many forms of occupational injustice in LMIC [17]. Future studies need to address the possible long-term maintenance of improvement associated with the use of the SADL-eM, and the impact of SADL-eM use during rehabilitation on other aspects, such as quality of life.

Limitations

We were unable to identify any study in LMIC that provides information about ADL performance among people with SCI measured by the SCIM-SR and SCIM-III. However, there are a number of potential limitations to the proposed study. This RCT employs strict inclusion criteria to improve the reliability of findings. Meanwhile, the incidence of SCI in the Gaza Strip is relatively low. Therefore, data collection is expected to continue for 12 to 14 months (April 2021-December 2022), during which different types of bias may be introduced. For example, sampling bias may occur due to a possible high rate of withdrawals and dropouts from the study. Familiarity of health professionals and people with SCI with the intervention is likely to create contamination bias. While the risk of maturity bias may occur due to age and long length of stay in the inpatient rehabilitation settings, exposure bias may occur due to different lengths of stay in the inpatient rehabilitation settings [42].

The intervention used in this RCT concurs with physical distancing that is currently required in clinical settings due to COVID-19. Considering this, it is safe and compatible with infection control guidelines [33,43].

Conclusions

The findings of the proposed study will highlight the importance of a culturally relevant educational intervention in people with SCI in LMIC and will, therefore, pave the road for more constructive and creative solutions to the lack of resources in these countries. This will encourage the shift in rehabilitation services toward more just and inclusive approaches. Future dissemination and implementation efforts will be critical to ensure that this cost-effective and easily accessible intervention is used to promote participation. The SADL-eM will be made freely available on the Stellenbosch University website in Arabic, with a summary in English. The study results will be further disseminated through conference presentations.

Data Availability

Anonymized data will be available for peer review or quality appraisal from the corresponding author. Any other data sharing will require approval from the authors (MAM, NAP, and MSB), ethical approval from the requesting party, and approval from the HREC of Stellenbosch University.

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Authors' Contributions

MAM, MSB, and NAP developed the concept for the trial, drafted the protocol, contributed to the trial design and methodology, developed the SADL-eM intervention, adapted the trial protocol as a protocol paper, reviewed and commented on drafts of the paper, and approved the final version. MAM, MSB, NAP, and BA developed the statistical analysis plan.

Conflicts of Interest

None declared.

References

1. Bashar J, Hughes C. Spinal cord injury. In: Pendleton H, Schultz-Krohn W, editors. Pedretti's Occupational Therapy: Practice Skills for Physical Dysfunction. 8th edition. Maryland Heights, MO: Mosby; 2017:1640-1683.
2. American Occupational Therapy Association. Occupational Therapy Practice Framework: Domain and Process. 3rd Edition. Am J Occup Ther 2014;68(Supplement_1):S1-S48 [FREE Full text] [doi: 10.5014/ajot.2014.682006]
3. Cogley C, D'Alton P, Nolan M, Smith E. "You were lying in limbo and you knew nothing": A thematic analysis of the information needs of spinal cord injured patients and family members in acute care. Disabil Rehabil 2021 Aug 31:1-11. [doi: 10.1080/09638288.2021.1970259] [Medline: 34465272]
4. Diviani N, Zanini C, Jaks R, Brach M, Gemperli A, Rubinelli S. Information seeking behavior and perceived health literacy of family caregivers of persons living with a chronic condition. The case of spinal cord injury in Switzerland. Patient Educ Couns 2020 Aug;103(8):1531-1537. [doi: 10.1016/j.pec.2020.02.024] [Medline: 32098740]
5. Emerich L, Parsons K, Stein A. Competent care for persons with spinal cord injury and dysfunction in acute inpatient rehabilitation. Top Spinal Cord Inj Rehabil 2012;18(2):149-166 [FREE Full text] [doi: 10.1310/sci1802-149] [Medline: 23460762]
6. Letts L, Martin Ginis KA, Faulkner G, Colquhoun H, Levac D, Gorczynski P. Preferred methods and messengers for delivering physical activity information to people with spinal cord injury: A focus group study. Rehabil Psychol 2011 May;56(2):128-137. [doi: 10.1037/a0023624] [Medline: 21574732]
7. May L, Day R, Warren S. Evaluation of patient education in spinal cord injury rehabilitation: Knowledge, problem-solving and perceived importance. Disabil Rehabil 2006 Apr 15;28(7):405-413. [doi: 10.1080/09638280500192439] [Medline: 16507503]
8. Shepherd JD, Badger-Brown KM, Legassic MS, Walia S, Wolfe DL. SCI-U: E-learning for patient education in spinal cord injury rehabilitation. J Spinal Cord Med 2013 Jul 19;35(5):319-329. [doi: 10.1179/2045772312y.0000000044]
9. Conti A, Dimonte V, Rizzi A, Clari M, Mozzone S, Garrino L, et al. Barriers and facilitators of education provided during rehabilitation of people with spinal cord injuries: A qualitative description. PLoS One 2020;15(10):e0240600 [FREE Full text] [doi: 10.1371/journal.pone.0240600] [Medline: 33057362]
10. Abu Mostafa M, Plastow NA, Savin-Baden M. The effectiveness of spinal cord injury ADL inpatient education on rehabilitation outcomes: A systematic review and meta-analysis. Br J Occup Ther 2019 Nov 05;83(1):15-28. [doi: 10.1177/0308022619879019]
11. Rice LA, Smith I, Kelleher AR, Greenwald K, Boninger ML. Impact of a wheelchair education protocol based on practice guidelines for preservation of upper-limb function: A randomized trial. Arch Phys Med Rehabil 2014 Jan;95(1):10-19.e11. [doi: 10.1016/j.apmr.2013.06.028] [Medline: 23856151]
12. Ljungberg I, Kroll T, Libin AS, Gordon S. Using peer mentoring for people with spinal cord injury to enhance self-efficacy beliefs and prevent medical complications. J Clin Nurs 2011 Feb;20(3-4):351-358. [doi: 10.1111/j.1365-2702.2010.03432.x] [Medline: 21219518]
13. Kennedy P, Hamilton L. The needs assessment checklist: A clinical approach to measuring outcome. Spinal Cord 1999 Feb;37(2):136-139. [doi: 10.1038/sj.sc.3100745] [Medline: 10065753]
14. Nasiri Ziba F, Shafie Bafti F, Seyedfatemi N, Doroudi T, Haghani H. Evaluation of the effect of self-care education on quality of life in people with spinal cord injury. Iran J Nur 2021 Oct 01;34(132):89-101. [doi: 10.52547/ijn.34.132.89]
15. Zarei F, Rashedi S, Tavousi M, Haeri-Mehrizi AA, Maasoumi R. A mobile-based educational intervention on sexo-marital life in Iranian men with spinal cord injury: A randomized controlled trial. Spinal Cord 2020 Nov;58(11):1189-1196. [doi: 10.1038/s41393-020-0489-4] [Medline: 32457513]
16. Chaffey L, Bigby C. 'I feel free': The experience of a peer education program with Fijians with spinal cord injury. J Dev Phys Disabil 2017 Nov 13;30(2):175-188. [doi: 10.1007/s10882-017-9578-5]
17. Yao DPG, Inoue K, Sy MP, Bontje P, Suyama N, Yatsu C, et al. Experience of Filipinos with spinal cord injury in the use of assistive technology: An occupational justice perspective. Occup Ther Int 2020;2020:6696296 [FREE Full text] [doi: 10.1155/2020/6696296] [Medline: 33304205]
18. GBD 2016 Traumatic Brain Injury and Spinal Cord Injury Collaborators. Global, regional, and national burden of traumatic brain injury and spinal cord injury, 1990-2016: A systematic analysis for the Global Burden of Disease Study 2016. Lancet Neurol 2019 Jan;18(1):56-87 [FREE Full text] [doi: 10.1016/S1474-4422(18)30415-0] [Medline: 30497965]

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19. Fehlings MG, Tetreault LA, Wilson JR, Kwon BK, Burns AS, Martin AR, et al. A clinical practice guideline for the management of acute spinal cord injury: Introduction, rationale, and scope. Global Spine J 2017 Sep;7(3 Suppl):84S-94S [FREE Full text] [doi: 10.1177/2192568217703387] [Medline: 29164036]
20. Yuen HK, Azuero A, London S. Association between seeking oral health information online and knowledge in adults with spinal cord injury: A pilot study. J Spinal Cord Med 2013 Jul 19;34(4):423-431. [doi: 10.1179/2045772311y.0000000020]
21. Abu Mostafa M, Plastow NA, Savin-Baden M. Participatory methods to develop health education for PW-SCI: Perspectives on occupational justice. Can J Occup Ther 2022 (forthcoming).
22. Moher D, Hopewell S, Schulz KF, Montori V, Gøtzsche PC, Devereaux PJ, et al. CONSORT 2010 explanation and elaboration: Updated guidelines for reporting parallel group randomised trials. BMJ 2010 Mar 23;340:c869 [FREE Full text] [doi: 10.1136/bmj.c869] [Medline: 20332511]
23. Bell ML, Whitehead AL, Julious SA. Guidance for using pilot studies to inform the design of intervention trials with continuous outcomes. Clin Epidemiol 2018 Jan;10:153-157. [doi: 10.2147/clep.s146397]
24. Quittner A, Espelage D, levers-Landis C, Drotar D. Measuring adherence to medical treatments in childhood chronic illness: Considering multiple methods and sources of information. J Clin Psychol Med Settings 2000;7(1):41-54. [doi: 10.1023/a:1009545319673]
25. Magill N, Knight R, McCrone P, Ismail K, Landau S. A scoping review of the problems and solutions associated with contamination in trials of complex interventions in mental health. BMC Med Res Methodol 2019 Jan 07;19(1):4 [FREE Full text] [doi: 10.1186/s12874-018-0646-z] [Medline: 30616508]
26. Polit DF, Beck C, Hungler BP. Essentials of Nursing Research: Methods, Appraisal, and Utilization. 5th edition. Philadelphia, PA: Lippincott Williams & Wilkins; 2001.
27. Fekete C, Eriks-Hoogland I, Baumberger M, Catz A, Itzkovich M, Lüthi H, et al. Development and validation of a self-report version of the Spinal Cord Independence Measure (SCIM III). Spinal Cord 2013 Jan;51(1):40-47. [doi: 10.1038/sc.2012.87] [Medline: 22890418]
28. Anderson K, Aito S, Atkins M, Biering-Sørensen F, Charlifue S, Curt A, Functional Recovery Outcome Measures Work Group. Functional recovery measures for spinal cord injury: An evidence-based review for clinical practice and research. J Spinal Cord Med 2008;31(2):133-144 [FREE Full text] [doi: 10.1080/10790268.2008.11760704] [Medline: 18581660]
29. Fetzer Institute and National Institute on Aging Working Group. Multidimensional Measurement of Religiousness/Spirituality for Use in Health Research: A Report of the Fetzer Institute/National Institute on Aging Working Group. Kalamazoo, MI: Fetzer Institute; 1999. URL: https://backend.fetzer.org/sites/default/files/resources/attachment/%5Bcurrent-date%3Atiny%5D/Multidimensional_Measurement_of_Religousness_Spirituality.pdf [accessed 2022-01-01]
30. Bodling A, Heneghan M, Walsh JC, Yoon DP, Johnstone B. The Brief Multidimensional Measure of Religiousness/Spirituality with an Irish sample: A factor analysis. Int J Ther Rehabil 2013 Feb 02;20(2):72-78. [doi: 10.12968/ijtr.2013.20.2.72]
31. De Las Cuevas C, Peñate W. Psychometric properties of the eight-item Morisky Medication Adherence Scale (MMAS-8) in a psychiatric outpatient setting. Int J Clin Health Psychol 2015;15(2):121-129 [FREE Full text] [doi: 10.1016/j.ijchp.2014.11.003] [Medline: 30487829]
32. Glass C, Tesio L, Itzkovich M, Soni B, Silva P, Mecci M, et al. Spinal Cord Independence Measure, version III: Applicability to the UK spinal cord injured population. J Rehabil Med 2009 Sep;41(9):723-728 [FREE Full text] [doi: 10.2340/16501977-0398] [Medline: 19774305]
33. DiSilvio B, Virani A, Patel S, Finoli L, Singh A, DuMont T, et al. Institutional COVID-19 protocols: Focused on preparation, safety, and care consolidation. Crit Care Nurs Q 2020;43(4):413-427. [doi: 10.1097/CNQ.0000000000000327] [Medline: 32833778]
34. Field A. Discovering Statistics Using SPSS. 3rd edition. London, UK: SAGE Publications Ltd; 2009.
35. McGough JJ, Faraone SV. Estimating the size of treatment effects: Moving beyond p values. Psychiatry (Edgmont) 2009 Oct;6(10):21-29 [FREE Full text] [Medline: 20011465]
36. Corallo V, Torre M, Ferrara G, Guerra F, Nicosia G, Romanelli E, et al. What do spinal cord injury patients think of their improvement? A study of the minimal clinically important difference of the Spinal Cord Independence Measure III. Eur J Phys Rehabil Med 2017 Aug;53(4):508-515. [doi: 10.23736/s1973-9087.17.04240-x]
37. Scivoletto G, Tamburella F, Laurenza L, Molinari M. The spinal cord independence measure: How much change is clinically significant for spinal cord injury subjects. Disabil Rehabil 2013 Oct;35(21):1808-1813. [doi: 10.3109/09638288.2012.756942] [Medline: 23343359]
38. Wirth B, van Hedel HJ, Kometer B, Dietz V, Curt A. Changes in activity after a complete spinal cord injury as measured by the Spinal Cord Independence Measure II (SCIM II). Neurorehabil Neural Repair 2008;22(2):145-153. [doi: 10.1177/1545968307306240] [Medline: 17761810]
39. Guindo LA, Wagner M, Baltussen R, Rindress D, van Til J, Kind P, et al. From efficacy to equity: Literature review of decision criteria for resource allocation and healthcare decision-making. Cost Eff Resour Alloc 2012 Jul 18;10(1):9 [FREE Full text] [doi: 10.1186/1478-7547-10-9] [Medline: 22808944]
40. Mortenson WB, Singh G, MacGillivray M, Sadeghi M, Mills P, Adams J, et al. Development of a self-management app for people with spinal cord injury. J Med Syst 2019 Apr 22;43(6):145. [doi: 10.1007/s10916-019-1273-x] [Medline: 31011881]

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41. Carney J, Fisher R, Augutis M, Charlifue S, Biering-Sørensen F, Höfers W, et al. Development of the International Spinal Cord Injury/Dysfunction Education Basic Data Set. Spinal Cord Ser Cases 2019;5:87 [FREE Full text] [doi: 10.1038/s41394-019-0229-1] [Medline: 31700685]
42. Stuckless S, Parfrey P. Bias in clinical research. Methods Mol Biol 2021;2249:17-34. [doi: 10.1007/978-1-0716-1138-8_2] [Medline: 33871836]
43. Wasson J. Practice standards for effective telemedicine in chronic care management after COVID-19. J Ambul Care Manage 2020;43(4):323-325. [doi: 10.1097/JAC.0000000000000355] [Medline: 32858735]

Abbreviations

ADL: activities of daily living
CONSORT: Consolidated Standards of Reporting Trials
HREC: Human Research Ethics Committee
ITT: intention-to-treat
LMIC: low- and middle-income countries
NAC: Needs Assessment Checklist
NAGPP: Needs Assessment and Goal Planning Programme
RCT: randomized controlled trial
SADL-eM: Spinal Cord Injury Activities of Daily Living Education Manual
SCI: spinal cord injury
SCIM-III: third version of the Spinal Cord Independence Measure
SCIM-SR: self-report version of the Spinal Cord Independence Measure

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Protocol

The Efficacy of Lumbar Support on Pain, Disability, and Motor Control in Women With Postpartum Pelvic Girdle Pain: Protocol for a Randomized Controlled Trial

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Abstract

Background: Pregnancy-related posterior pelvic girdle pain (PPGP) is one of the most important clinical manifestations of postpartum back pain. Those affected often complain of discomfort during daily activities. It is hypothesized that altered motor control is associated with perceived pain. Pelvic support can regulate possible underlying altered motor control mechanisms and decrease pain. However, the influence of a lumbosacral orthosis, which is broader support that allows for a wider contact area and more skin sensory stimulation to restore proper motor function, has not yet been investigated in women with postpartum PPGP.

Objective: This study investigates the efficacy of broader lumbar support and narrower pelvic support on pain, proprioception, disability, and muscle strength in women with pregnancy-related PPGP.

Methods: This study will be a single-center, 3-armed, participant-blinded, randomized controlled trial. In total, 84 women diagnosed with pregnancy-related PPGP will be recruited and randomly assigned into 3 groups. Intervention groups A and B will receive pelvic and lumbar supports, respectively. Group C (control) will receive only a patient education leaflet containing advice on strengthening exercises, comfortable positions, and other practical information. The study outcomes are pain, effort score during the active straight leg raising test, maximum isometric hip flexion force, maximum isometric hip external rotation force, maximum isometric trunk rotation force, and joint position reproduction of hip abduction. The study outcomes will be measured at 4 time points: baseline (T1), immediately after the intervention (T2), 4 weeks following interventions began (at this time, the intervention period is completed) (T3), and 1 week after discontinuing the interventions (T4) to evaluate the possible lasting effects of wearing supports. Multivariate analysis of variance will be used to test between- and within-group differences.

Results: Recruitment for this study will be started in summer 2022 and is expected to be completed by the end of fall 2022.

Conclusions: This study will examine the efficacy of broader lumbar support as an early rehabilitative treatment for women receiving postpartum posterior pelvic pain support compared to those receiving a narrower pelvic support. We expect the broader lumbar support to impact pain management and disability better than the current narrower pelvic belt. Long-term follow-up studies will help determine whether such lumbosacral orthosis reduces pain and improves daily activities in women with pregnancy-related PPGP.

Trial Registration: Iranian Registry of Clinical Trials IRCT20150210021034N11; https://www.irct.ir/trial/54808

International Registered Report Identifier (IRRID): PRR1-10.2196/40553

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KEYWORDS

sacroiliac joint; pain; disability; motor control; lumbosacral orthosis; postpartum

Introduction

Pregnancy-related posterior pelvic girdle pain (PPGP) is a common musculoskeletal disorder affecting women's well-being in the postpartum period [1]**.** Nearly half of the involved population demonstrates moderate to severe disability [2]. This painful condition is related to physical and psychosocial aspects, including kinesiophobia, psychological distress, beliefs regarding curability, financial stress, and social isolation [3-6]. The alteration of motor control in people with pelvic pain has been documented [7] and can affect a change in the load transfer ability at the pelvis [8]. Pregnancy-related PPGP is commonly localized in the vicinity of the sacroiliac joint (SIJ) [9]. One of the SIJ's functions is transmitting the upper body weight to the pelvis and lower extremities and vice versa [10]. Dynamic control of mechanical and neural systems acting on the pelvis allows the lumbopelvic movements to be smooth, painless, and effortless under changing conditions [11]. Pregnancy-related PPGP includes the dysfunction of sensorimotor pathways that control load transfer through the SIJ [11,12]. The altered spinal and abdominal muscle activations and perceived pain affect the function of the SIJ in postnatal women [13]. Those with pregnancy-related PPGP often complain of discomfort during load transfer tasks through the pelvis [14]. The active straight leg raise (ASLR), as a biomechanical test, is proposed to check load transfer between the spine and legs via the pelvis [14,15].

Many preventive or therapeutic strategies are used for the management of pregnancy-related PPGP. Current pain relief recommendations include avoiding certain physical loads, relaxation, massage, medications, exercise, physical therapy, and pelvic or lumbar supports [16]. Among the recommendations for managing pregnancy-related PPGP, it was noted that pelvic or lumbar support is widely used to manage painful symptoms [17,18]. Pelvic or lumbar support, also known as soft orthosis, can work through a combination of mechanisms to address the SIJ instability. First, the circumferential supports are expected to apply a compressive force on the pelvis to promote anatomical alignment [19], stiffness [20], and increase the function of the SIJ [21]. Second, soft orthoses can also provide potent stimuli to improve neuromuscular control required for lumbopelvic function [22]. It has been shown that the gentle pressure soft orthoses applied to the skin receptors can positively affect proprioceptive acuity [20,23], pain intensity [17,24], joint stability [25,26], and physical function [17,27].

Emerging research has highlighted the sensorimotor effectiveness of narrow pelvic supports in pregnancy-related PPGP [27,28]. Furthermore, previous research has indicated that lumbar support effectively improved proprioceptive awareness in healthy subjects [22]. However, the effect of broader lumbar supports that allow for a wider contact area and greater skin sensory stimulation in women with pregnancy-related PPGP remains unclear. Therefore, this study first aims to investigate whether using lumbar support reduces pain in women with pregnancy-related PPGP versus controls. Secondly, it aims to examine whether broader lumbar support is more beneficial than narrower pelvic support on disability and sensorimotor outcomes (eg, joint positions reproduction) in the lumbopelvic area in women with pregnancy-related PPGP.

Methods

Study Design

A prospective 3-armed, participant-blinded, randomized controlled trial (interventions versus control group) will be performed to investigate the aims. The Template for Intervention Description and Replication (TIDieR) checklist and related guidelines will be used to report the study process [29,30]. The TIDieR checklist describes a standard way to document details carefully and allows authors to write interventions in their studies clearly [29]. The CONSORT-EHEALTH (Consolidated Standards of Reporting Trials of Electronic and Mobile Health Applications and onLine TeleHealth) checklist will be used to report data efficiently as an eHealth intervention trial [31].

Setting

Participants will be recruited from Isfahan University of Medical Sciences (IUMS), Isfahan, Iran.

Ethics Approval

The local ethical committee of IUMS approved the study protocol (IR.MUI.NUREMA.REC.1400.007). The study protocol was registered in the Iranian Registry of Clinical Trials on April 31, 2021 (IRCT20150210021034N11).

Sample Size

In total, 84 women with postpartum PPGP will be recruited. The optimal sample size was calculated on the basis of the results of a previous study [32]. The pain intensity for intervention groups was 58.2 (SD 13.93) and 64.4 (SD 13.96) at baseline, respectively [32]. We estimated a sample size of 25 in each study arm, which would yield 60% power (α=.1) and an effect size of 0.44 (Cohen *d*) in accordance with calculations performed using G*power software (Version 3.1, Universität Düsseldorf). We also considered an overall dropout rate of 10% (eg, lost to follow-up). Therefore, we aimed to recruit 84 participants (28 in each study arm).

Participants

Women with postpartum PPGP will be recruited through a simple (convenience) sampling method from the obstetric outpatient clinics of IUMS. The examiner will confirm the diagnosis with the presence of PPGP, and positive diagnostic tests include the following: ASLR, posterior pelvic pain provocation (also known as P4) test, Patric-Faber test, and Gaenslen's test [33]. The inclusion criteria of the study are (1) primipara women who experienced natural delivery (one month before); (2) age between 18 and 45 years; (3) self-reported

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pregnancy-related PPGP; (4) a pain score of at least 40 out of 100 mm on the visual analog scale (VAS) [17]; and (5) a score of higher than 2 out of 5 on a 6-point Likert scale for perceived effort during the ASLR test [34]. The exclusion criteria were as follows: (1) the presence of lower back or pelvic pain before pregnancy; (2) history of any fracture in the pelvis and lower extremities; (3) history of spine, pelvis, and lower extremity surgery; (4) neurological diseases; (5) limb length discrepancy; (6) congenital anomaly in the spine, pelvis, and lower extremities; and (7) using any other conservative treatment for pain relief during the study, such as physiotherapy treatment methods. All eligible participants will provide informed consent and sign the consent form before inclusion in the trial. Participants will be free to withdraw at any time during the study.

Assignment, Randomization, and Blinding (Masking) Procedures

Once participants are confirmed to be eligible, they will be randomly assigned with equal allocation at a 1:1:1 ratio (one control participant per treatment participant) to one of 3 groups: (A) pelvic (narrower) support (n=28), (B) lumbar (broader) support (n=28), and (C) control group (patient-education leaflet) (n=28). Block randomization will be used, with a block size of 6 to achieve balance in allocating participants to study arms [35]. The assessor will perform randomization with a Random Allocation Software (version 1.0) [36]. The nature of this study will not allow for masking of the assessor after assignment to interventions. Only participants will be masked to group assignment at the point of allocation.

Adverse Events and Dropouts

Adverse events will be mentioned and recorded throughout the trial for participant safety. Information about adverse events, including the date and participant's experience, will be summarized in tables. Information about participants who discontinued the study will be recorded. Furthermore, the reasons for dropout, such as COVID-19 symptoms, loss to follow-up, and sickness, will be reported.

Study Arms and Content

There will be 3 different study arms. As intervention groups (A and B), the first and second arms will receive pelvic or lumbar supports for 4 weeks. As the control group (C), the third arm will only receive a patient education leaflet containing advice on strengthening exercises, comfortable positions, and other practical information. The outcomes include pain, effort score during the ASLR test, maximum isometric hip flexion force, maximum isometric hip external rotation force, maximum isometric trunk rotation force, and joint position reproduction (JPR) of hip abduction. The study outcomes will be measured at 4 time points: baseline (T1), immediately after the intervention (T2), 4 weeks after the interventions began (at this time, the intervention period is completed) (T3), and 1 week after discontinuing the interventions (T4) to evaluate the possible lasting effects of wearing supports. The study process is outlined in Figure 1.

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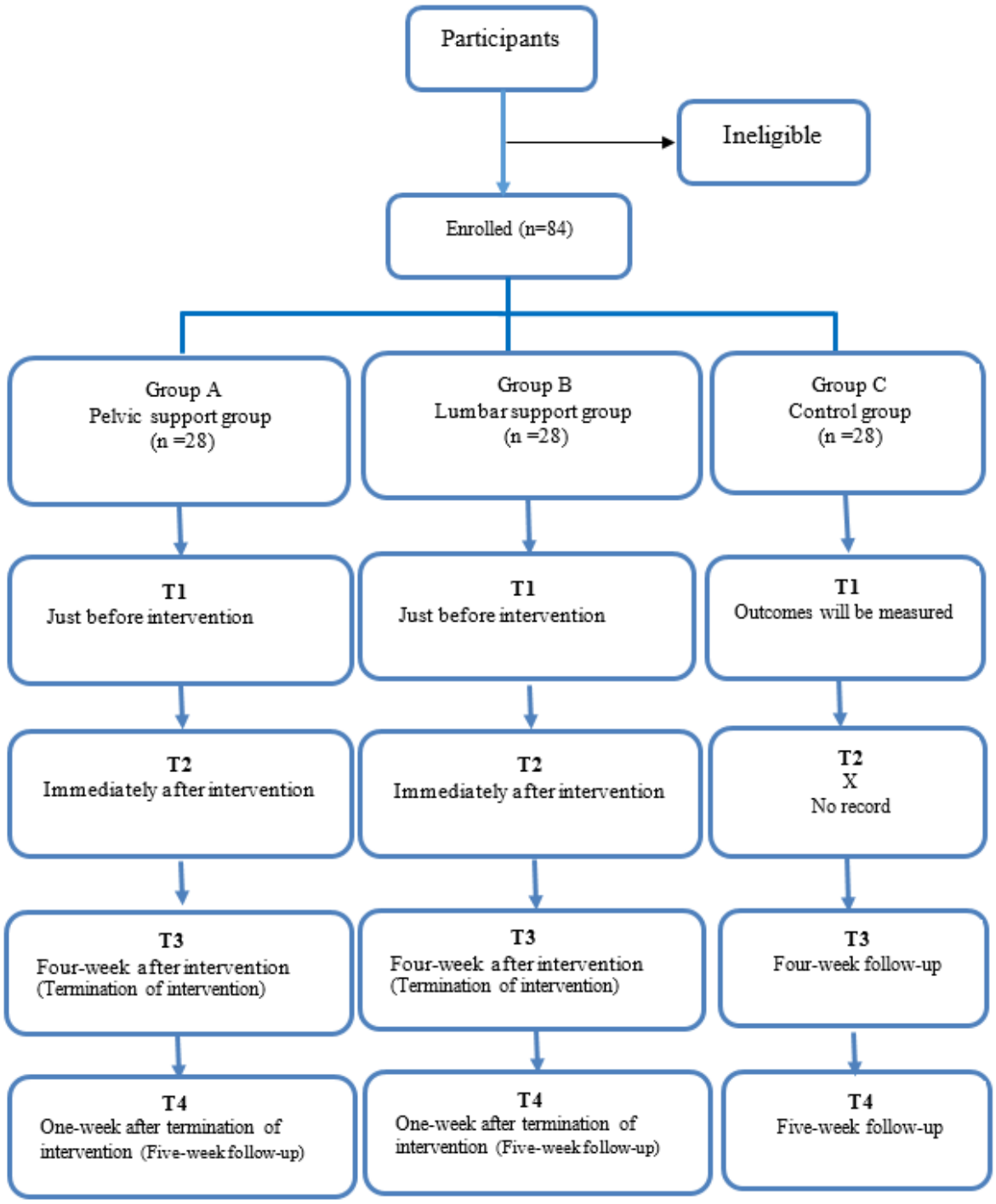
Figure 1. The study flowchart for the randomized controlled trial.



Intervention

This study will use 2 orthoses: pelvic (Group A) and lumbar (Group B) support (Teb Darman Co). Both orthoses are made of breathable textile material to comfort the participant. Orthoses can be worn on top of or under daytime clothes. The pelvic support will be an adjustable strap (10-15–cm width) fastened below the anterior superior iliac spine (Figure 2A). The lumbar support consists of a pelvic belt attached to the lumbar corset. Lumbar support has a 25-cm width anteriorly and extends from the xiphoid process to the pelvis. It has a 35-cm width posteriorly and extends down from the lower angle of the scapula to gluteal prominences (Figure 2B). Group C (control) will receive only a patient education leaflet containing advice on strengthening exercises, comfortable positions, and other practical information. Participants will be instructed to incorporate the regular activities into their daily routines and not use pain relief medication or other treatment during the following 5 weeks. Although we do not expect participants to experience any trial-related harm, they will be provided with a direct number to contact should they have any questions or

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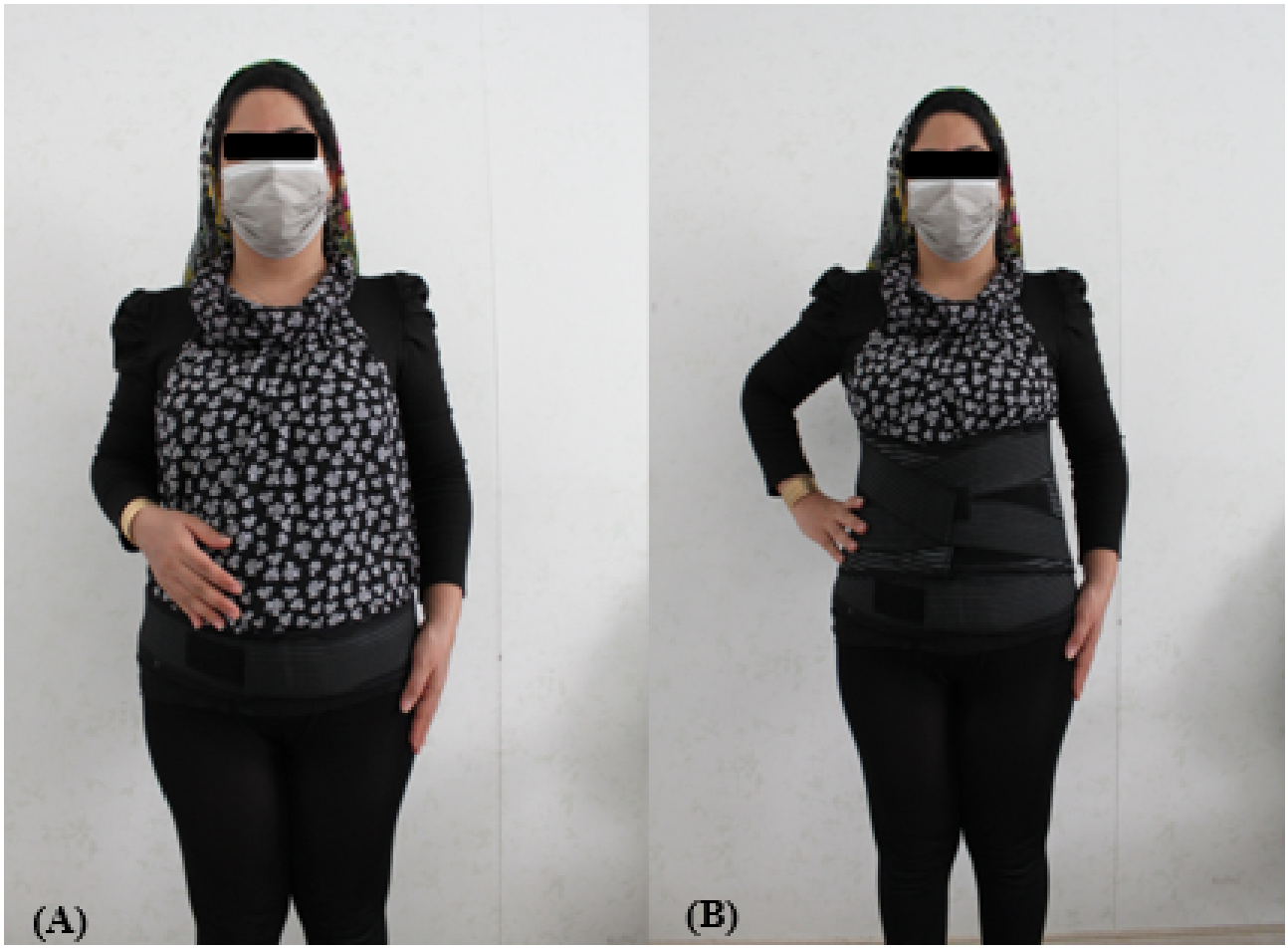
queries and report any symptoms related to interventions or any discomfort experienced while wearing their orthoses.

Figure 2. Study interventions: (A) pelvic support and (B) lumbar support.



Outcome Measures

All tests will be carried out with a certified orthotic practitioner. Table 1 outlines the outcome measures and shows how outcome measures will be measured at different time points throughout the study.

Table 1. The outcome measures of the study.

Measures	Baseline (T1)	Immediate effect (T2)	Fourth week (T3)	Fifth week (T4)	
Overall pain	✓	✓	✓	✓	Visual analog scale
Effort score during active straight leg raise	✓	✓	✓	✓	6-point Likert scale
Maximum isometric hip flexion force	✓	✓	✓	✓	Digital force gauge
Maximum isometric trunk rotation force	✓	✓	✓	✓	Digital force gauge
Maximum isometric hip external rotation force	✓	✓	✓	✓	Digital force gauge
Joint position reproduction of hip abduction	✓	✓	✓	✓	Kinovea software
Activity limitation	✓	✗	✓	✓	Modified Oswestry Disability Index

Primary Outcome Measures

Pain

The participant will indicate the severity of pain related to the lumbopelvic region during the previous week on a 10-point VAS ranging from 0 to 10, where 0=no pain and 10=the worst imaginable pain [24]. The VAS is documented and recommended as reliable in subjects with lower back pain (SE 0.09, intraclass correlation coefficient [ICC] 0.90) [37].

Modified Oswestry Disability Index for Lower Back Pain

The Persian version of the Oswestry Disability Index (ODI) will quantify disability in women with postpartum PPGP [38]. This self-reported 10-item questionnaire has been introduced

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as a valid and reliable tool compatible with spine-related disabilities [39]. The first item evaluates the pain intensity. The other items ask about pain intensity experienced while carrying out typical daily activities, including personal care, lifting, walking, sitting, standing, sleeping, social life, traveling, and employment/homemaking. Each item scored 0-5; higher scores imply higher pain intensity and disability. The ODI has been introduced as a gold standard for lower back functional outcome tools and has good psychometric properties, which can be used in various settings [40]. The ODI shows a good construct validity, acceptable internal consistency (Cronbach α=.69-.87) [38,41,42], and high test-retest reliability (r=0.83-0.99) in people with lower back pain [41-43].

Secondary Outcome Measures

Effort Score During ASLR

With the participant lying in supine position on the examination table, they will be instructed to keep their knee straight with their feet 20 cm apart during tests. The raising height during the ASLR test will be defined by placing a metal bar 20 cm above the examination table (target position) [44]. The perceived effort will be scored while the participant raises their leg to the target position. They will indicate their perceived difficulty in performing the test on a 6-point Likert scale ranging from 0 to 5, where 0=no problem and 5=unable to do [44]. The test-retest reliability of the ASLR test was reportedly high in women with pregnancy-related PPGP (information coefficient 0.82) [44].

Maximum Isometric Force

Maximum isometric muscle force measures will be obtained with a portable digital force gauge (SF-500, Akurasi, R.O.C). It will be periodically calibrated in accordance with the manufacturer's information manual.

Maximum Isometric Hip Flexion Force

A digital force gauge will be attached to the metal bar and adjusted to be placed immediately above the ankle. The participant will be asked to raise their involved leg and compress the force gauge probe while their leg is still lying on the table [15]. The maximum isometric hip flexion force test correlates well with the ASLR test. The test will be repeated 3 times at a 20-second interval. The mean value will be recorded.

Maximum Isometric Hip External Rotation Force

The participant will undergo isometric muscle strength testing for external hip rotation using a digital force gauge and a stabilization strap. He/she will be asked to sit upright on the chair with his/her hip and knee positioned in approximately 90° flexion [45]. The stabilization strap will be placed immediately proximal to the ankle joint of the involved limb and fastened firmly around the chair's leg. A force gauge will be secured between the medial side of the leg and the stabilization strap. The participant will be instructed to pull his/her leg inward with maximal effort until the force value is displayed on the force gauge. The test will be repeated 3 times at a 20-second interval. The mean value will be recorded [45]. The maximum isometric hip external rotation test was reported reliable in healthy subjects (SE 3.9, ICC 0.88) [45].

Maximum Isometric Trunk Rotation Force

The participant will be positioned on the chair in the sitting position with feet resting on the floor. Two nonelastic belts will pass diagonally over the chest and shoulder and finally are wrapped and secured around the back of the chair. Another belt will be fastened on the thighs to prevent extraneous pelvic movement. The force gauge will be fixed between the subclavicular area and the diagonal strap at one side. The participant will be asked to rotate his/her trunk toward the opposite side and exert isometric force to the force-probe, held in this position for 5 seconds. The test will be repeated thrice at a 20-second interval. The mean value will be recorded. The test will be performed on the opposite side using the same procedure [46]. A portable dynamometer provides suitable reliability and validity values to test different trunk muscles and populations [47]. Adequate reliability for the measurement of trunk rotator muscles was presented in subjects with stroke (ICC 0.64-0.99, SEM was considered low) [46] and older adults (ICC≥0.75) [48].

JPR of Hip Abduction

Hip proprioception will be measured using the active JPR while standing. The participant will stand with closed eyes on the uninvolved leg on a 10-cm-high wooden block. The involved leg will be allowed to freely move and abduct the hip joint. The participant will maintain his/her balance throughout the tests by touching a horizontal bar at hip joint height. During the first trial, the examiner will sit behind the participant and check the reference position and target angle. The hip abduction angle will be quantified using a large protractor attached in front of the participant on the wall. The protractor and hip joint center (greater trochanter) will be matched before starting the trial. The reference position is when the tested leg is placed parallel to the supporting limb in which the medial side of the tested leg is adjusted on the zero degrees of the protractor. The participant will randomly select the target angle within 10° to 40° for 4 trials. Three reflective markers will be attached to the apex of the iliac crest, greater trochanter, and lateral femur epicondyle [49]. The movement of the reflective markers will be recorded using a Canon camera (EOS-500D, DS126231) placed behind the participant at a distance of 2.5 m. The participant will be asked to actively move his/her leg from the reference position to the selected target angle at their self-selected velocity.

In the first trial, the examiner will instruct the participant on the "STOP" command to inform him/her of reaching the target angle. The participant will hold their leg at the target angle for approximately 4 seconds to memorize it. Then, the examiner will ask the participant to return his/her leg to a reference position of 0° by saying "Return" and holding the leg there for 3 seconds. Next, the participant will be asked to actively reproduce the previous target angle 3 times [49]. The camera's tracking angles will be analyzed using Kinovea software (Version 0.9.2). Kinovea software is a valid and reliable tool to measure angle and distance accurately [50]. Intrasession reliability for angular error in hip abduction movement in healthy adults was reported between 0.39° and 0.96°, indicating a lower measurement error or more precise score for the hip joint proprioception test [49].

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Demographic and Clinical Data

Demographic and clinical characteristics, including age, weight, height, BMI, duration of symptoms, and involved limb, will be prospectively collected and recorded on report forms.

Data Analysis

All data will be saved with identification codes to maintain confidentiality. Every effort will be made to follow up on all subjects by the examiner. All enrolled participants, including those who do not complete treatment, will be included in the analysis on the basis of the intention-to-treat principle. Missing data will be replaced by the mean imputation technique, in which the mean of the observed values will be calculated and reported. Descriptive statistics will present demographic characteristics and outcome measures for each intervention group. Multivariate ANOVA will be used to test between- and within-group differences. Data will be controlled for outliers and checked for the normality and homogeneity assumptions. Post hoc (Bonferroni) tests will be conducted to report pair-wise comparisons. SPSS (version 17.0; SPSS, Inc) will be used for statistical analysis, and statistical significance will be set at a *P* value of <.05.

Results

This study will start in summer 2022 and be complete by fall 2022.

Discussion

Expected Findings

It is generally accepted that rehabilitative modalities, including pelvic support, are suitable for PPGP [17]. Previous research has shown that lumbosacral orthosis effectively improved motor control and lumbopelvic function among patients with lower back pain [22]. The pathomechanics of lower back pain and PPGP are similar and include dysfunction of load transfer across the pelvis; hence, it has been hypothesized that wearing lumbar support could have beneficial effects for women with PPGP.

This study protocol will compare the impact of pelvic and lumbar supports on pain, disability, and hip repositioning in postpartum PPGP. The study results can be helpful for clinical decision-making. We anticipate that the study results will have significant implications for practitioners and specialists by increasing the scientific basis and contributing to the successful implementation of effective rehabilitation programs in clinical settings. Earlier studies have shown that both pelvic compression belts in pregnant women with PPGP [28] and lumbosacral orthosis in low back pain can significantly decrease pain [51] and improve proprioception [52], which can be explained by the biomechanical support provided [53] and proprioceptive impact of the orthosis [22]. At present, it is impossible to quantify which support is superior in reducing pain and improving proprioception and quality of life in women with PPGP. Suppose the lumbar support offers more favorable effects than the pelvic support in terms of pain reduction and improved sensorimotor outcomes. In that case, new orthotic interventions can be advised for women with postnatal PPGP.

This clinical study will evaluate repositioning in women with PPGP. For this repositioning, the JPR will be tested in a standing position. The upright position is a functionally relevant condition often occurring during daily activities. The hip abduction was selected since more precise scores for the proprioception test for the hip joint are assessed during this movement [49]. If pelvic and lumbar supports could affect the pain or load transfer at the SIJ, it could be reflected in the precision of JPR. The maximum force generation during trunk and external hip rotation is planned to quantify the possible effects of wearing the pelvic or lumbar support on the load transfer across the lumbopelvic area.

Strengths and Limitations

The strength of this study will be the investigation of the effectiveness of newly designed lumbar support for the management of PPGP. There may be limitations to this study. The inclusion and exclusion criteria set in this study can limit the generalizability of the results. Another limitation could be that some participants may be excluded because of incomplete trial time or not being interested in wearing the support.

Acknowledgments

The authors would like to sincerely thank the research deputy of Isfahan University of Medical Sciences for supporting this study protocol.

Data Availability

The data sets will be included in the main manuscript and available from the corresponding author at reasonable request.

Authors' Contributions

F-SJ, GY, and ES-D contributed substantially to the conception and design and drafted the manuscript. Participants' eligibility criteria will be confirmed under the supervision of MJ-H. F-SJ will complete data collection and analysis with ES-D and MJ-H guidance. All authors reviewed and revised the manuscript for important intellectual content and approved the final version.

Conflicts of Interest

None declared.

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Multimedia Appendix 1
Peer-review reports from the Isfahan University of Medical Sciences - Office for Research and Technology (Isfahan, Iran).
[PDF File (Adobe PDF File), 107 KB - researchprotocols_v11i7e40553_fig.pdf]

References

1. Wu WH, Meijer OG, Uegaki K, Mens JMA, van Dieën JH, Wuisman PIJM, et al. Pregnancy-related pelvic girdle pain (PPP), I: Terminology, clinical presentation, and prevalence. Eur Spine J 2004 Nov 27;13(7):575-589 [FREE Full text] [doi: 10.1007/s00586-003-0615-y] [Medline: 15338362]
2. Gutke A, Lundberg M, Östgaard HC, Öberg B. Impact of postpartum lumbopelvic pain on disability, pain intensity, health-related quality of life, activity level, kinesiophobia, and depressive symptoms. Eur Spine J 2011 Mar 1;20(3):440-448 [FREE Full text] [doi: 10.1007/s00586-010-1487-6] [Medline: 20593205]
3. Beales D, O'Sullivan P. A person centred biopsychosocial approach to assessment and management of pelvic girdle pain. In: Grieve's modern musculoskeletal physiotherapy. London: Elsevier; 2015:488-495.
4. Beales D, Slater H, Palsson T, O'Sullivan P. Understanding and managing pelvic girdle pain from a person-centred biopsychosocial perspective. Musculoskelet Sci Pract 2020 Aug;48:102152. [doi: 10.1016/j.msksp.2020.102152] [Medline: 32560860]
5. Bunzli S, Smith A, Schütze R, Lin I, O'Sullivan P. Making Sense of Low Back Pain and Pain-Related Fear. J Orthop Sports Phys Ther 2017 Sep;47(9):628-636. [doi: 10.2519/jospt.2017.7434] [Medline: 28704621]
6. Hodges PW, Cholewicki J, Popovich JM, Lee AS, Aminpour P, Gray SA, et al. Building a Collaborative Model of Sacroiliac Joint Dysfunction and Pelvic Girdle Pain to Understand the Diverse Perspectives of Experts. PM R 2019 Aug 23;11 Suppl 1(S1):S11-S23. [doi: 10.1002/pmrj.12199] [Medline: 31169360]
7. O'Sullivan PB, Beales DJ. Diagnosis and classification of pelvic girdle pain disorders--Part 1: a mechanism based approach within a biopsychosocial framework. Man Ther 2007 May;12(2):86-97. [doi: 10.1016/j.math.2007.02.001] [Medline: 17449432]
8. Aldabe D, Milosavljevic S, Bussey MD. Is pregnancy related pelvic girdle pain associated with altered kinematic, kinetic and motor control of the pelvis? A systematic review. Eur Spine J 2012 Sep 21;21(9):1777-1787 [FREE Full text] [doi: 10.1007/s00586-012-2401-1] [Medline: 22718046]
9. Gutke A, Boissonnault J, Brook G, Stuge B. The Severity and Impact of Pelvic Girdle Pain and Low-Back Pain in Pregnancy: A Multinational Study. J Womens Health (Larchmt) 2018 Apr;27(4):510-517. [doi: 10.1089/jwh.2017.6342] [Medline: 28832267]
10. Bussey MD. Mechanics of pelvic girdle stability and self-bracing in SIJ-related pelvic girdle pain: a review. Physical Therapy Reviews 2015 May 15;20(3):168-177. [doi: 10.1179/1743288x15y.0000000010]
11. Reeves NP, Cholewicki J, van Dieën JH, Kawchuk G, Hodges PW. Are Stability and Instability Relevant Concepts for Back Pain? J Orthop Sports Phys Ther 2019 Jun;49(6):415-424. [doi: 10.2519/jospt.2019.8144] [Medline: 31021689]
12. Snijders C, Vleeming A, Stoeckart R. Transfer of lumbosacral load to iliac bones and legs. Clinical Biomechanics 1993 Nov;8(6):285-294. [doi: 10.1016/0268-0033(93)90002-y]
13. Coldron Y, Stokes MJ, Newham DJ, Cook K. Postpartum characteristics of rectus abdominis on ultrasound imaging. Man Ther 2008 May;13(2):112-121. [doi: 10.1016/j.math.2006.10.001] [Medline: 17208034]
14. Mens JM, Huis In 't Veld YH, Pool-Goudzwaard A. The Active Straight Leg Raise test in lumbopelvic pain during pregnancy. Man Ther 2012 Aug;17(4):364-368. [doi: 10.1016/j.math.2012.01.007] [Medline: 22365484]
15. de Groot M, Pool-Goudzwaard A, Spoor C, Snijders C. The active straight leg raising test (ASLR) in pregnant women: differences in muscle activity and force between patients and healthy subjects. Man Ther 2008 Feb;13(1):68-74. [doi: 10.1016/j.math.2006.08.006] [Medline: 17188924]
16. Liddle S, Pennick V. Interventions for preventing and treating low-back and pelvic pain during pregnancy. Cochrane Database Syst Rev 2015 Sep 30(9):CD001139 [FREE Full text] [doi: 10.1002/14651858.CD001139.pub4] [Medline: 26422811]
17. Mens JM, Damen L, Snijders CJ, Stam HJ. The mechanical effect of a pelvic belt in patients with pregnancy-related pelvic pain. Clin Biomech (Bristol, Avon) 2006 Feb;21(2):122-127. [doi: 10.1016/j.clinbiomech.2005.08.016] [Medline: 16214275]
18. Suehiro T, Yakushijin Y, Nuibe A, Ishii S, Kurozumi C, Ishida H. Effect of pelvic belt on the perception of difficulty and muscle activity during active straight leg raising test in pain-free subjects. J Exerc Rehabil 2019 Jun 26;15(3):449-453 [FREE Full text] [doi: 10.12965/jer.1938140.070] [Medline: 31316940]
19. Morino S, Ishihara M, Umezaki F, Hatanaka H, Yamashita M, Kawabe R, et al. The effects of pelvic belt use on pelvic alignment during and after pregnancy: a prospective longitudinal cohort study. BMC Pregnancy Childbirth 2019 Aug 22;19(1):305 [FREE Full text] [doi: 10.1186/s12884-019-2457-6] [Medline: 31438891]
20. Jung H, Jeon H, Oh D, Kwon O. Effect of the pelvic compression belt on the hip extensor activation patterns of sacroiliac joint pain patients during one-leg standing: a pilot study. Man Ther 2013 Apr;18(2):143-148. [doi: 10.1016/j.math.2012.09.003] [Medline: 23111368]
21. Pel J, Spoor C, Goossens R, Pool-Goudzwaard A. Biomechanical model study of pelvic belt influence on muscle and ligament forces. J Biomech 2008 Jan;41(9):1878-1884. [doi: 10.1016/j.jbiomech.2008.04.002] [Medline: 18501363]

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22. Cholewicki J, Shah KR, McGill KC. The effects of a 3-week use of lumbosacral orthoses on proprioception in the lumbar spine. J Orthop Sports Phys Ther 2006 Apr;36(4):225-231. [doi: 10.2519/jospt.2006.36.4.225] [Medline: 16676872]
23. Barss TS, Pearcey GEP, Munro B, Bishop JL, Zehr EP. Effects of a compression garment on sensory feedback transmission in the human upper limb. J Neurophysiol 2018 Jul 01;120(1):186-195 [FREE Full text] [doi: 10.1152/jn.00581.2017] [Medline: 29641310]
24. Sawle L, Freeman J, Marsden J, Matthews MJ. Exploring the effect of pelvic belt configurations upon athletic lumbopelvic pain. Prosthet Orthot Int 2013 Apr;37(2):124-131. [doi: 10.1177/0309364612448806] [Medline: 22751218]
25. Mens JMA, Pool-Goudzwaard A, Stam HJ. Mobility of the pelvic joints in pregnancy-related lumbopelvic pain: a systematic review. Obstet Gynecol Surv 2009 Mar;64(3):200-208. [doi: 10.1097/OGX.0b013e3181950f1b] [Medline: 19228440]
26. Mitchell DA, Esler DM. Pelvic instability - Painful pelvic girdle in pregnancy. Aust Fam Physician 2009 Jun;38(6):409-410 [FREE Full text] [Medline: 19521584]
27. Delshad B, Zarean E, Yeowell G, Sadeghi-Demneh E. The immediate effects of pelvic compression belt with a textured sacral pad on the sacroiliac function in pregnant women with lumbopelvic pain: A cross-over study. Musculoskelet Sci Pract 2020 Aug;48:102170. [doi: 10.1016/j.msksp.2020.102170] [Medline: 32560872]
28. Bertuit J, Van Lint CE, Rooze M, Feipel V. Pregnancy and pelvic girdle pain: Analysis of pelvic belt on pain. J Clin Nurs 2018 Jan 03;27(1-2):e129-e137. [doi: 10.1111/jocn.13888] [Medline: 28544276]
29. Cotterill S, Knowles S, Martindale A, Elvey R, Howard S, Coupe N, et al. Getting messier with TIDieR: embracing context and complexity in intervention reporting. BMC Med Res Methodol 2018 Jan 18;18(1):12 [FREE Full text] [doi: 10.1186/s12874-017-0461-y] [Medline: 29347910]
30. Hoffmann TC, Glasziou PP, Boutron I, Milne R, Perera R, Moher D, et al. Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide. BMJ 2014 Mar 07;348(mar07 3):g1687-g1687. [doi: 10.1136/bmj.g1687] [Medline: 24609605]
31. Eysenbach G, CONSORT-EHEALTH Group. CONSORT-EHEALTH: improving and standardizing evaluation reports of Web-based and mobile health interventions. J Med Internet Res 2011 Dec 31;13(4):e126 [FREE Full text] [doi: 10.2196/jmir.1923] [Medline: 22209829]
32. Kordi R, Abolhasani M, Rostami M, Hantoushzadeh S, Mansournia MA, Vasheghani-Farahani F. Comparison between the effect of lumbopelvic belt and home based pelvic stabilizing exercise on pregnant women with pelvic girdle pain; a randomized controlled trial. BMR 2013 Apr 29;26(2):133-139. [doi: 10.3233/bmr-2012-00357]
33. Laslett M, Aprill CN, McDonald B, Young SB. Diagnosis of sacroiliac joint pain: validity of individual provocation tests and composites of tests. Man Ther 2005 Aug;10(3):207-218. [doi: 10.1016/j.math.2005.01.003] [Medline: 16038856]
34. Mens JMA, Vleeming A, Snijders CJ, Koes BW, Stam HJ. Validity of the active straight leg raise test for measuring disease severity in patients with posterior pelvic pain after pregnancy. Spine (Phila Pa 1976) 2002 Jan 15;27(2):196-200. [doi: 10.1097/00007632-200201150-00015] [Medline: 11805667]
35. Efird J. Blocked randomization with randomly selected block sizes. Int J Environ Res Public Health 2011 Jan 23;8(1):15-20 [FREE Full text] [doi: 10.3390/ijerph8010015] [Medline: 21318011]
36. Saghaei M. Random allocation software for parallel group randomized trials. BMC Med Res Methodol 2004 Nov 09;4(1):26 [FREE Full text] [doi: 10.1186/1471-2288-4-26] [Medline: 15535880]
37. Paungmali A, Sitilertpisan P, Taneyhill K, Pirunsan U, Uthaikhup S. Intrarater reliability of pain intensity, tissue blood flow, thermal pain threshold, pressure pain threshold and lumbo-pelvic stability tests in subjects with low back pain. Asian J Sports Med 2012 Mar 01;3(1):8-14 [FREE Full text] [doi: 10.5812/asjsm.34718] [Medline: 22461960]
38. Baradaran A, Ebrahimzadeh MH, Birjandinejad A, Kachooei AR. Cross-Cultural Adaptation, Validation, and Reliability Testing of the Modified Oswestry Disability Questionnaire in Persian Population with Low Back Pain. Asian Spine J 2016 Apr;10(2):215-219 [FREE Full text] [doi: 10.4184/asj.2016.10.2.215] [Medline: 27114759]
39. Vianin M. Psychometric properties and clinical usefulness of the Oswestry Disability Index. J Chiropr Med 2008 Dec;7(4):161-163 [FREE Full text] [doi: 10.1016/j.jcm.2008.07.001] [Medline: 19646379]
40. Fairbank J, Couper J, Davies J, O'Brien JP. The Oswestry low back pain disability questionnaire. Physiotherapy 1980 Aug;66(8):271-273. [Medline: 6450426]
41. Fairbank JCT, Pynsent PB. The Oswestry Disability Index. Spine (Phila Pa 1976) 2000 Nov 15;25(22):2940-2952; discussion 2952. [doi: 10.1097/00007632-200011150-00017] [Medline: 11074683]
42. Roland M, Fairbank J. The Roland-Morris Disability Questionnaire and the Oswestry Disability Questionnaire. Spine (Phila Pa 1976) 2000 Dec 15;25(24):3115-3124. [doi: 10.1097/00007632-200012150-00006] [Medline: 11124727]
43. Davidson M, Keating JL. A comparison of five low back disability questionnaires: reliability and responsiveness. Phys Ther 2002 Jan;82(1):8-24. [doi: 10.1093/ptj/82.1.8] [Medline: 11784274]
44. Mens JMA, Vleeming A, Snijders CJ, Koes BW, Stam HJ. Reliability and validity of the active straight leg raise test in posterior pelvic pain since pregnancy. Spine (Phila Pa 1976) 2001 May 15;26(10):1167-1171. [doi: 10.1097/00007632-200105150-00015] [Medline: 11413432]
45. Bazett-Jones DM, Squier K. Measurement properties of hip strength measured by handheld dynamometry: Reliability and validity across the range of motion. Phys Ther Sport 2020 Mar;42:100-106. [doi: 10.1016/j.ptsp.2020.01.005] [Medline: 31958744]

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46. Aguiar LT, Martins JC, Lara EM, Albuquerque JA, Teixeira-Salmela LF, Faria CDCM. Dynamometry for the measurement of grip, pinch, and trunk muscles strength in subjects with subacute stroke: reliability and different number of trials. Braz J Phys Ther 2016 Jul 11;20(5):395-404 [FREE Full text] [doi: 10.1590/bjpt-rbf.2014.0173] [Medline: 27410161]
47. Souza LACE, Martins JC, Teixeira-Salmela LF, Godoy MR, Aguiar LT, Faria CDCDM. Avaliação da força muscular pelo teste do esfigmomanômetro modificado: uma revisão da literatura. Fisioter Mov 2013 Jun;26(2):437-452. [doi: 10.1590/s0103-51502013000200021]
48. Kienbacher T, Paul B, Habenicht R, Starek C, Wolf M, Kollmitzer J, et al. Reliability of isometric trunk moment measurements in healthy persons over 50 years of age. J Rehabil Med 2014 Mar;46(3):241-249 [FREE Full text] [doi: 10.2340/16501977-1266] [Medline: 24473577]
49. Arvin M, Hoozemans MJM, Burger BJ, Verschueren SMP, van Dieën JH, Pijnappels M. Reproducibility of a knee and hip proprioception test in healthy older adults. Aging Clin Exp Res 2015 Apr 2;27(2):171-177. [doi: 10.1007/s40520-014-0255-6] [Medline: 24986332]
50. Puig-Diví A, Padullés-Riu J, Busquets-Faciaben A, Padullés-Chando X, Escalona-Marfil C, Marcos-Ruiz D. Validity and reliability of the kinovea program in obtaining angular and distance dimensions. Preprints Preprint posted online October 9, 2017. [doi: 10.20944/preprints201710.0042.v1]
51. Calmels P, Queneau P, Hamonet C, Le Pen C, Maurel F, Lerouvreur C, et al. Effectiveness of a lumbar belt in subacute low back pain: an open, multicentric, and randomized clinical study. Spine (Phila Pa 1976) 2009 Feb 01;34(3):215-220. [doi: 10.1097/BRS.0b013e31819577dc] [Medline: 19179915]
52. Newcomer K, Laskowski ER, Yu B, Johnson JC, An K. The effects of a lumbar support on repositioning error in subjects with low back pain. Arch Phys Med Rehabil 2001 Jul;82(7):906-910. [doi: 10.1053/apmr.2001.23281] [Medline: 11441376]
53. van Poppel MNM, de Looze MP, Koes BW, Smid T, Bouter LM. Mechanisms of action of lumbar supports: a systematic review. Spine (Phila Pa 1976) 2000 Aug 15;25(16):2103-2113. [doi: 10.1097/00007632-200008150-00016] [Medline: 10954643]

Abbreviations

ASLR: active straight leg raise
CONSORT-EHEALTH: Consolidated Standards of Reporting Trials of Electronic and Mobile Health Applications and onLine TeleHealth
ICC: intraclass correlation coefficient
IUMS: Isfahan University of Medical Sciences
JPR: joint position reproduction
ODI: Oswestry Disability Index
PPGP: posterior pelvic girdle pain
SIJ: sacroiliac joint
TIDieR: Template for Intervention Description and Replication
VAS: visual analogue scale

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Protocol

An Adapted Cognitive Behavioral Stress and Self-management Intervention for Sexual Minority Men Living With HIV and Cancer Using the SmartManage eHealth Platform: Protocol and Study Design

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Abstract

Background: Sexual minority men are disproportionately affected by HIV. Medical advances in HIV treatment have extended life expectancy, and as this group ages, medical and psychological challenges become more prominent. Older people with HIV experience a higher incidence of cancer and other comorbidities; these burdens along with sexual minority stress can strain coping resources and diminish health-related quality of life. Interventions such as cognitive behavioral stress and self-management (CBSM) can mitigate some of this burden; however, no manualized, eHealth-based interventions have focused on the unique needs of sexual minority men living with HIV and cancer.

Objective: This study aims to refine and finalize a web-based, CBSM-based intervention to meet the unique needs of this population, including sexual health, comanagement of 2 chronic conditions, and coping with sexual minority stress.

Methods: This mixed methods study used a previously completed qualitative phase (n=6) to inform the development of a web-based platform and intervention called SmartManage. The pilot phase study (n=50) involved randomization (1:1) into either 10 sessions of adapted CBSM or an attention control health promotion. Both conditions used the SmartManage platform, a web-based eHealth program designed to deliver CBSM and health promotion content and host *live* groups. Feasibility and acceptability (eg, rates of participant engagement and retention) were the primary outcomes.

Results: Participant-related activities are expected to be completed by November 2022, and results are expected to be submitted for publication by February 2023.

Conclusions: We hypothesize that participants would find the intervention acceptable (compared with engagement and retention rates observed in similar CBSM studies). We also hypothesize that participants receiving the SmartManage intervention would have reduced symptom burden and improved health-related quality of life before and after treatment compared with those who do not.

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KEYWORDS

intervention; HIV; cancer; participant; SmartManage; cognitive behavioral stress and self-management

Introduction

With the advent of highly active antiretroviral treatment in the late 1990s, the life expectancy of people living with HIV now nearly matches that of people without HIV. However, the aging cohort of people living with HIV faces substantial health disparities, including higher rates of non–AIDS-defining cancers including liver, lung, and colorectal cancers [1], and for some of these people, these cancers may develop at a younger age [2]. Sexual minority men (SMM) are disproportionately affected by HIV, and many face societal stigma related to both HIV and sexual minority status. The demands of simultaneously managing 2 chronic conditions in the context of this stigma can negatively impact health-related quality of life (HRQoL) and health outcomes. For example, many sexual minority patients miss or delay the needed medical care because of provider bias [3-5]. Relative to heterosexual men, gay men may not be screened for less common cancers in heterosexual communities, such as anal cancer [6,7]. Gay men also report lower satisfaction with their cancer care, which is associated with greater anxiety and poor quality of life [8,9]. Collectively, these challenges place patients who are SMM at a greater risk of late-presenting advanced cancer, leading to worse treatment outcomes and HRQoL.

Psychosocial interventions, including cognitive behavioral stress and self-management (CBSM), can ameliorate symptom burden and improve HRQoL among patients with prostate or breast cancer [10,11]. CBSM also shows favorable effects in SMM (eg, reduced distress and improved mood) [12,13]. However, there are limitations to the standard CBSM for those with HIV and cancer, particularly SMM with HIV and cancer. They face the additional burden of managing complex medical regimens in an often-fragmented care model and in the presence of enduring stigmas around HIV and sexual minority status. Many SMM report experiences with chronic discrimination and nonaffirming providers, leading to apprehension about self-disclosure of sexual minority status to cancer providers or support services (eg, support groups) [14,15]. For group therapy participants and medical patients, societal pressure to conceal their identity can interfere with treatment and leave important needs unaddressed. An equally important challenge is the lack of focus on specific problems for this population, including sexual health and difficulties specific to HIV and cancer comanagement [16].

To address this treatment gap, we are adapting and piloting our CBSM intervention using the *SmartManage* platform (an eHealth-based program for stress management and relaxation training management). SmartManage is a web-based, synchronous platform that hosts all components of our CBSM intervention, which delivers evidence-based techniques to improve self-management, psychosocial or physiological adaptation, and HRQoL. The 9 distinct CBSM intervention targets are listed in Textbox 1.

Textbox 1. Additional treatment targets integrated into adapted cognitive behavioral stress and self-management (CBSM) for issues relevant to sexual minority men (SMM) living with HIV and cancer.

Treatment issues

- HIV and cancer stigma
- Coping with social and medical challenges of 2 major chronic illnesses
- Sexual minority status often disclosed with HIV serostatus
- Medication and treatment adherence for 2 major chronic illnesses
- Care coordination across medical appointments and providers
- Sexual health and intimacy for SMM in the context of cancer and HIV treatments
- Managing treatment fatigue
- Finding appropriate lesbian, gay, bisexual, transgender, and questioning resources for medical information and support and mental health care
- Recognizing and managing cognitive, emotional, and physical effects of minority stress

This initial trial will use CBSM via the SmartManage platform to address the unique needs of SMM who are HIV positive cancer survivors, both related to specific medical concerns and psychosocial factors that contribute to health disparities. Our primary aim is to evaluate the usability, acceptability, and feasibility of the adapted CBSM intervention; our secondary aim is to evaluate the intended effects (eg, improvements in HRQoL and stress management) relative to an attention control condition. In this paper, we describe (1) the intervention development strategy by using both qualitative and quantitative assessments and (2) a single-site randomized controlled pilot study of the adapted CBSM.

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Methods

Ethics Approval

All study procedures and assessment materials have been approved by the institutional review board at the University of Miami (IRB #20190762) and by the University of Miami Sylvester Comprehensive Cancer Center Protocol Review and Monitoring Committee.

Study Design

This pilot intervention development study will test the feasibility, acceptability, and intended effects of an adapted CBSM intervention. Pre–pilot testing and qualitative feedback (see Textbox 2 for qualitative interview questions) were used to refine the intervention, which will be tested in a randomized controlled pilot trial.

Textbox 2. Categorical breakdown of qualitative questions for study phase 1 (usability).

Aesthetic appearance

- "What was your first impression of the website?"
- "What words would you use to describe the appearance of the website? Feel free to comment on the following: layout, colors, size, fonts, etc."

User experience

- "In general, how did you feel about using the website?"
- "Was it fairly intuitive to use?"
- "How easily could you locate what you were looking for?"
- "How was the speed of the site? (Ex: did text, images, sound, and/or video take a short or long time to load?)"
- "What did you like about using the website?"
- "What would you change about the website?"
- "What type of device would you be most likely to use for accessing this site: computer, tablet, or smartphone?"

Content related to health and health care

- "In general, how much did you like the information presented on the website?"
- "Were the topics we included relevant to your experience as an HIV+ cancer survivor?"
- "What specifically did you learn that you can use to improve your health and well-being?"
- "What problems or challenges do you have that were not addressed appropriately or to your satisfaction?"
- "What else would you like to see included on the site?"

All study procedures involving participants are intended to be completed remotely via secure Health Insurance Portability and Accountability Act–compliant video conferencing software. This includes the documentation of informed consent and administration of assessments, both of which will be captured using the secure REDCap (Research Electronic Data Capture; Vanderbilt University) platform.

The pilot study will enroll 50 SMM who are HIV positive with a history of a nonmetastatic solid tumor or blood cancer, who will be randomly assigned (1:1) to receive either 10 individual sessions of video-adapted health promotion (HP) content (educational control) or 10 group-based sessions of the SmartManage intervention facilitated by trained interventionists (Figure 1). Before randomization, participants will complete a self-report assessment battery (baseline or T1; Table 1), which they will complete again immediately after treatment (T2). Participants will be compensated US $20 for completing the T1 questionnaire, US $10 for each of the 10 intervention or control sessions, and US $30 for the T2 questionnaire, yielding a maximum of US $150 compensation for completing the study procedures.

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Figure 1. SmartManage session 1 screenshot.

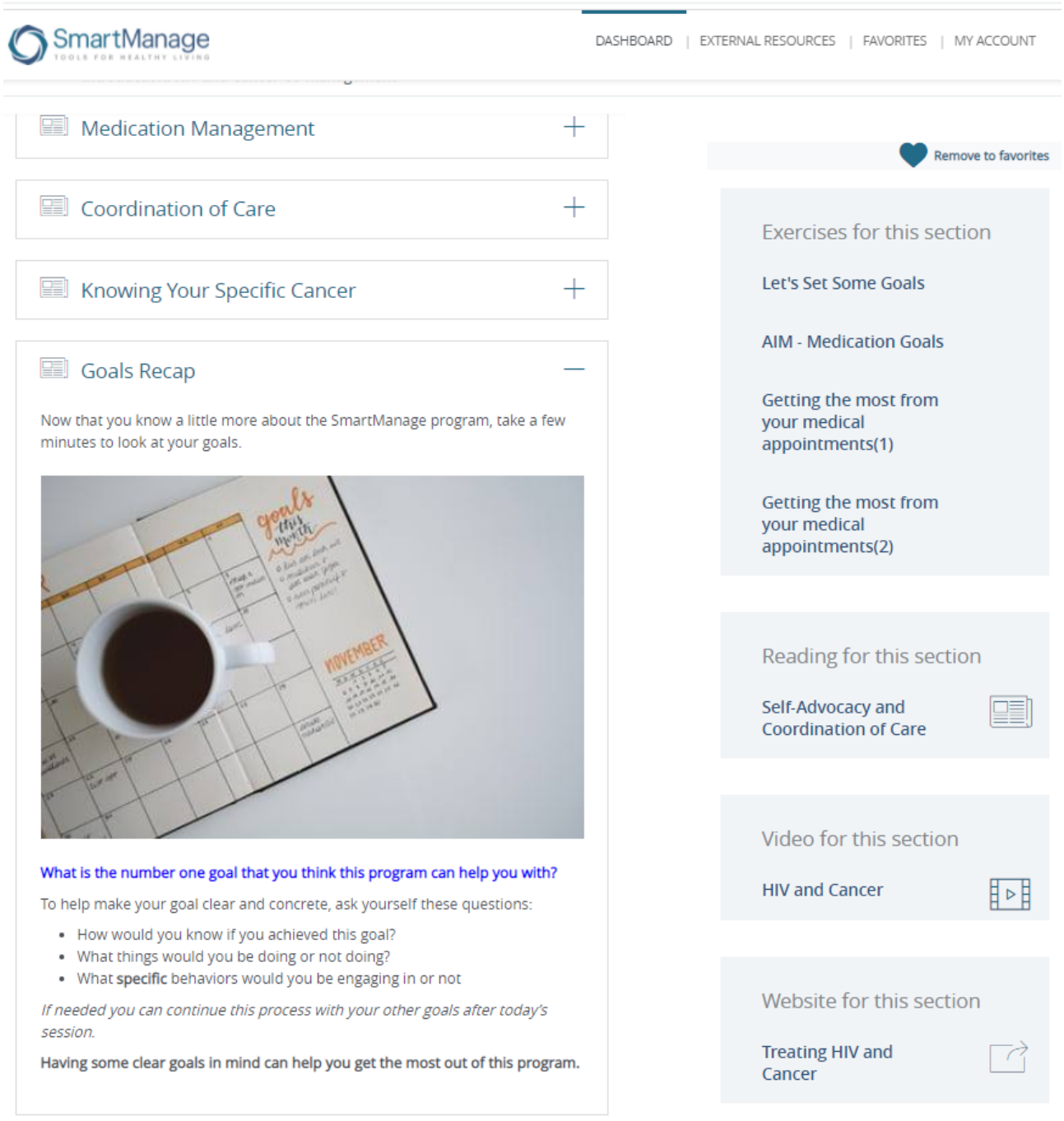

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Table 1. Usability and pilot phase measures.

Measure name	Usability phase	Pilot phase
Demographics Survey (baseline only)	✓	✓
Disease Information Form (baseline only)	✓	✓
ACTG[a] HIV medication Adherence measure	✓	✓
Barriers to HIV Care survey	✓	✓
Participant Survey on Website Feedback (ie, USE[b] Questionnaire; postintervention)	✓	✓
Coping Self-Efficacy Scale		✓
Interpersonal Support Evaluation List		✓
Bidimensional Acculturation Scale for Hispanics		✓
Computer Proficiency Questionnaire		✓
Perceived Stress Scale (General Stress)		✓
Impact of Event Scale (disease or dual diagnosis–related distress)		✓
Functional Assessment of Cancer Therapy Scale-General (HRQoL[c])		✓
Medical Outcomes Study HIV Survey (HRQoL)		✓
SmartManage Acceptability Evaluation (postintervention only)	✓	✓
Communication Assessment Tool-revised		✓
International Physical Activity Questionnaire—short form		✓
PROMIS[d] Bother Regarding Sexual Function		✓
PROMIS Factors Interfering with Sexual Satisfaction		✓
Pittsburgh Sleep Quality Index		✓
COVID-19: Impact of the pandemic and HRQoL on patients with cancer and survivors		✓
COVID-19: Impact on sexual health—SGM[e]		✓
Everyday Discrimination—Sexual Orientation		✓

[a]ACTG: AIDS Clinical Trials Group.

[b]USE: Usefulness, Satisfaction, and Ease of Use.

[c]HRQoL: health-related quality of life.

[d]PROMIS: Patient-Reported Outcomes Measurement Information System.

[e]SGM: sexual and gender minority.

Participants in phase 1 and participants who are randomized to the CBSM SmartManage intervention (Table 2) condition in phase 2 will be asked to consent to audio recordings of these visits for qualitative analysis and fidelity monitoring. The weekly topics of the educational control HP condition are listed in Textbox 3.

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Table 2. SmartManage cognitive behavioral stress and self-management for HIV and cancer weekly session topics and key subtopics.

Weekly sessions	Major topic	Subtopic	Relaxation exercises
Session 1	Introduction: HIV and Cancer Comanagement	Goal setting	__[a]
Session 2	Stress and Stress Management	Medication adherence	Breathing meditation
Session 3	Linking Thoughts and Emotions	Cognitive appraisal	Introduction to meditation and mindfulness
Session 4	Linking Thoughts and Emotions: Part 2	Cognitive distortions	Meditation for working with difficulties
Session 5	Sex and Intimacy	Focus on SMM[b] sexual health	Loving kindness meditation
Session 6	Effective Communication and Managing Emotions	Anger management	Body scan for sleep
Session 7	Partnering With My Health System or Providers	Assertiveness training	Breathing meditation (audio)
Session 8	Social Connections	Building a social support network	Sitting meditation
Session 9	Healthy Behaviors	Coping with information overload	Brief “stop” meditation
Session 10	Wrap up and Program Summary	Plan for continuing work toward goals	Brief 3-minute meditation

[a]None.

[b]SMM: sexual minority men.

Textbox 3. SmartManage educational control health promotion topics.

Weekly sessions and topic
Session 1: Introduction to health promotion
Session 2: Disease and healthy lifestyle
Session 3: Aging
Session 4: Exercise
Session 5: Diet
Session 6: Memory and cognition
Session 7: Sexuality
Session 8: Quality of life
Session 9: Information overload
Session 10: Review and summary

Textbox 3 describes weekly educational control sessions.

Participants

We enrolled 6 qualitative participants (phase 1) and will enroll 50 pilot participants (phase 2) recruited from specific departments within the University of Miami Hospital (Infectious Diseases and AIDS Clinical Research Unit), University of Miami medical affiliates (Sylvester Comprehensive Cancer Center), consent to contact databases (Center for HIV and Research in Mental Health—CHARM Registry), and via social media.

Participants will meet the following inclusion criteria: (1) ≥18 years of age; (2) fluent in English; (3) diagnosed with at least 1 form of nonmetastatic solid tumor or blood cancer; (4) ≥30 days after the completion of active primary treatment (eg, surgery, radiation, and chemotherapy); (5) self-identify as a sexual minority, cisgender man (ie, self-identify as something other than heterosexual or straight; assigned male at birth and identify as male); (6) self-report having been diagnosed with HIV; and (7) have reliable access to a device with internet access. Adjuvant therapies such as hormone treatment for prostate cancer are not considered exclusionary. Participants will be excluded if they (1) have one of the following exclusionary cancer types: nonmelanoma skin cancer only, brain cancer, eye cancer, or remote history of pediatric cancer only without a history of cancer as an adult; (2) have a history of metastatic cancer of any type; (3) are currently undergoing primary treatment for their cancer; (4) have had inpatient treatment for serious mental illness in the past 12 months, overt signs of serious mental illness, or moderate or higher risk of suicidality at the time of screening; (5) appear actively intoxicated or otherwise unable to provide full informed consent; or (6) have any medical conditions resulting in a predicted life expectancy of <12 months per participant self-report. The

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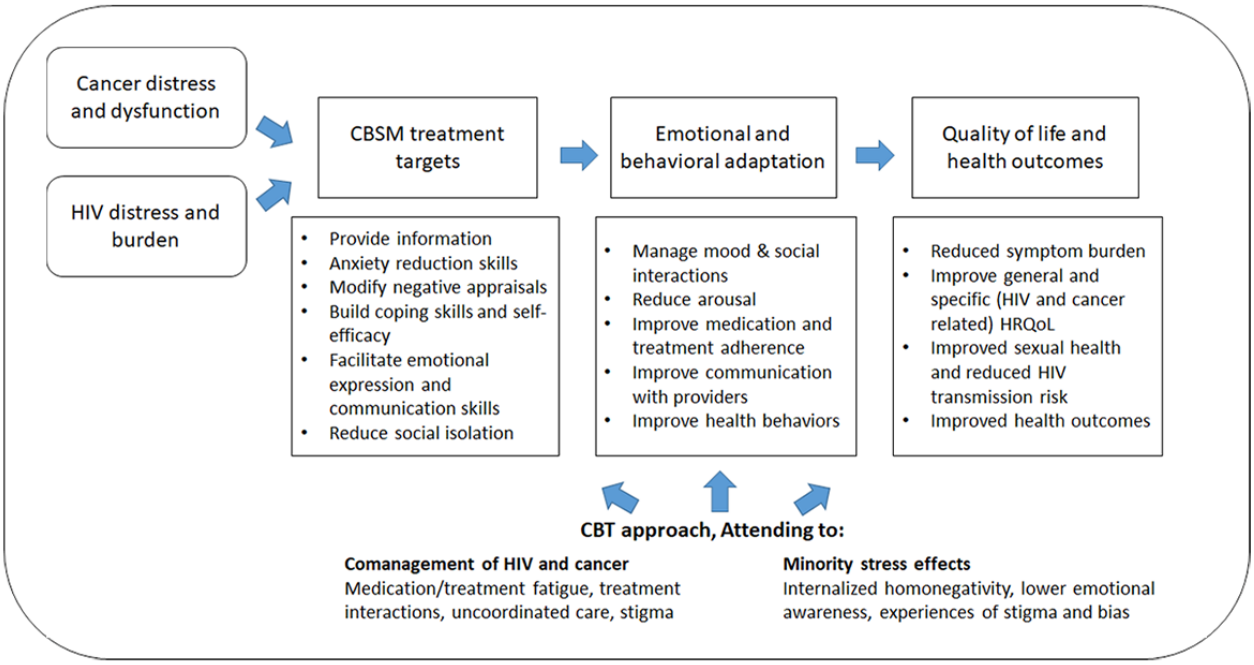
intention behind the specificity of these inclusion and exclusion criteria is to minimize the enrollment of participants whose illness is likely to significantly interfere with their ability to engage with the study material (eg, eye cancer) or complete study participation (eg, metastatic illness with a life expectancy of <12 months). The research team felt that this was necessary given the small sample size of this study; however, we also recognize that some patients excluded from this study could benefit from the intervention. We intended to expand inclusion criteria in larger subsequent studies to allow broader medical inclusion and applicability to participants of other genders and sexual orientations.

SmartManage for HIV and Cancer Survivors: Adapted CBSM for Lesbian, Gay, Bisexual, Transgender, and Questioning Individuals Dually Diagnosed With HIV and Cancer

The SmartManage CBSM intervention was adapted from the manualized CBSM intervention [17], with an additional focus on psychosocial issues relevant to SMM, as well as focus on comanaging HIV and cancer. The adapted CBSM SmartManage for HIV and cancer intervention incorporates cognitive behavioral therapy techniques to facilitate changes in domains known to impact symptom burden, HRQoL, physical functioning, and self-management (see Table 2 for the session outline). The CBSM intervention using the SmartManage platform seeks to promote coping and resilience through the use of practical tools (relaxation training, increasing physical activity, and social support), general and diagnosis-specific information, and cognitive behavioral therapy–based strategies (eg, cognitive restructuring), with added focus on the role of sexual minority stress and issues relevant to SMM (see Figure 2 for conceptual model). Throughout the 10 sessions that lasted for 90 minutes, participants are taught to recognize the antecedents of negative mood and systematically evaluate cognitive distortions to improve symptom management, interpersonal adjustment, and HRQoL. Intervention groups consist of 4 to 6 participants led by a trained therapist (master's level or psychology doctoral students) with experience in working with sexual minority clients. Participants are encouraged to share relevant experiences and to practice skills during the session. For example, a participant who expresses anger that a friend did not call him back may apply Socratic questioning with the help of the group to identify and challenge cognitive distortions. Participants will be asked to complete live worksheets through the web-based platform, and they will be asked to complete weekly home exercises using downloadable materials. Therapists will troubleshoot and track the prior week's home practice at the beginning of each subsequent session.

Figure 2. Integrated model of cognitive behavioral stress and self-management (CBSM) for comanagement of cancer and HIV. CBT: cognitive behavior therapy; HRQoL: health-related quality of life.



To adapt the intervention for SMM comanaging HIV and cancer, we drew upon our earlier work and newer research with sexual and gender minority clients. Our prior research on interventions to manage prostate cancer survivorship or HIV infection in SMM guided content changes that may be important for SMM with HIV and cancer. We also conducted qualitative interviews with this cohort to determine the usability of the SmartManage website and to allow participants to share what they felt was lacking in the nonadapted interventions [10,18]. We then incorporated these changes within the conceptual framework of the minority stress model, which posits that chronic exposure to societal stigma and bias drives internal stress processes that exacerbate psychological distress and increase the risk of maladaptive coping strategies [19,20]. The resulting CBSM intervention for HIV and cancer using the SmartManage platform therefore includes changes ranging from cosmetic (SMM-specific images and text) to content, with an emphasis on intervention elements most likely to address the interaction of minority stress and the comanagement of cancer and HIV.

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HIV and Cancer SmartManage Content and Format

Participants in phase 2 of the study will be randomly assigned to receive 10 sessions of either the SmartManage CBSM intervention or SmartManage-based HP educational control. Both interventions will be delivered weekly over 10 weeks. Given that this study is intended primarily for intervention development and evaluation of usability, feasibility, and acceptability among the target population, the intervention and control conditions are not matched in terms of dose (session length) or format. Both conditions provide participants with broadly relevant HP information; however, the control content does not contain population-specific adaptations (eg, focus on minority stress) or active psychotherapeutic techniques (eg, cognitive restructuring). Each week involves a prescheduled live web-based group meeting with 4 to 6 members led by a therapist who delivers the session material while collaborating with the participants to guide them through exercises and elicit personally relevant content. Weekly relaxation and stress management topics for the SmartManage-based CBSM condition for the HIV and cancer condition are listed in Table 2. Specific intervention techniques designed to address HIV-, cancer-, and SMM-specific challenges are listed in Textbox 4. Sessions will be audio recorded for later analysis and fidelity rating. Group members will be addressed by their first name only to limit the potential disclosure of personal information. Therapists will discuss with the participants the standard rules and expectations of group treatment, including the importance of maintaining group confidentiality. They will also remind participants of the limits of confidentiality as described in the consent form, acknowledging the possibility that another group member could potentially disclose one's personal information.

Textbox 4. SmartManage cognitive behavioral stress and self-management for HIV and cancer intervention techniques to address HIV and cancer and sexual and gender minority community–specific challenges. HRQoL: health-related quality of life.

Topic

Minority Stress Model

- Introduce model—Acknowledge that minority stress has a measurable negative effect on mental health and HRQoL
- Explore participants' experiences with stigma and bias
- Validate that the onus for minority stress lies with society and bias, not with the minority group

HIV and cancer comanagement

- Explore and problem solve individual and common challenges related to managing cancer and HIV (eg, medication adherence, managing multiple provider appointments, and coordination and communication with providers)
- Screening for secondary cancers, recurrences, and disease progression

Sex and intimacy

- Strategies to prevent HIV transmission with serodiscordant partners
- Talking to providers about sexual health concerns, including anal sex
- Problem solving and practical skills to manage sexual difficulties related to illness (HIV or cancer), treatment side effects, and aging

Interpersonal

- Acknowledge that internalized homonegativity is often related to less assertive behavior
- Assertiveness skill building

HP Educational Control

We adapted a manualized, didactic HP workbook to be delivered to the control participants using the SmartManage web-based format. The content for each of the 10 sessions was converted to a slide format, which we then converted into videos with voiceover narration. The session duration ranged from 10 to 20 minutes, and topics included descriptions of age-related and other diseases (eg, diabetes and cardiovascular disease), complications that may arise in the course of each condition, information on various disease treatments and side effects, cancer and HIV information, and other HP content. The control material does not include any content or instruction related to stress and self-management techniques or other psychotherapeutic content. Participants will be invited to log onto the web-based platform to view 1 new video every week over the course of 10 weeks. Built-in diagnostic software will track when participants have finished viewing each video. The HP topics are listed in Textbox 3.

Data Collection

Sociodemographic and Medical History or Status

Participants in both phases will report sociodemographic data including age, race, ethnicity, sex assigned at birth, gender identity, education, income, and household makeup. Participants in both phases will also self-report information about their cancer, HIV, and relevant health behaviors. This includes diagnosis dates, past and current treatments, and medication or treatment adherence. Cancer-specific questions include the type of cancer and whether their cancer has metastasized. HIV-specific questions relate to the frequency of contact with HIV care providers, current viral load, and CD4 count. We will

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also ask about any barriers they face regarding access to HIV care, such as difficulty obtaining medications or feeling stigmatized by health care providers. Participants in phase 2 will be reassessed after the intervention for information that may change (eg, HIV viral load and cancer prognosis). Table 1 lists all study measures collected.

Primary Outcomes: Feasibility and Acceptability

As the main purpose of the SmartManage study is intervention development, quantitative primary outcomes are focused on participant engagement in phase 2 (pilot testing). For the adapted SmartManage CBSM for HIV and cancer intervention to be considered feasible, 70% of the participants who begin the intervention will attend at least 70% of all intervention sessions, and 85% of the enrolled participants will be retained throughout the study. These proportions are based on previously successful CBSM trials in other populations [21-23]. We will also examine cost indicators of implementation feasibility by documenting personnel time, space requirements (eg, for intervention delivery and study administration), and supply costs, including the maintenance and management of the SmartManage website.

We will evaluate intervention acceptability in two ways: (1) the proportion of eligible SMM in phase 2 who agree to participate versus decline (≥30%) and (2) via 2 exit surveys administered after participants have completed the SmartManage intervention. One such survey is the commonly used Usefulness, Satisfaction, and Ease of Use (USE) questionnaire [24], which assesses participants' impressions of the intervention's usefulness, ease of use, ease of learning, as well as overall satisfaction with the intervention. We also created an intervention-specific measure to evaluate participants' views on SmartManage elements that are not assessed in the USE questionnaire. These include perceptions of relevance to health needs, how helpful the program is for SMM with HIV and cancer, and the willingness to recommend the program to similar peers. Both intervention acceptability measures ask participants to rate items on a 7-point Likert scale ranging from *strongly agree* to *strongly disagree*. Both measures also include qualitative questions with open text response fields allowing participants to share thoughts on what they found most and least helpful, what important areas were not addressed sufficiently, and recommendations to improve the intervention.

Secondary Outcomes: Intended Effects of Intervention, Other Psychosocial Factors, and Nature of Illness

Intended Effects of Intervention

This study is not intended to test the efficacy of SmartManage; however, we will examine the intended treatment effects of the intervention. We expect that relative to the educational control condition, SMM who participate in SmartManage-based CBSM for HIV and cancer will show improvements in health behaviors, HRQoL or disease-related distress, stress, and coping. Health behaviors include adherence to HIV medication regimen, as measured by the AIDS Clinical Trials Group HIV medication adherence measure [25], and frequency and duration of exercise, as measured by the International Physical Activity Questionnaire-Short Form [26]. HRQoL is captured by two measures: Functional Assessment of Cancer Therapy Scale–General [27] and Medical Outcomes Study HIV Survey [28]. Both measures assess illness-related physical, social, and functional well-being as influenced by cancer or HIV, respectively. We will also capture the impact of sexual dysfunction by using the Patient-Reported Outcomes Measurement Information System—Bother Regarding Sexual Function scale [29]. The general stress level over the past 30 days will be measured using the Perceived Stress Scale-14 [30]. Finally, aspects of distress and coping will be assessed using two measures: the Impact of Event Scale [31], which asks participants how much they have been bothered over the past week by memories and intrusive thoughts about past stressful events, and the Coping Self-Efficacy Scale [32], which measures the confidence that one can use a wide range of coping strategies when faced with adversity. Table 1 lists the study measures.

Other Psychosocial Factors

Although the SmartManage CBSM for HIV and cancer intervention is designed to address common targets of psychotherapy (stress management and coping skills), we will also conduct exploratory analyses to examine more stable and dispositional factors that may moderate intervention effects. Among these are the frequency and emotional impact of chronic social stigma and bias, which will be measured using the Everyday Discrimination—Sexual Orientation instrument [33], modified to include sexual orientation-specific questions. We will also look at the acculturation level using the Bidimensional Acculturation Scale [34], which assesses *Americanism* and *Hispanicism* independently to categorize individuals according to the quadrant model of acculturation by Berry [35]. This is particularly relevant in Miami-Dade County, where >53% of residents are foreign born and nearly 70% identify as Hispanic [36].

Nature of Illness

The target population for SmartManage for HIV and cancer is likely to be more heterogeneous than that of prior CBSM studies, given the widely varying impact of different cancer types. Therefore, we will examine the variability in intervention responses based on specific types of cancer (eg, prostate vs lung). We will also explore the practical and psychological impact of COVID-19 using 1 measure specifically for patients with cancer and 1 to assess how COVID-19 has affected the sexual health and behavior of SMM, both developed by Penedo et al (Penedo FJ, unpublished data, May 2020).

Data Analytic Plan

Aim 1: Conduct Usability Testing and Finalize SmartManage for HIV and Cancer Intervention

For phase 1, we will summarize the participants' demographic, psychosocial, and clinical information by using descriptive statistics. Audio-recorded participant responses will be transcribed, coded, and qualitatively analyzed using NVivo Pro (version 12.6; QSR International) software. Two independent raters will develop a codebook following a conventional content analysis approach in which codes emerge solely from the data. Throughout coding development, raters will use the constant comparative method to identify themes. Coding will follow an iterative process in which each preceding group will refine

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themes to accommodate new information until saturation is reached and raters reach consensus. The larger study team will review a summary of the findings to inform and refine the development of the program modules, program content, study documents (including recruitment materials), and study procedures.

Aim 2: Randomized Controlled Pilot Testing of Intervention (Feasibility, Acceptability, and Intended Effects)

For phase 2, descriptive statistics will be used to characterize the sample and inspect data quality. We will examine the amount, pattern, and randomness of missing data to determine appropriate statistical methods to handle missingness. Type 1 error will be set to 5% (α=.05) for calculating CIs and performing hypothesis testing. The α values will be adjusted for multiple comparisons, as needed.

We will examine feasibility via engagement and retention rates as well as cost indicators. Intervention acceptability will be evaluated using continuous data from the exit survey (USE questionnaire). These analyses will be primarily descriptive; however, we will use general linear modeling (eg, independent samples 2-tailed *t* test and ANOVA) to determine whether there are significant differences in feasibility and acceptability by sociodemographic, medical, and psychosocial variables. We will examine the distributions to determine whether alterations to the data analytic plan are needed, for example, using nonparametric methods. If >10% of the data are missing completely at random, we will use multiple imputation techniques.

To evaluate the intended effects of the intervention, we will analyze continuous scores on measures of stress, disease-related distress, and HRQoL. We will use paired samples *t* tests to examine whether these variables improve significantly within groups from pre- to postintervention measurement. We will use repeated measures ANOVA to determine whether these potential changes remain significant, accounting for the sociodemographic, medical, and psychosocial covariates described earlier. We will also use independent samples *t* tests to analyze potential differences in outcomes between the study groups (SmartManage intervention vs educational control). These will be analyzed using repeated measures ANOVA to explore whether effects remain when accounting for sociodemographic, medical, and psychosocial covariates.

Results

Participant qualitative enrollment began in February 2022, and phase 2 enrollment began in April 2022. All intervention and assessment procedures are expected to be completed no later than November 2022. Both the qualitative and quantitative outcomes are expected to be submitted for publication by February 2023.

Discussion

In this study, we seek to build on prior research by incorporating population-specific content and emphasizing targeted areas of treatment to address the disproportionate health burden on SMM living with HIV and cancer. We drew upon relevant theoretical models (minority stress and syndemic theory) that have shown their utility in guiding the development of efficacious interventions for marginalized populations [37,38]. Although the appropriate application of theory and thorough evaluation of prior research are necessary steps in developing an intervention tailored for the sexual and gender minority community, we also recognize the vital contribution of stakeholder feedback and involvement in this process [39]. Therefore, the primary purpose of this study was to systematically evaluate participant feedback and provide insights to guide further refinement of the treatment model. We also anticipate that those who receive the experimental intervention will show measurable improvement in stress burden, coping self-efficacy, and overall HRQoL.

Despite improved HIV treatment that allows those living with the virus to live longer and healthier lives relative to those infected earlier in the HIV epidemic, the large and growing cohort of aging SMM living with HIV continues to face stigma and bias related to HIV status and sexual minority status, as well as unanticipated health problems, including higher rates of cancer. Together, these factors contribute to poorer HRQoL, diminished rates of cancer survivorship, and higher rates of mental health concerns such as depression and anxiety [40,41]. There are few intervention programs intended to address the specific needs of SMM living with HIV and cancer despite the widely acknowledged critical role of mental health treatment in ending the HIV epidemic [42]. We seek to further the process that will eventually address this need by using qualitative and quantitative (mixed) methods to develop an intervention program to address the disproportionate symptom burden and diminished HRQoL among SMM living with HIV and cancer.

The rationale for creating this adapted intervention for a relatively small subset of the total population is similar to the reasons behind specialized interventions such as panic control treatment [43] or any culturally adapted treatment, that is, unmet needs in an identifiable community, and significant negative consequences that could be ameliorated with appropriate care. The need is even more pronounced in our target population (SMM with HIV and cancer) because of the syndemic conditions that both concentrate disease risk and maintain conditions detrimental to the overall health trajectory over time within minority populations [44-48]. This study is not designed to determine whether the disproportionate health burden present in our target population is attributable to syndemic factors; however, we do know that the effects of societal bias and minority stress are ubiquitous within this group. Without intervention, the ongoing corrosive impact of these and other syndemic factors create a high likelihood of suboptimal health trajectories in this population. Therefore, our approach is a person-centered method of providing the necessary tools and skills via an intervention that integrates evidence-based techniques to improve self-management, self-efficacy, communication skills, stress awareness, and management to improve physiological and psychosocial adaptation on the one hand and HRQoL and health outcomes on the other hand. It is a broader goal that social and structural factors that lead to

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syndemic conditions can be addressed such that negative health outcomes can be prevented. Therefore, our immediate goal is to facilitate improved coping and offer practical strategies that can improve health outcomes in this critically challenged subgroup of cancer survivors.

Although this is a pilot study intended as an early developmental stage for the treatment model, there are some inherent limitations. One limitation is the inclusion of participants who have many types of cancer because of the relative infrequency of study participants with both HIV and cancer. The progression of illness, nature of treatment, and common sequelae of different forms of cancer can vary widely. We also hope to further tailor the interventions to address the specific needs of the participants. Some participants will likely have unique needs that cannot be fully addressed in a time-limited group session format. We anticipate that these data gathered in this study will allow us to refine the intervention to address the most pressing needs and guide the creation of a comprehensive resource where participants can get help with problems not addressed in the session. Wider implementation of this model would allow further refinement and could facilitate more targeted cancer groups (eg, prostate cancer and blood cancer), given that the web-based format allows participants to join from any location.

Similarly, we recognize that limiting enrollment to those with nonmetastatic cancer who have completed primary cancer treatment excludes a significant number of potential participants. Active treatment and metastasis have a high potential to interfere with group attendance, which is problematic given the small sample size of this study. In future iterations, we will seek to broaden the inclusion criteria and tailor the content to address the acute needs of such individuals.

We also recognize that most people in our current catchment area (South Florida) are Hispanic, and this study is conducted only in English. This may limit our ability to generalize feasibility and acceptability findings, given a large number of Spanish monolingual speakers. To address this limitation, our collaborators are culturally adapting the SmartManage intervention for Hispanic participants to be tested concurrently with this study. This culturally adapted version will be piloted in English and then translated and tested in Spanish.

In addition, we believe that a web-based intervention is a significant strength; however, it is also a potential limitation. The intent of this format is to make group sessions accessible to those for whom in-person meetings are not feasible owing to physical limitations, lack of transportation, and location of residency. However, the requirement for a video-equipped device and stable internet is prohibitive for those who are most vulnerable, including those who are unstably housed. A potential solution that we used for other studies during the COVID-19 pandemic is to provide computer-equipped therapy rooms where participants can join the web-based group in a secure, private setting. This requires accessible facilities and reintroduces the travel burden, both of which may require additional creative solutions.

We expect that this study will inform the development of an intervention to specifically address the needs of an underserved and highly burdened population. This study will provide much-needed information regarding the utility and acceptability of a web-based group format, which will inform future iterations, bringing treatment options to those without access. We also expect that the information gathered will contribute to the literature by providing both qualitative and quantitative data describing the experiences and needs of a marginalized population living with multiple chronic illnesses. Although this is a relatively small sample, the lessons learned may be generalizable to other marginalized communities facing multiple challenges and may inform large-scale randomized controlled trials with long-term follow-up to assess the clinical utility of these programs.

Acknowledgments

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Data Availability

As this is a pilot intervention development study, outcome data will not be publicly available but will be available from the corresponding author (FJP) on reasonable request.

Conflicts of Interest

FJP is a paid consultant for Blue Note Therapeutics, which is a digitizing component of the cognitive behavioral stress and self-management intervention for cancer survivors.

References

1. Silverberg MJ, Lau B, Achenbach CJ, Jing Y, Althoff KN, D'Souza G, et al. Cumulative incidence of cancer among persons with HIV in North America. Ann Intern Med 2015 Oct 06;163(7):507-518. [doi: 10.7326/m14-2768]

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2. Brooks JT, Buchacz K, Gebo KA, Mermin J. HIV infection and older Americans: the public health perspective. Am J Public Health 2012 Aug;102(8):1516-1526. [doi: 10.2105/ajph.2012.300844]
3. Simpson TL, Balsam KF, Cochran BN, Lehavot K, Gold SD. Veterans administration health care utilization among sexual minority veterans. Psychol Serv 2013 May;10(2):223-232. [doi: 10.1037/a0031281] [Medline: 23730965]
4. Tracy JK, Lydecker AD, Ireland L. Barriers to cervical cancer screening among lesbians. J Womens Health (Larchmt) 2010 Feb;19(2):229-237 [FREE Full text] [doi: 10.1089/jwh.2009.1393] [Medline: 20095905]
5. Lisy K, Peters MD, Schofield P, Jefford M. Experiences and unmet needs of lesbian, gay, and bisexual people with cancer care: a systematic review and meta-synthesis. Psychooncology 2018 Jun 15;27(6):1480-1489. [doi: 10.1002/pon.4674] [Medline: 29462496]
6. Boehmer U, Cooley TP, Clark MA. Cancer and men who have sex with men: a systematic review. Lancet Oncol 2012 Dec;13(12):e545-e553. [doi: 10.1016/s1470-2045(12)70347-9]
7. Haviland K, Swette S, Kelechi T, Mueller M. Barriers and facilitators to cancer screening among LGBTQ individuals with cancer. Oncol Nurse Forum 2020 Jan 1;47(1):44-55. [doi: 10.1188/20.onf.44-55]
8. Hart TL, Coon DW, Kowalkowski MA, Zhang K, Hersom JI, Goltz HH, et al. Changes in sexual roles and quality of life for gay men after prostate cancer: challenges for sexual health providers. J Sex Med 2014 Sep;11(9):2308-2317. [doi: 10.1111/jsm.12598] [Medline: 24888965]
9. Jabson JM, Kamen CS. Sexual minority cancer survivors' satisfaction with care. J Psychosoc Oncol 2016 Nov 17;34(1-2):28-38 [FREE Full text] [doi: 10.1080/07347332.2015.1118717] [Medline: 26577277]
10. Penedo FJ, Traeger L, Dahn J, Molton I, Gonzalez JS, Schneiderman N, et al. Cognitive behavioral stress management intervention improves quality of life in Spanish monolingual Hispanic men treated for localized prostate cancer: results of a randomized controlled trial. Int J Behav Med 2007 Sep;14(3):164-172. [doi: 10.1007/bf03000188]
11. Wang AW, Bouchard LC, Gudenkauf LM, Jutagir DR, Fisher HM, Jacobs JM, et al. Differential psychological effects of cognitive-behavioral stress management among breast cancer patients with high and low initial cancer-specific distress. J Psychosom Res 2018 Oct;113:52-57 [FREE Full text] [doi: 10.1016/j.jpsychores.2018.07.011] [Medline: 30190048]
12. Antoni MH, Carrico AW, Durán RE, Spitzer S, Penedo F, Ironson G, et al. Randomized clinical trial of cognitive behavioral stress management on human immunodeficiency virus viral load in gay men treated with highly active antiretroviral therapy. Psychosom Med 2006;68(1):143-151. [doi: 10.1097/01.psy.0000195749.60049.63] [Medline: 16449425]
13. Berger S, Schad T, von Wyl V, Ehlert U, Zellweger C, Furrer H, et al. Effects of cognitive behavioral stress management on HIV-1 RNA, CD4 cell counts and psychosocial parameters of HIV-infected persons. AIDS 2008 Mar 30;22(6):767-775. [doi: 10.1097/QAD.0b013e3282f511dc] [Medline: 18356607]
14. Qiao S, Zhou G, Li X. Disclosure of same-sex behaviors to health-care providers and uptake of hiv testing for men who have sex with men: a systematic review. Am J Mens Health 2018 Sep 27;12(5):1197-1214 [FREE Full text] [doi: 10.1177/1557988318784149] [Medline: 29947563]
15. Sabin JA, Riskind RG, Nosek BA. Health care providers' implicit and explicit attitudes toward lesbian women and gay men. Am J Public Health 2015 Sep;105(9):1831-1841. [doi: 10.2105/ajph.2015.302631]
16. Fallin-Bennett K. Implicit bias against sexual minorities in medicine: cycles of professional influence and the role of the hidden curriculum. Acad Med 2015 May;90(5):549-552. [doi: 10.1097/ACM.0000000000000662] [Medline: 25674911]
17. Penedo F. Cognitive-Behavioral Stress Management for Prostate Cancer Recovery: Workbook. Oxfordshire, England, UK: Oxford University Press; 2008.
18. Antoni M, Schneiderman N, Esterling B, Ironson G. Stress management and adjustment to HIV-1 infection. Homeostasis Health Disease 1994;35(3):149-160.
19. Meyer IH. Prejudice, social stress, and mental health in lesbian, gay, and bisexual populations: conceptual issues and research evidence. Psychol Bull 2003 Sep;129(5):674-697 [FREE Full text] [doi: 10.1037/0033-2909.129.5.674] [Medline: 12956539]
20. Sun S, Hoyt WT, Pachankis JE. Sexual risk behaviors in the internet age: the case of Chinese men who have sex with men. AIDS Care 2020 Mar 18;32(3):302-309 [FREE Full text] [doi: 10.1080/09540121.2019.1668525] [Medline: 31533450]
21. Campbell LC, Keefe FJ, Scipio C, McKee DC, Edwards CL, Herman SH, et al. Facilitating research participation and improving quality of life for African American prostate cancer survivors and their intimate partners. A pilot study of telephone-based coping skills training. Cancer 2007 Jan 15;109(2 Suppl):414-424 [FREE Full text] [doi: 10.1002/cncr.22355] [Medline: 17173280]
22. Kissane DW, Grabsch B, Clarke DM, Smith GC, Love AW, Bloch S, et al. Supportive-expressive group therapy for women with metastatic breast cancer: survival and psychosocial outcome from a randomized controlled trial. Psychooncology 2007 Apr;16(4):277-286. [doi: 10.1002/pon.1185] [Medline: 17385190]
23. Yanez B, McGinty HL, Mohr DC, Begale MJ, Dahn JR, Flury SC, et al. Feasibility, acceptability, and preliminary efficacy of a technology-assisted psychosocial intervention for racially diverse men with advanced prostate cancer. Cancer 2015 Dec 15;121(24):4407-4415. [doi: 10.1002/cncr.29658] [Medline: 26348661]
24. Lund A. Measuring usability with the USE questionnaire. Usability Interface 2001;8(2):3-6 [FREE Full text]
25. Chesney MA, Ickovics JR, Chambers DB, Gifford AL, Neidig J, Zwickl B, et al. AIDS Care 2000 Jun;12(3):255-266. [doi: 10.1080/09540120050042891] [Medline: 10928201]

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26. Craig CL, Marshall AL, Sjöström M, Bauman AE, Booth ML, Ainsworth BE, et al. International physical activity questionnaire: 12-country reliability and validity. Med Sci Sports Exerc 2003 Aug;35(8):1381-1395. [doi: 10.1249/01.MSS.0000078924.61453.FB] [Medline: 12900694]
27. Cella DF, Tulsky DS, Gray G, Sarafian B, Linn E, Bonomi A, et al. The Functional Assessment of Cancer Therapy scale: development and validation of the general measure. J Clin Oncol 1993 Mar;11(3):570-579. [doi: 10.1200/JCO.1993.11.3.570] [Medline: 8445433]
28. Wu A, Revicki D, Jacobson D, Malitz F. Evidence for reliability, validity and usefulness of the Medical Outcomes Study HIV Health Survey (MOS-HIV). Qual Life Res 1997;6:481-493. [doi: 10.1023/A:1018451930750]
29. Weinfurt KP, Lin L, Bruner DW, Cyranowski JM, Dombeck CB, Hahn EA, et al. Development and initial validation of the PROMIS(®) sexual function and satisfaction measures version 2.0. J Sex Med 2015 Sep;12(9):1961-1974. [doi: 10.1111/jsm.12966] [Medline: 26346418]
30. Cohen S, Kamarck T, Mermelstein R. A global measure of perceived stress. J Health Social Behav 1983 Dec;24(4):385. [doi: 10.2307/2136404]
31. Weiss DS. The impact of event scale: revised. In: Wilson JP, Tang CS, editors. Cross-Cultural Assessment of Psychological Trauma and PTSD. Boston, MA: Springer; 2007.
32. Chesney M, Neilands TB, Chambers DB, Taylor JM, Folkman S. A validity and reliability study of the coping self-efficacy scale. Br J Health Psychol 2006 Sep;11(Pt 3):421-437 [FREE Full text] [doi: 10.1348/135910705X53155] [Medline: 16870053]
33. Clark R, Coleman AP, Novak JD. Brief report: initial psychometric properties of the everyday discrimination scale in black adolescents. J Adolesc 2004 Jun;27(3):363-368. [doi: 10.1016/j.adolescence.2003.09.004] [Medline: 15159094]
34. Marin G, Gamba RJ. A new measurement of acculturation for Hispanics: the Bidimensional acculturation scale for Hispanics (BAS). Hispanic J Behav Sci 2016 Jul 25;18(3):297-316. [doi: 10.1177/07399863960183002]
35. Berry JW. Immigration, acculturation, and adaptation. Applied Psychol 1997 Jan;46(1):5-34. [doi: 10.1111/j.1464-0597.1997.tb01087.x]
36. QuickFacts Miami-Dade County, Florida. United States Census Bureau. URL: https://www.census.gov/quickfacts/fact/table/miamidadecountyflorida/POP060210 [accessed 2021-08-25]
37. Pachankis JE, Harkness A, Maciejewski KR, Behari K, Clark KA, McConocha E, et al. LGBQ-affirmative cognitive-behavioral therapy for young gay and bisexual men's mental and sexual health: a three-arm randomized controlled trial. J Consult Clin Psychol 2022 Apr 28 (forthcoming). [doi: 10.1037/ccp0000724] [Medline: 35482652]
38. O'Cleirigh C, Safren SA, Taylor SW, Goshe BM, Bedoya CA, Marquez SM, et al. Cognitive Behavioral Therapy for Trauma and Self-Care (CBT-TSC) in men who have sex with men with a history of childhood sexual abuse: a randomized controlled trial. AIDS Behav 2019 Sep;23(9):2421-2431 [FREE Full text] [doi: 10.1007/s10461-019-02482-z] [Medline: 30993478]
39. Pachankis JE, Soulliard ZA, Morris F, Seager van Dyk I. A model for adapting evidence-based interventions to be LGBQ-affirmative: putting minority stress principles and case conceptualization into clinical research and practice. Cognit Behav Pract 2022 Jan (forthcoming). [doi: 10.1016/j.cbpra.2021.11.005]
40. Bränström R, van der Star A, Pachankis JE. Untethered lives: barriers to societal integration as predictors of the sexual orientation disparity in suicidality. Soc Psychiatry Psychiatr Epidemiol 2019 Jul 12;55(1):89-99. [doi: 10.1007/s00127-019-01742-6]
41. Rice CE, Vasilenko SA, Fish JN, Lanza ST. Sexual minority health disparities: an examination of age-related trends across adulthood in a national cross-sectional sample. Ann Epidemiol 2019 Mar;31:20-25 [FREE Full text] [doi: 10.1016/j.annepidem.2019.01.001] [Medline: 30792064]
42. Remien RH, Stirratt MJ, Nguyen N, Robbins RN, Pala AN, Mellins CA. Mental health and HIV/AIDS: the need for an integrated response. AIDS 2019 Jul 15;33(9):1411-1420 [FREE Full text] [doi: 10.1097/QAD.0000000000002227] [Medline: 30950883]
43. Barlow DH, Craske MG, Cerny JA, Klosko JS. Behavioral treatment of panic disorder. Behav Ther 1989;20(2):261-282. [doi: 10.1016/s0005-7894(89)80073-5]
44. Scheer JR, Clark KA, Maiolatesi AJ, Pachankis JE. Syndemic profiles and sexual minority men's HIV-risk behavior: a latent class analysis. Arch Sex Behav 2021 Oct 22;50(7):2825-2841 [FREE Full text] [doi: 10.1007/s10508-020-01850-4] [Medline: 33483851]
45. Singer M. Aids and the health crisis of the U.S. urban poor; the perspective of critical medical anthropology. Social Sci Med 1994 Oct;39(7):931-948. [doi: 10.1016/0277-9536(94)90205-4]
46. Singer M, Bulled N, Ostrach B, Mendenhall E. Syndemics and the biosocial conception of health. Lancet 2017 Mar;389(10072):941-950. [doi: 10.1016/s0140-6736(17)30003-x]
47. Stall R, Friedman M, Catania J. Interacting epidemics and gay men's health: a theory of syndemic production among urban gay men. In: Wolitski RJ, Stall R, Valdiserri RO, editors. Unequal Opportunity: Health Disparities Affecting Gay and Bisexual Men in the United States. Oxfordshire, England, UK: Oxford University Press; 2007.
48. Stall R, Mills TC, Williamson J, Hart T, Greenwood G, Paul J, et al. Association of co-occurring psychosocial health problems and increased vulnerability to HIV/AIDS among urban men who have sex with men. Am J Public Health 2003 Jun;93(6):939-942. [doi: 10.2105/ajph.93.6.939] [Medline: 12773359]

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Abbreviations

CBSM: cognitive behavioral stress and self-management
HP: health promotion
HRQoL: health-related quality of life
REDCap: Research Electronic Data Capture
SMM: sexual minority men
USE: Usefulness, Satisfaction, and Ease of Use

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Protocol

Drill-Hole Bone Defects in Animal Models of Bone Healing: Protocol for a Systematic Review

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Abstract

Background: Bone fractures are common conditions of the musculoskeletal system. Several animal models of bone fractures have been established to help elucidate the complex process of bone healing. In the last decades, drill-hole bone defects have emerged as a method to study bone healing. Animal models of drill-hole defects are easy to standardize and do not require external fixation of the bone. However, current studies of drill-hole bone defects lack detailed descriptions of techniques and interstudy standardization.

Objective: This systematic review aims to present a detailed description of the different methods used to induce drill-hole bone defects in long bones of laboratory animals and to provide a comprehensive overview of their methodology and potential for investigation of bone healing.

Methods: A systematic search of PubMed and Embase will be performed of abstracts containing variations of the following four keywords: “long bone,” “drill-hole,” “regeneration,” and “animal model.” Abstract screening and full-text screening will be performed independently by 2 reviewers, and data will be extracted to a predesigned extraction protocol. The primary outcome of the included studies is the technique used to create the drill-hole bone defect, and secondary outcomes are any measurements or analyses of bone defect and regeneration. A narrative synthesis will be used to present the primary outcome, while information on secondary outcomes will be displayed graphically. The study protocol follows the PRISMA-P (Preferred Reporting Items for Systematic Review and Meta-analysis Protocols) guidelines.

Results: Abstract and full-text screening is ongoing and is expected to be completed by October 2022. Data extraction will commence immediately after, and the manuscript is expected to be completed by December 2023. The systematic review will follow the PRISMA statement.

Conclusions: The strength of this systematic review is that it provides a comprehensive methodological overview of the different drill-hole methods and their advantages and disadvantages. This will assist researchers in choosing which model to use when studying different aspects of bone healing.

Trial Registration: International Prospective Register of Systematic Reviews CRD42020213076; https://tinyurl.com/bp56wdwe

International Registered Report Identifier (IRRID): PRR1-10.2196/34887

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KEYWORDS

systematic review; animal models; preclinical; bone defect; drill-hole; fracture model; bone; bone healing; protocol; bone fracture; animal model; healing; bone healing; laboratory; laboratory animal

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Introduction

Bone fractures are a common condition of the musculoskeletal system. A recent study reported an incidence rate of 3.6 fractures per 100 person years and a lifetime fracture prevalence of 38.2% for any fracture [1]. Most fractures heal easily if the fracture is sufficiently stabilized [2]. However, bone regeneration is a complex process involving multiple different cells and tissues [3-5]. Because of its complexity, sometimes, the healing process fails, and this may lead to fractures healing slowly or not at all [6]. Delayed fracture healing is more often seen in patients with comorbidities such as osteoporosis, diabetes, or old age [7-9]. In fact, as many as 5%-10% of the fractures devolve into delayed bone healing [10,11]—either as a significantly increased healing time or as a complete lack of healing resulting in a nonunion fracture. Patients with nonunion fractures experience lower quality of life than those with diabetes mellitus, stroke, or AIDS [12].

Owing to the complexity of fracture healing, studies performed in animals are often used to investigate the mechanisms of bone healing and test potential new treatment regimens [13,14]. There are multiple advantages of studying diseases in animal models [15]. Through a controlled environment and a homogenous population, disease pathology and temporal development can be studied more thoroughly than is possible in humans [16].

The bone structure comprises two types of bone tissue: cortical bone constitutes the compact shell surrounding the bone, while trabecular bone forms a porous network of interconnected bone found in the medullary space of metaphyseal and epiphyseal bone [17]. Healing of cortical and trabecular bones differs; cortical bone heals through both endochondral and intramembranous ossification [4], while trabecular bone heals through direct membranous bone formation [18].

Numerous methods of inducing bone fractures have been established in animal models [19], from resection of a bone segment [20,21] to fractures obtained by 3-point bending [22]. Most of these studies investigate healing at the diaphysis of a long bone [18,23]. Recently, drill-hole bone defects have been used increasingly as a model of bone injury [24-27]. While this method is less directly translational to clinical fractures, they nevertheless have several advantages in basic research: they are better suited for investigation of trabecular bone healing in, for example, the metaphysis, they are easier to standardize and require no external fixation of the bone [25]. In most fracture models, it is difficult to achieve uniform fracture fixation, and variations in fracture fixation are bound to occur. Fracture fixation is a crucial factor of optimal bone healing [5], and elimination of this variable is a major advantage of the drill-hole methods.

Currently, there is little consistency in the methodology of the drill-hole bone defects. Therefore, the purpose of this systematic review is to present a narrative synthesis of the different animal models of long bone drill-hole bone defects and their potential use in preclinical and translational research.

Methods

Overview

This review is registered with the PROSPERO (International Prospective Register of Systematic Reviews; CRD42020213076) and has been written in accordance with the current guidelines of the PRISMA-P (Preferred Reporting Items for Systematic review and Meta-analysis Protocols) guidelines [28].

Eligibility Criteria

Overview

This systematic review aims to provide a detailed description of the different methods used to induce drill-hole bone defects in long bones of laboratory animals and to provide a comprehensive overview of their methodology and potential for investigation of bone healing. This research question has been formulated following the Population, Intervention, Comparison, and Outcome (PICO) framework [29].

Population

This review will include all in vivo animal studies using drill-hole bone defects.

Intervention

All types of drill-hole bone defects generated in long bones will be included.

Comparator or Control Group

Studies will be included if they comprise a control group with a drill-hole defect that receives no treatment to influence healing of the defect, or if they encompass an unoperated or a sham-operated control group.

Outcome

The primary outcome is the surgical procedure used to generate the drill-hole injury and the anatomical location of the defect. Secondary outcomes are healing time and methods used to analyze the healing of the bone defect.

Information Sources and Search Strategy

A systematic literature search will be performed in the PubMed and Embase databases without date restriction. The search strategy consists of 4 blocks:

- First block: specifies that only long bones will be investigated.
- Second block: specifies that only drill-hole defects are included.
- Third block: specifies that a secondary outcome of bone regeneration must be investigated.
- Fourth block: specifies that all animal species can be included using a search filter for PubMed and Embase [30].

The search strategy (Textbox 1) aims to include all original animal studies of drill-hole defects as a disease model of bone fracture. The search string has been developed in cooperation with an expert information specialist of systematic reviews. Furthermore, free-hand searches in Google Scholar will be performed, and any relevant articles will be included.

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Textbox 1. Search strategy for PubMed and Embase.

First block:

- PubMed: ("long bone"[Tiab] OR "long bones"[Tiab] OR tibia*[Tiab] OR "Tibia"[Mesh] OR fibul*[Tiab] OR "Fibula"[Mesh] OR femur*[Tiab] OR femor*[Tiab] OR "Femur"[Mesh] OR metatar*[Tiab] OR "Metatarsal Bones"[Mesh] OR phalanx*[Tiab] OR "Finger Phalanges"[Mesh] OR "Toe Phalanges"[Mesh] OR "Humerus"[Mesh] OR humeru*[Tiab] OR humera*[Tiab] OR radius[Tiab] OR "Radius"[Mesh] OR "Radius"[Mesh] OR ulna*[Tiab] OR "Ulna"[Mesh] OR metacar*[Tiab] OR "Metacarpal Bones"[Mesh] OR diaphysis[Tiab] OR diaphyses[Tiab] OR "Diaphyses"[Mesh] OR epiphysis[Tiab] OR epiphyses[Tiab] OR "Epiphyses"[Mesh])
- Embase: ("long bone":ti,ab,kw OR "long bones":ti,ab,kw OR tibia*:ti,ab,kw OR 'tibia'/exp OR fibul*:ti,ab,kw OR 'fibula'/exp OR femur*:ti,ab,kw OR femor*:ti,ab,kw OR 'femur'/exp OR metatar*:ti,ab,kw OR 'metatarsal bone'/exp OR phalanx*:ti,ab,kw OR 'phalanx'/exp OR humeru*:ti,ab,kw OR humera*:ti,ab,kw OR 'humerus'/exp OR radius:ti,ab,kw OR 'radius'/exp OR ulna*:ti,ab,kw OR 'ulna'/exp OR metacar*:ti,ab,kw OR 'metacarpal bone'/exp OR diaphysis:ti,ab,kw OR diaphyses:ti,ab,kw OR 'diaphysis'/exp OR epiphysis:ti,ab,kw OR epiphyses:ti,ab,kw OR 'epiphysis'/exp)

AND

Second block:

- PubMed: (drill*[Tiab] OR burr*[Tiab] OR bur[Tiab] OR circular[Tiab])
- Embase: (drill*:ti,ab,kw OR burr*:ti,ab,kw OR bur:ti,ab,kw OR circular:ti,ab,kw)

AND

Third block:

- PubMed: (Heal*[Tiab] OR regener*[Tiab] OR growth[Tiab] OR repa*[Tiab] OR formati*[Tiab] OR osteogenesis[MeSH] OR "bone regeneration"[MeSH])
- Embase: (Heal*:ti,ab,kw OR regener*:ti,ab,kw OR growth:ti,ab,kw OR repa*:ti,ab,kw OR formati*:ti,ab,kw OR 'bone development'/exp OR 'bone regeneration'/exp)

AND

Fourth block:

- PubMed: Search filter by van der Mierden et al [30]
- Embase: Search filter by van der Mierden et al [30]

Data Management and Selection Process

Overview

All studies found through the search strategy will be uploaded to the web-based screening and data extraction tool *Covidence*, and titles and abstracts will be screened by 2 independent reviewers. Prior to abstract screening, the 2 reviewers will practice screening of 50 abstracts to ensure a uniform screening. Then, the included studies will undergo full-text screening for eligibility by the same reviewers. Any disagreements over eligibility will first be discussed internally by the 2 reviewers, and if no agreement can be reached, the eligibility will be decided by an independent arbitrator. Following were the screening inclusion and exclusion criteria.

Animals or Population

- Inclusion criteria: Animal studies where a drill-hole defect is created in a long bone (all species, sexes, and ages).
- Exclusion criteria: Nonanimal studies, human studies, and in vitro or ex vivo studies.

Intervention or Exposure

- Inclusion criteria: Studies creating a drill-hole defect in any long bone. All types of drills, burrs, or other instruments creating circular bone defects will be included.
- Exclusion criteria: Bone defects created without usage of a drill, burr, or similar instruments or any bone defect that needs fixation. As this is a review of drill-hole models used as a bone healing model and not as a model of osseointegration, all studies with permanent implants placed in a drill hole (titanium, screws, etc) will be excluded.

Comparator or Control

- Inclusion criteria: Studies including a control group. Either a healthy control group not subjected to a drill-hole defect or a control group subjected to the drill-hole defect without treatment of the defect.
- Exclusion criteria: Studies not using a control group as described above.

Outcome Measures

- Inclusion criteria:
  - Primary outcome: Information about the anatomical location of the defect, type of defect, defect size, number of defects, and depth of the defect.
  - Secondary outcomes: Information about defect repair, including healing time (only for untreated groups), bone characteristics (dual energy x-ray absorptiometry [DEXA], computed tomography [CT], µCT, histomorphometry, mechanical strength, etc).
- Exclusion criteria: No relevant information about the method of defect creation. No follow-up of the healing defect.

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Publication Type

- Inclusion criteria: Full-text original research papers.
- Exclusion criteria: Any type of review, meta-analysis, or conference abstract.

List of Exclusion Criteria for Screening

- Not a full-text study
- Study not written in English
- Not an original animal study
- No defect is created
- The defect is not created by a drill- or burr-like technique
- The defect is not created in a long bone
- The bone injury is fixated
- No control group is included
- No relevant outcome is obtained as follow-up on the defect healing

Data Collection Process

Overview

All eligible studies will have relevant data extracted by a reviewer to a predesigned data extraction protocol in *Covidence*. To ensure uniform data extraction and to reduce the risk of error in the data extraction process, 2 independent reviewers will perform data extraction on 10 full-text studies prior to full data extraction. The extracted data will be compared to verify that there is no disparity in the extraction. Should there be differences in the extracted data, the data extraction protocol will be refined, and the reviewers will perform full-text screening on 10 new full-text studies as a quality check.

Data Items and Availability

Data extracted from articles will include study characteristics (type of study, sample size calculations, duration of the study, number of groups, and number of animals per group), animal characteristics (species, strain, sex, age, genetic modifications, and body weight), method of drill-hole creation (description of drill methodology, type of drill-hole, size of the drill-hole, anatomical bone and site, number of defects, type of drill, drill speed, and depth of the drill-hole), and method of analysis (initial and final defect size, healing time [only for untreated groups], DEXA, CT, μCT, histomorphometry, and mechanical strength). This list is not exhaustive and may be updated upon refinement of the extraction protocol or during full-text data extraction. Data from graphs and figures will be collected with assistance of a web-based tool. All data from the data extraction protocol will be available upon request from the corresponding author.

Bias Assessment

The focus of this systematic review is the available methods of drill-hole bone defects in the literature and not the treatment of bone defects. Therefore, we include the healing time of any untreated group, as we believe this is an important aspect of any bone injury model. However, since we do not compare or analyze any treatment effect, no assessment of treatment bias is planned. To ensure uniformity between groups prior to creation of the bone defect, allocation method of animals (both blinding and randomization), sample size calculation, and baseline characteristics (sex, age, weight, species, strains, housing conditions, and provider of the animals) will be assessed. No analysis of meta-bias will be conducted.

Data Synthesis

The main outcome of this systematic review is methods used for creating drill-hole bone defects. Therefore, a narrative synthesis will be performed to describe all methods of creating bone defects in the included studies. Data on animal models will be tabulated to show similarities and differences in technique, anatomical location, and bone healing between the included drill-hole models clearly. Furthermore, data related to the main outcome (type of model, anatomical bone or site, and animal species or strain) will be presented graphically in bar or pie charts for improved clarity. The type of drill-hole injury and drill-hole site will also be presented and subdivided by animal species. Finally, the advantages and disadvantages of the injury model, bone site, and animal selection will be presented in the Discussion section.

Confidence in Cumulative Evidence

This is a narrative synthesis of animal models for preclinical investigation of bone healing. As such, no assessment is planned.

Results

Abstract and full-text screening is ongoing and is expected to be completed by October 2022. Data extraction will commence immediately after, and the manuscript is expected to be completed by December 2023. The study is expected to be published in a peer-reviewed journal once work is complete. The systematic review will follow the PRISMA statement [31].

Discussion

Expected Findings

Owing to the complexity of bone healing and its different healing processes, no single animal model can be used to study all aspects of the process. Therefore, the availability of different models and knowledge of their advantages and disadvantages allows researchers to choose the best-suited model based on their research question.

Drill-hole bone defects are relatively new methods used to investigate bone healing. These methods may help elucidate some of the mechanisms of bone healing in the diaphysis and especially in the metaphysis of long bones, and the interaction between cortical and trabecular bone healing. Understanding the healing processes in trabecular bone and the differences and similarities compared to the healing processes in cortical bone is highly relevant [18]. Hip fractures are common in older or osteoporotic individuals and involve healing of both cortical and trabecular bones in the proximal femoral metaphysis [32,33]. Until recently, most animal studies of fracture healing were performed at the middiaphysis, where little or no trabecular bone is found. Therefore, drill-hole defect models may increase options for preclinical studies of metaphyseal fractures, where healing of both trabecular and cortical bones can be studied. However, literature on drill-hole models suffer from a lack of standardization between studies, and often only inadequate descriptions of the applied technique are available.

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Therefore, this review aims to present a systematic overview of the drill-hole methods, describe the methodologies and techniques, and highlight their potential to elucidate aspects of the bone healing process. In the future, the review will hopefully assist researchers in selecting an appropriate model when planning their study protocols.

Strengths and Limitations

The strength of this systematic review is that it will present a comprehensive methodological overview of the different drill-hole methods and their advantages and disadvantages, and that abstract and full-text screening will be performed by 2 independent reviewers to increase reproducibility.

One limitation of this study is that some abstracts found from the search string are not written in English and cannot be included owing to the lack of linguistic proficiency in those languages in our research team. Another limitation is that owing to current lack of standardization, relevant articles may not be found if the abstract does not sufficiently describe the method of inducing a drill-hole bone defect.

Acknowledgments

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Authors' Contributions

FDB is the guarantor of the review, created the search strategy, performed data extraction, and drafted the manuscript. MBB assisted with the search strategy. FDB and MBB performed the abstract and full-text screening. All authors participated in the study design, manuscript revision, and approval of the final manuscript.

Conflicts of Interest

None declared.

References

1. Donaldson LJ, Reckless IP, Scholes S, Mindell JS, Shelton NJ. The epidemiology of fractures in England. J Epidemiol Community Health 2008 Feb;62(2):174-180. [doi: 10.1136/jech.2006.056622] [Medline: 18192607]
2. Claes L, Recknagel S, Ignatius A. Fracture healing under healthy and inflammatory conditions. Nat Rev Rheumatol 2012 Jan 31;8(3):133-143. [doi: 10.1038/nrrheum.2012.1] [Medline: 22293759]
3. Bolander ME. Regulation of fracture repair by growth factors. Proc Soc Exp Biol Med 1992 Jun;200(2):165-170. [doi: 10.3181/00379727-200-43410a] [Medline: 1374563]
4. Einhorn TA. The cell and molecular biology of fracture healing. Clin Orthop Relat Res 1998 Oct(355 Suppl):S7-21. [doi: 10.1097/00003086-199810001-00003] [Medline: 9917622]
5. Einhorn TA, Gerstenfeld LC. Fracture healing: mechanisms and interventions. Nat Rev Rheumatol 2015 Jan;11(1):45-54 [FREE Full text] [doi: 10.1038/nrrheum.2014.164] [Medline: 25266456]
6. Kostenuik P, Mirza FM. Fracture healing physiology and the quest for therapies for delayed healing and nonunion. J Orthop Res 2017 Feb 19;35(2):213-223 [FREE Full text] [doi: 10.1002/jor.23460] [Medline: 27743449]
7. Zura R, Xiong Z, Einhorn T, Watson JT, Ostrum RF, Prayson MJ, et al. Epidemiology of Fracture Nonunion in 18 Human Bones. JAMA Surg 2016 Nov 16;151(11):e162775. [doi: 10.1001/jamasurg.2016.2775] [Medline: 27603155]
8. Hobby B, Lee MA. Managing atrophic nonunion in the geriatric population: incidence, distribution, and causes. Orthop Clin North Am 2013 Apr;44(2):251-256. [doi: 10.1016/j.ocl.2013.01.011] [Medline: 23544828]
9. Lavery LA, Lavery DC, Green T, Hunt N, La Fontaine J, Kim PJ, et al. Increased Risk of Nonunion and Charcot Arthropathy After Ankle Fracture in People With Diabetes. J Foot Ankle Surg 2020;59(4):653-656. [doi: 10.1053/j.jfas.2019.05.006] [Medline: 32600558]
10. Einhorn TA. Enhancement of fracture-healing. J Bone Joint Surg Am 1995 Jun;77(6):940-956. [doi: 10.2106/00004623-199506000-00016] [Medline: 7782368]
11. Bahney CS, Hu DP, Miclau T, Marcucio RS. The multifaceted role of the vasculature in endochondral fracture repair. Front Endocrinol (Lausanne) 2015 Feb 05;6:4 [FREE Full text] [doi: 10.3389/fendo.2015.00004] [Medline: 25699016]
12. Schottel PC, O'Connor DP, Brinker MR. Time Trade-Off as a Measure of Health-Related Quality of Life: Long Bone Nonunions Have a Devastating Impact. J Bone Jt Surg 2015;97(17):1406-1410. [doi: 10.2106/jbjs.n.01090]
13. Haffner-Luntzer M, Hankenson KD, Ignatius A, Pfeifer R, Khader BA, Hildebrand F, et al. Review of Animal Models of Comorbidities in Fracture-Healing Research. J Orthop Res 2019 Dec;37(12):2491-2498 [FREE Full text] [doi: 10.1002/jor.24454] [Medline: 31444806]
14. Bigham-Sadegh A, Oryan A. Selection of animal models for pre-clinical strategies in evaluating the fracture healing, bone graft substitutes and bone tissue regeneration and engineering. Connect Tissue Res 2015 Jun;56(3):175-194. [doi: 10.3109/03008207.2015.1027341] [Medline: 25803622]

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15. Barré-Sinoussi F, Montagutelli X. Animal models are essential to biological research: issues and perspectives. Future Sci OA 2015 Nov;1(4):FSO63 [FREE Full text] [doi: 10.4155/fso.15.63] [Medline: 28031915]
16. Denayer T, Stöhrn T, Van RM. Animal models in translational medicine: Validation and prediction. New Horiz Transl Med 2014;2(1):5-11. [doi: 10.1016/j.nhtm.2014.08.001]
17. Clarke B. Normal bone anatomy and physiology. Clin J Am Soc Nephrol 2008 Nov;3 Suppl 3:S131-S139 [FREE Full text] [doi: 10.2215/CJN.04151206] [Medline: 18988698]
18. Sandberg OH, Aspenberg P. Inter-trabecular bone formation: a specific mechanism for healing of cancellous bone. Acta Orthop 2016 Oct;87(5):459-465 [FREE Full text] [doi: 10.1080/17453674.2016.1205172] [Medline: 27357416]
19. Garcia P, Histing T, Holstein JH, Klein M, Laschke MW, Matthys R, et al. Rodent animal models of delayed bone healing and non-union formation: a comprehensive review. Eur Cell Mater 2013 Jul 16;26:1-12; discussion 12 [FREE Full text] [doi: 10.22203/ecm.v026a01] [Medline: 23857280]
20. Wittbjer J, Palmer B, Thorngren KG. Osteogenetic properties of reimplanted decalcified and undecalcified autologous bone in the rabbit radius. Scand J Plast Reconstr Surg 1982;16(3):239-244. [doi: 10.3109/02844318209026214] [Medline: 6762656]
21. Kasten P, Vogel J, Geiger F, Niemeyer P, Luginbühl R, Szalay K. The effect of platelet-rich plasma on healing in critical-size long-bone defects. Biomaterials 2008 Oct;29(29):3983-3992. [doi: 10.1016/j.biomaterials.2008.06.014] [Medline: 18614227]
22. Brüel A, Olsen J, Birkedal H, Risager M, Andreassen TT, Raffalt AC, et al. Strontium is incorporated into the fracture callus but does not influence the mechanical strength of healing rat fractures. Calcif Tissue Int 2011 Feb;88(2):142-152. [doi: 10.1007/s00223-010-9439-z] [Medline: 21153023]
23. Claes L, Veeser A, Göckelmann M, Simon U, Ignatius A. A novel model to study metaphyseal bone healing under defined biomechanical conditions. Arch Orthop Trauma Surg 2009 Jul;129(7):923-928. [doi: 10.1007/s00402-008-0692-9] [Medline: 18654792]
24. Meadows TH, Bronk JT, Chao YS, Kelly PJ. Effect of weight-bearing on healing of cortical defects in the canine tibia. J Bone Joint Surg Am 1990 Aug;72(7):1074-1080. [Medline: 2384507]
25. Uusitalo H, Rantakokko J, Ahonen M, Jämsä T, Tuukkanen J, KäHäri V, et al. A metaphyseal defect model of the femur for studies of murine bone healing. Bone 2001 Apr;28(4):423-429. [doi: 10.1016/s8756-3282(01)00406-9] [Medline: 11336924]
26. Vegger JB, Brüel A, Sørensen TG, Thomsen JS. Systemic Treatment with Strontium Ranelate Does Not Influence the Healing of Femoral Mid-shaft Defects in Rats. Calcif Tissue Int 2016 Feb;98(2):206-214. [doi: 10.1007/s00223-015-0077-3] [Medline: 26543033]
27. He Y, Zhang G, Pan X, Liu Z, Zheng L, Chan C, et al. Impaired bone healing pattern in mice with ovariectomy-induced osteoporosis: A drill-hole defect model. Bone 2011 Jun 01;48(6):1388-1400. [doi: 10.1016/j.bone.2011.03.720] [Medline: 21421090]
28. Moher D, Shamseer L, Clarke M, Ghersi D, Liberati A, Petticrew M, PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. Syst Rev 2015 Jan 01;4:1 [FREE Full text] [doi: 10.1186/2046-4053-4-1] [Medline: 25554246]
29. Richardson WS, Wilson MC, Nishikawa J, Hayward RS. The well-built clinical question: a key to evidence-based decisions. ACP J Club 1995;123(3):A12-A13. [Medline: 7582737]
30. van der Mierden S, Hooijmans C, Tillema A, Rehn S, Bleich A, Leenaars C. Laboratory animals search filter for different literature databases: PubMed, Embase, Web of Science and PsycINFO. Lab Anim 2021 Sep 24:236772211045485 [FREE Full text] [doi: 10.1177/00236772211045485] [Medline: 34559023]
31. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021 Mar 29;372:n71 [FREE Full text] [doi: 10.1136/bmj.n71] [Medline: 33782057]
32. Gullberg B, Johnell O, Kanis JA. World-wide projections for hip fracture. Osteoporos Int 1997;7(5):407-413. [doi: 10.1007/pl00004148] [Medline: 9425497]
33. Wehren LE, Magaziner J. Hip fracture: risk factors and outcomes. Curr Osteoporos Rep 2003 Sep;1(2):78-85. [doi: 10.1007/s11914-003-0013-8] [Medline: 16036069]

Abbreviations

CT: computed tomography
DEXA: dual energy x-ray absorptiometry
PICO: Population, Intervention, Comparison, and Outcome
PRISMA-P: Preferred Reporting Items for Systematic review and Meta-Analysis Protocols
PROSPERO: The International Prospective Register of Systematic Reviews

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Protocol

Cultural Competence Interventions for Health Care Providers Working With Racialized Foreign-born Older Adults: Protocol for a Systematic Review

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Abstract

Background: Integrating culturally competent approaches in the provision of health care services is recognized as a promising strategy for improving health outcomes for racially and ethnically diverse populations. Person-centered care, which ensures patient values guide care delivery, necessitates cultural competence of health care providers to reduce racial/ethnic health disparities. Previous work has focused on interventions to improve cultural competence among health care workers generally; however, little investigation has been undertaken regarding current practices focused on racialized foreign-born older adults.

Objective: We seek to synthesize evidence from existing literature in the field to gain a comprehensive understanding of interventions to improve the cultural competence of health professionals who care for racialized foreign-born older adults. The aim of this paper is to outline a protocol for a systematic review of available published evidence.

Methods: Our protocol will follow the PRISMA-P (Preferred Reporting Items for Systematic Reviews and Meta-Analyses–Protocols) for systematic review protocols. We will conduct a systematic search for relevant studies from four electronic databases that focus on health and social sciences (PubMed, CINAHL, Scopus, and Cochrane Database). After selecting relevant papers using the inclusion and exclusion criteria, data will be extracted, analyzed, and synthesized to yield recommendations for practice and for future research.

Results: The systematic review is currently at the search phase where authors are refining the search strings for the selected databases; the search strings will be finalized by July 2022. We anticipate the systematic review to be completed by December 2022.

Conclusions: This study will inform the future development and implementation of interventions to support culturally competent, person-centered care of racialized foreign-born older adults.

Trial Registration: PROSPERO CRD42021259979; https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=259979

International Registered Report Identifier (IRRID): PRR1-10.2196/31691

(JMIR Res Protoc 2022;11(7):e31691) doi:10.2196/31691

KEYWORDS

cultural competence; racialized older adults; person-centered care; immigrants; health systems interventions

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Introduction

Background

Recent changes in population demographics, as a result of increased migration across national borders, have led to the reconsideration of traditional health care practices [1-3]. The rapid increase in migration and globalization patterns in high-income countries has important implications for health systems, health care workers, and the health of individuals [4,5]. Health and quality of life consequences for immigrants of racial and ethnic disparities in health care have been well documented [2,6,7]. Challenges faced by racialized foreign-born older adults (FBOAs) include greater difficulty accessing health services, lower likelihood of routine services, and an overall lower quality of care [8-13]. For FBOAs, access and quality of services is of particular concern [3,14]. Studies assessing the disparities in health care and health outcomes among racialized groups, including older adults, have identified race, ethnicity, and cultural variables as predictors of poorer health outcomes [4,14,15]. Health status disparities result in higher rates of mortality and morbidity among FBOAs even though immigrants report better health outcomes compared to non-FBOAs upon arrival [4,16]. The lack of clarity in health care systems on how to best cater social and health services for FBOAs further exacerbates health disparities [4,13,17].

Increased cultural competency of health care professionals is recognized as important for improving the provision of health care for racial/ethnic minority groups [7,18,19]. For older adults, it has been recognized that cultural competence is essential to meet the needs of what is becoming a larger and more diverse population [20]. The value of cultural competence lies in understanding how cultural variables impact and inform the health care experiences of older adults [21,22]. However, early literature commonly framed cultural competence as a list of "dos and don'ts" that may result in stereotypical thinking [14,23,24]. Instead, health care workers should view cultural competence as a core component of clinical competence [21,24].

There is increasing recognition of the importance of including patient perspectives on the quality of health care delivery, which has traditionally been driven solely by health care professionals and policy makers [23,25]. Consequently, person-centered care, which prioritizes viewing older adults as partners in receiving, planning, and monitoring care, has received significant traction over the last few decades [26,27]. Ensuring patients are involved and central to their care is now recognized as a key component of supporting high-quality health care [26,27]. Because older adults from culturally diverse backgrounds are often miscategorized as a homogenous group despite the prominent sociocultural differences that exist among them, person-centered care merits considerable attention in the care of FBOAs [28]. By moving away from a "one-size-fits-all" approach, person-centered care necessitates that care providers tailor care delivery to the participants' specific sociocultural backgrounds [26,27]. As such, person-centered care is a crucial component of cultural competence in health care settings, and each informs the other [29,30].

Several systematic reviews have been conducted on cultural competency in various care settings and within various disease modalities. One such review sought to compile the perceptions of culturally competent care for lesbian, gay, bisexual, and transgender (LGBT) long-term care (LTC) residents [31]. It was found that staff lack training when caring for LGBT residents in LTC and report negative feelings toward same-sex relationships among older adults [31]. Similarly, in a study assessing the impact of being a language minority in LTC, Batista and colleagues [32] reported that the capacity to deliver care in residents' languages could impact health outcomes. Reviews on other populations beyond racialized FBOAs found that culturally competent care, including the use of interpreters, staff cultural training, and culturally appropriate training, could reduce racial and ethnic disparities [31].

Truong and colleagues [33] conducted a systematic review of reviews that sought to synthesize existing reviews investigating the effectiveness of cultural competence interventions. They found, within a broad array of contexts and study types, that interventions addressing cultural competence produced moderate improvements in provider and health care access outcomes, and weak improvements in patient outcomes [33]. This review, however, did not distinguish between foreign-born and non–foreign-born older adults [33]. This highlights the need for a systematic review that emphasizes the role of health care providers in managing and improving the health of racialized FBOAs and the need for further investigation surrounding culturally competent care in the health care system [34].

We propose to look at all interventions pertaining to culturally competent practices and training for health care professionals working with FBOAs. This will allow us to better understand the merit of existing interventions and highlight similarities and differences with relevant implications for care provided. Both culture and competence are multidimensional and multifactorial concepts [35,36]. As a result, several different terminologies such as cultural competence, cultural safety, or multi- or cross-cultural competence, are used interchangeably owing to the lack of consistent and clear definitions [33,37-39]. Consequently, health care professionals view the term through the lens of their respective disciplines [33,37,38]. For the purposes of our review, the widely used definition of cultural competence provided by Cross and colleagues [40] will be used, that being, "a set of congruent behaviors, attitudes, and policies that come together in a system, agency, or among professionals and enables that system, agency, or those professionals to work effectively in cross-cultural situations." Additionally, the definition of cultural competence interventions provided by Truong and colleagues [33] will be used, that being, any intervention that aims to improve health care effectiveness and accessibility for people belonging to racial or ethnic minorities by increasing the provider and patient knowledge, skills, or awareness. As a byproduct of this synthesis, we aim to reach consensus and refine the definition of cultural competence and gain a better understanding of what cultural competence entails specifically relating to FBOAs. The overall aim of the proposed systematic review is to synthesize current best practices regarding interventions to promote cultural competence for health care professionals working with FBOAs.

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Study Rationale

Cultural competence allows health care professionals to account for the specific cultural contexts of older adults from different ethnic and racial backgrounds [14,18,19]. In recent years, substantial evidence from public health reports and research findings indicated that racialized immigrants are underserved and have a higher likelihood of receiving negative and differential health outcomes compared to their nonimmigrant counterparts [4,13,17]. In response, health systems in countries with high immigrant populations have attempted to incorporate cultural competence in their health delivery practices and policies to improve quality of care for racially and ethnically diverse populations [8,41,42]. Although racialized FBOAs account for a large portion of the overall population in these countries, published research for understanding the needs of this subpopulation, particularly older adults, is limited [8]. We anticipate most of these studies will come from western and high-income countries, but we do not wish to limit or exclude studies from low-income countries. Despite culturally competent interventions showing promise in promoting positive health outcomes, there has been a lack of recent systematic appraisal of its impact for racialized FBOAs [43]. As such, the review will not be limited to the interventions conducted in any one country or by the origins of the FBOAs under study within the studies. Any older adult belonging to a racialized group who have migrated to a country outside of their birth country will be considered. Any intervention aiming to improve the quality of cultural competence within the practitioners caring for those FBOAs will be considered.

Study Objective

To improve health outcomes of older adults, it is important to understand if health care systems reinforce health disparities, including assessment of how inadequate services affect the well-being of racialized FBOAs. To do so, we need to understand the impact of culture on health care experiences, delivery, and planning; whether the unique health care needs of ethnic and racial older adults are being adequately met; and the merits of provider cultural competence interventions for racialized FBOAs. This paper will outline the protocol for a systematic review that will review all interventions pertaining to culturally competent practices and training for health care professionals working with racialized FBOAs that have been implemented across various care settings. This will allow us to better understand the value of existing interventions and highlight similarities and differences with relevant implications for care provided.

Methods

Protocol Design

Our systematic review protocol (PROSPERO registration CRD42021259979) follows the PRISMA-P (Preferred Reporting Items for Systematic Reviews and Meta-Analyses–Protocols) reporting guidelines [44].

Eligibility Criteria

The systematic review will consider all relevant health interventions aimed to improve culturally competent care for FBOAs throughout the health system. The papers selected will include peer-reviewed publications published in English until December 31, 2021. Prior reviews regarding cultural competence interventions only included articles published after the year 2000, when cultural competence started to gain recognition as an issue of concern in the health care field [33]. To capture a broader range of information, as well as information that may have served as a prelude to the recognition of cultural competence as a necessity in health care, no early date limit will be used. Papers selected for the review will include qualitative, quantitative, and mixed methods studies that describe and apply culturally competent practices across health care settings. The review will consider a variety of health settings that include but are not limited to LTC, hospital care, and home and community care. The inclusion of a wide range of health settings helps inform the trajectory and progress of culturally competent care throughout the health literature. Following the World Health Organization's guidelines, we will use the age range of >60 years to define older adults [45]. Following Ontario's Human Rights Code, we use the term "racialized" to describe persons of color and visible minority populations [46-48]. "Foreign-born" persons include those who were born in a country that is different than the one they reside in, as defined by the Organisation for Economic Co-operation and Development, the US Census Bureau, and Ontario's Human Rights Code [46-48]. Our selected population will include older adults (aged ≥60 years) who are racialized FBOAs. To be included, a study must consider the care of a racialized FBOA by any health care provider. For the purposes of this paper, health care providers include health care professionals or other paid health care workers who work in any community or institutional health care setting, including hospitals and LTC homes. Studies focusing on adults who are not 60 years or older will be excluded, as well as studies that do not consider cultural competence interventions given to health care providers. All studies not written in English and all gray literature will not be included.

Search Methods

A systematic search of the published literature will be performed using defined search terms. The systematic review will use four databases (PubMed, CINAHL, Scopus, and the Cochrane Database) to search for peer-reviewed articles, with dates ranging from inception to December 2021. Selected databases and search strategies have been developed by all authors with the guidance of a health sciences librarian.

The search strategy for the review was developed for PubMed and will be used as a template for the remaining databases. The search strategy will use Medical Subject Headings (MeSH) terms and keywords identified in relevant papers. In adherence to the PRISMA-P guidelines, the protocol paper describes a draft of the search string as well as the number of results obtained [44]. The initial search results that have been developed for PubMed, as of April 25, 2022, are shown in Textbox 1. The titles and abstracts of articles will be used for the initial screening. Upon completing screening for abstracts and full papers, reference lists of selected journal articles will be hand searched for additional papers.

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Textbox 1. PubMed search strategy (762 PubMed search results).

Cultural competence

("cultural competenc*"[Text Word] OR "cultural diversity*"[Text Word] OR "cultural appropriateness*"[Text Word] OR "cultural responsiveness*"[Text Word] OR "cultural sensitivity*"[Text Word] OR "multicultural education"[Text Word] OR "cultural self-efficacy"[Text Word])

Older Adults

("elder*"[Text Word] OR "senior*"[Text Word] OR "older adults"[Text Word] OR "aged"[MeSH Terms])

Racialized foreign-born

("emigration and immigration"[MeSH Terms] OR "ethnicity"[MeSH Terms] OR "ethnic group"[Text Word] OR "refugee*"[Text Word] OR "newcomer*"[Text Word] OR "migrant*"[Text Word] OR "immigrant*"[Text Word])

The final search strategy prepared for this systematic review will be completed and recorded on June 28, 2022. Study selection on Covidence [49] will begin on July 4, 2022, to allow for some time to review the retrieved articles, prepare the study selection tool, and train reviewers to apply the inclusion and exclusion criteria. It is expected that title and abstract selection will take 1 month, at which point full-text selection will begin and last for approximately 3 weeks. Following study selection, data extraction and risk of bias assessments will be conducted and are expected to take an additional month to complete. It is expected that data synthesis and reporting will begin in August 2022 and will take approximately 2 months to complete, at which point discussion and finalization of the report will take an additional month to complete. Following this, the final systematic review will be submitted for publication in a journal relating to public health by the end of 2022.

Data Collection and Analysis

Selection of Studies

This review will consist of a two-stage article screening procedure. Results obtained from our search will be imported into Covidence, a web-based software that facilitates systematic review management [49]. Two pairs of reviewers will independently screen each identified article's titles and abstracts based on the predetermined inclusion and exclusion criteria. Reviewers will be blinded to each other's decisions. Discrepancies will be resolved through discussion among authors to reach a final decision, and articles deemed irrelevant by the majority (at least three of the four reviewers) will be eliminated from the review. Reasons for excluding articles will be noted throughout the process.

Following title and abstract review, two pairs or two reviewers will independently conduct full-text screening to finalize the included articles prior to data extraction. Any emerging disagreements between reviewers will be resolved by consulting the other coauthors. Furthermore, a group training session will be held prior to screening to ensure that all authors follow a consistent approach when screening studies. This group session will include an overview of the mechanics of Covidence, and a discussion of how to consistently apply the inclusion and exclusion criteria. The results of the previously mentioned steps will be recorded and presented according to the PRISMA-P flow diagram [50].

Data Extraction and Management

Data extraction will proceed separately for quantitative and qualitative studies (see Multimedia Appendices 1 and 2 for sample extraction tables [51,52]). If mixed methods studies are identified, a separate extraction table will be created based on the main categories described below. The review team, consisting of four of the reviewing authors, will be trained on extraction categories using Cochrane's training resources [53]. All reviewers will pilot test the data extraction table to ensure consistency. This process will ensure that reviewers are extracting similar types of data. Any discrepancies that arise throughout the extraction process will be discussed by the team and documented. If necessary, the extraction form will be adjusted to reflect team decisions, and a second sample of research studies will be reviewed to ensure reviewers are extracting similar data. Any discrepancies that arise throughout the extraction process will be discussed by the team and documented. If necessary, the extraction form will be adjusted to reflect team decisions, and a second sample of research studies will be reviewed to ensure reviewers are extracting similar data. From selected studies, we expect the following overarching information will be extracted: study identification items (ie, authors and year of publication), study characteristics (eg, country, care setting, and participant characteristics), study design and methods, findings/results, and definition of cultural competence. The extracted data from the papers will be compiled into data sheets independently by all four authors. The reviewers will then compare data sheets and as a group compile a final extraction table. Any discrepancies will be resolved by consulting other coauthors.

Outcomes

Due to the likely heterogeneous nature of the studies to be included within the review, target outcome measures were not specified a priori. However, following Bronfenbrenner's Ecological-Environmental model, we expect that, for both qualitative and quantitative studies, outcomes can be broadly classified under patient (micro-level), organization (meso-level), or system-level outcomes (macro-level) [54]. The studies are unlikely to be statistically comparable, since we expect the interventions and outcomes to be disparate, but we will consider outcomes and impacts at each of the specified levels.

Assessing Bias

To assess the risk of bias in quantitative studies included within the review, the Risk of Bias 2 (ROB2) and Risk of Bias In Non-randomized Studies of Interventions (ROBINS-1) tools

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will be used [55,56]. The ROB2 tool was designed to assess the risk of bias in randomized trials along five domains: bias arising from the randomization process, bias due to deviations from intended interventions, bias due to missing outcome data, bias in measurement of the outcome, and bias in the selection of the reported result [55]. The ROBINS-1 tool is used to assess risk of bias in nonrandomized studies along seven domains: bias due to confounding, bias in selection of participants, bias in classification of interventions, bias due to deviations from intended interventions, bias due to missing data, bias in measurement of outcomes, and bias in the selection of the reported result [56].

Quality Assessment

Quantitative studies included within the review will be assessed using The Effective Public Health Practice Project Quality Assessment Tool for Quantitative Studies, which is a validated tool designed to assess the quality of articles within systematic reviews [57]. This tool assesses eight indicators—selection bias, study design, confounders, blinding, data collection methods, withdrawals and dropouts, intervention integrity, and analysis—and rates items as either strong, moderate, or weak [57]. These ratings are then aggregated to create an overall rating of each paper to be listed under one of three categories [57]. This tool was selected because it allows for a broad array of studies to be assessed. Two reviewers will independently assess each article that meets inclusion criteria, and in the case of a disagreement, a third author will assess the study.

Qualitative studies selected for the review will be assessed using the Critical Appraisal Skills Programme Qualitative Checklist [58]. This appraisal tool consists of 10 questions and can be used to determine the strengths and limitations of different qualitative studies [58]. Two reviewers will independently assess selected articles, and in the case of a disagreement, a third author will provide input.

Mixed methods studies selected for review will be assessed for methodological validity by two independent reviewers according to the procedures outlined by the Methodology for Joanna Briggs Institute Mixed Methods Systematic Reviews [59]. Any disagreements that arise between reviewers will be resolved by consulting a third author.

Ethical Considerations

Since the systematic review will involve data collection from publicly available resources, this study will not require ethics approval.

Results

The results will be reported according to the outcomes specified above. We anticipate that our findings will be useful for those aiming to develop or implement interventions that support culturally competent care for racialized FBOAs and as a basis for future research. Results of the review will be disseminated widely, and the review will be submitted for publication at a peer-reviewed journal.

Discussion

We expect that this systematic review will comprehensively synthesize the existing literature surrounding interventions aimed at improving the cultural competence of health care professionals who care for racialized FBOAs. We anticipate that the findings will be heterogeneous but will nonetheless prove valuable in highlighting interventions that improve the competence of health care professionals, from both a quantitative and qualitative perspective. The results of this systematic review will aid in program planning and training of health care professionals who care for racialized FBOAs by providing evidence for effective strategies to increase cultural competence. The final manuscript produced for this study will be disseminated through a peer-reviewed academic journal and will be distributed widely to stakeholders within the health care field.

Acknowledgments

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Conflicts of Interest

None declared.

Multimedia Appendix 1
Quantitative data extraction sheet.
[DOCX File , 15 KB - resprot_v11i7e31691_app1.docx]

Multimedia Appendix 2
Qualitative data extraction sheet.
[DOCX File , 16 KB - resprot_v11i7e31691_app2.docx]

References

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1. Schmidt S, Hendricks V, Griebenow R, Riedel R. Demographic change and its impact on the health-care budget for heart failure inpatients in Germany during 1995-2025. Herz 2013 Dec;38(8):862-867. [doi: 10.1007/s00059-013-3955-3] [Medline: 24065050]
2. Gushulak BD, Pottie K, Hatcher Roberts J, Torres S, DesMeules M, Canadian Collaboration for Immigrant and Refugee Health. Migration and health in Canada: health in the global village. CMAJ 2011 Sep 06;183(12):E952-E958 [FREE Full text] [doi: 10.1503/cmaj.090287] [Medline: 20584934]
3. Setia MS, Quesnel-Vallee A, Abrahamowicz M, Tousignant P, Lynch J. Access to health-care in Canadian immigrants: a longitudinal study of the National Population Health Survey. Health Soc Care Community 2011 Jan;19(1):70-79 [FREE Full text] [doi: 10.1111/j.1365-2524.2010.00950.x] [Medline: 21054621]
4. Markides K, Rote S. The healthy immigrant effect and aging in the United States and other western countries. Gerontologist 2019 Mar 14;59(2):205-214. [doi: 10.1093/geront/gny136] [Medline: 30383212]
5. Hamilton T, Hagos R. Race and the healthy immigrant effect. Public Policy Aging Rep 2021;31(1):14-18 [FREE Full text] [doi: 10.1093/ppar/praa042] [Medline: 33462550]
6. Riley WJ. Health disparities: gaps in access, quality and affordability of medical care. Trans Am Clin Climatol Assoc 2012;123:167-72; discussion 172 [FREE Full text] [Medline: 23303983]
7. Mullings DV, Gien L. Culturally Competent i (Appropriate) health and long-term care services for older immigrants in a small urban center Of Newfoundland. Int J Humanit Soc Sci Invent 2013;2(9):81-89.
8. Butler M, McCreedy E, Schwer N, Burgess D, Call K, Przedworski J, Kane RL. Improving Cultural Competence to Reduce Health Disparities. Rockville, MD: Agency for Healthcare Research and Quality (US); 2016.
9. Bempong N, Sheath D, Seybold J, Flahault A, Depoux A, Saso L. Critical reflections, challenges and solutions for migrant and refugee health: 2nd M8 Alliance Expert Meeting. Public Health Rev 2019;40:3 [FREE Full text] [doi: 10.1186/s40985-019-0113-3] [Medline: 30923641]
10. Jakab Z, Severoni S, Ostlin P, Verschuuren M, Stein CE. Refugee and migrant health: a priority in the WHO European Region. Lancet 2015 Dec 19;386(10012):2477-2478. [doi: 10.1016/S0140-6736(15)01102-2] [Medline: 26738713]
11. Sheath D, Flahault A, Seybold J, Saso L. Diverse and complex challenges to migrant and refugee mental health: reflections of the M8 Alliance Expert Group on Migrant Health. Int J Environ Res Public Health 2020 May 18;17(10):3530 [FREE Full text] [doi: 10.3390/ijerph17103530] [Medline: 32443521]
12. Abbas M, Aloudat T, Bartolomei J, Carballo M, Durieux-Paillard S, Gabus L, et al. Migrant and refugee populations: a public health and policy perspective on a continuing global crisis. Antimicrob Resist Infect Control 2018;7:113 [FREE Full text] [doi: 10.1186/s13756-018-0403-4] [Medline: 30250735]
13. Kobayashi KM, Prus SG. Examining the gender, ethnicity, and age dimensions of the healthy immigrant effect: factors in the development of equitable health policy. Int J Equity Health 2012 Feb 16;11:8 [FREE Full text] [doi: 10.1186/1475-9276-11-8] [Medline: 22336144]
14. Lai DWL, Chau SBY. Predictors of health service barriers for older Chinese immigrants in Canada. Health Soc Work 2007 Feb;32(1):57-65. [doi: 10.1093/hsw/32.1.57] [Medline: 17432742]
15. Nair L, Adetayo O. Cultural competence and ethnic diversity in healthcare. Plast Reconstr Surg Glob Open 2019 May;7(5):e2219 [FREE Full text] [doi: 10.1097/GOX.0000000000002219] [Medline: 31333951]
16. Gee EM, Kobayashi KM, Prus SG. Examining the healthy immigrant effect in mid- to later life: findings from the Canadian Community Health Survey. Can J Aging 2004;23 Suppl 1:S61-S69. [Medline: 15660311]
17. De Maio FG. Immigration as pathogenic: a systematic review of the health of immigrants to Canada. Int J Equity Health 2010 Nov 24;9:27 [FREE Full text] [doi: 10.1186/1475-9276-9-27] [Medline: 21106100]
18. Brottman MR, Char DM, Hattori RA, Heeb R, Taff SD. Toward cultural competency in health care: a scoping review of the diversity and inclusion education literature. Acad Med 2020 May;95(5):803-813. [doi: 10.1097/ACM.0000000000002995] [Medline: 31567169]
19. Taylor S, Lurie N. The role of culturally competent communication in reducing ethnic and racial healthcare disparities. Am J Manag Care 2004 Sep;10 Spec No:SP1-SP4 [FREE Full text] [Medline: 15481430]
20. Periyakoil VS. Building a culturally competent workforce to care for diverse older adults: scope of the problem and potential solutions. J Am Geriatr Soc 2019 May;67(S2):S423-S432. [doi: 10.1111/jgs.15939] [Medline: 31074850]
21. Geiger HJ. Racial stereotyping and medicine: the need for cultural competence. CMAJ 2001 Jun 12;164(12):1699-1700 [FREE Full text] [Medline: 11450212]
22. Mayberry RM, Mili F, Ofili E. Racial and ethnic differences in access to medical care. Med Care Res Rev 2000;57 Suppl 1:108-145. [doi: 10.1177/1077558700057001S06] [Medline: 11092160]
23. Epner D, Baile W. Patient-centered care: the key to cultural competence. Ann Oncol 2012 Apr;23 Suppl 3:33-42. [doi: 10.1093/annonc/mds086] [Medline: 22628414]
24. Stevens S, Jussim L, Stevens L, Anglin S. Cultural competence: a form of stereotype rationality: an evaluation of current status and future directions. In: Cultural Competence in Applied Psychology. Cham: Springer; 2018.
25. Castillo R, Guo K. A framework for cultural competence in health care organizations. Health Care Manag (Frederick) 2011;30(3):205-214. [doi: 10.1097/HCM.0b013e318225dfe6] [Medline: 21808172]

XSL•FO
RenderX

26. Howard MC, Hoffman ME. Variable-centered, person-centered, and person-specific approaches. Organizational Res Methods 2017 Dec 10;21(4):846-876. [doi: 10.1177/1094428117744021]
27. Kaehne A. Care integration - from "One Size Fits All" to person centred care: comment on "Achieving Integrated Care for Older People: Shuffling the Deckchairs or Making the System Watertight for the Future?". Int J Health Policy Manag 2018 Oct 01;7(10):955-957 [FREE Full text] [doi: 10.15171/ijhpm.2018.51] [Medline: 30316248]
28. Leach CW, van Zomeren M, Zebel S, Vliek MLW, Pennekamp SF, Doosje B, et al. Group-level self-definition and self-investment: a hierarchical (multicomponent) model of in-group identification. J Pers Soc Psychol 2008 Jul;95(1):144-165. [doi: 10.1037/0022-3514.95.1.144] [Medline: 18605857]
29. Papadopoulos I, Lees S. Developing culturally competent researchers. J Adv Nurs 2002 Feb;37(3):258-264. [doi: 10.1046/j.1365-2648.2002.02092.x] [Medline: 11851796]
30. Saha S, Beach MC, Cooper LA. Patient centeredness, cultural competence and healthcare quality. J Natl Med Assoc 2008 Nov;100(11):1275-1285 [FREE Full text] [doi: 10.1016/s0027-9684(15)31505-4] [Medline: 19024223]
31. Caceres B, Travers J, Primiano J, Luscombe R, Dorsen C. Provider and LGBT individuals' perspectives on LGBT issues in long-term care: a systematic review. Gerontologist 2020 Apr 02;60(3):e169-e183 [FREE Full text] [doi: 10.1093/geront/gnz012] [Medline: 30726910]
32. Batista R, Prud'homme D, Hsu AT, Guérin E, Bouchard L, Rhodes E, et al. The health impact of living in a nursing home with a predominantly different spoken language. J Am Med Dir Assoc 2019 Dec;20(12):1649-1651. [doi: 10.1016/j.jamda.2019.06.003] [Medline: 31351860]
33. Truong M, Paradies Y, Priest N. Interventions to improve cultural competency in healthcare: a systematic review of reviews. BMC Health Serv Res 2014 Mar 03;14:99 [FREE Full text] [doi: 10.1186/1472-6963-14-99] [Medline: 24589335]
34. Anderson LM, Scrimshaw SC, Fullilove MT, Fielding JE, Normand J, Task Force on Community Preventive Services. Culturally competent healthcare systems. A systematic review. Am J Prev Med 2003 Apr;24(3 Suppl):68-79. [doi: 10.1016/s0749-3797(02)00657-8] [Medline: 12668199]
35. Asad AL, Kay T. Toward a multidimensional understanding of culture for health interventions. Soc Sci Med 2015 Nov;144:79-87. [doi: 10.1016/j.socscimed.2015.09.013] [Medline: 26397866]
36. Sue DW. Multidimensional facets of cultural competence. Counseling Psychol 2016 Jun 30;29(6):790-821. [doi: 10.1177/0011000001296002]
37. Sharifi N, Adib-Hajbaghery M, Najafi M. Cultural competence in nursing: a concept analysis. Int J Nurs Stud 2019 Nov;99:103386. [doi: 10.1016/j.ijnurstu.2019.103386] [Medline: 31404821]
38. Cai D. A concept analysis of cultural competence. Int J Nurs Sci 2016 Sep;3(3):268-273. [doi: 10.1016/j.ijnss.2016.08.002]
39. Betancourt JR, Green AR, Carrillo J, Ananeh-Firempong O. Defining cultural competence: a practical framework for addressing racial/ethnic disparities in health and health care. Public Health Rep 2003;118(4):293-302 [FREE Full text] [doi: 10.1093/phr/118.4.293] [Medline: 12815076]
40. Cross T, Bazron B, Dennis K, Isaacs M. Towards a Culturally Competent System of Care: A Monograph on Effective Services for Minority Children Who Are Severely Emotionally Disturbed. Washington, DC: CASSP Technical Assistance Centre, Georgetown University Child Development Program; 1989:13.
41. Shepherd SM, Willis-Esqueda C, Newton D, Sivasubramaniam D, Paradies Y. The challenge of cultural competence in the workplace: perspectives of healthcare providers. BMC Health Serv Res 2019 Feb 26;19(1):135 [FREE Full text] [doi: 10.1186/s12913-019-3959-7] [Medline: 30808355]
42. Handtke O, Schilgen B, Mösko M. Culturally competent healthcare - a scoping review of strategies implemented in healthcare organizations and a model of culturally competent healthcare provision. PLoS One 2019;14(7):e0219971 [FREE Full text] [doi: 10.1371/journal.pone.0219971] [Medline: 31361783]
43. Brach C, Fraser I. Can cultural competency reduce racial and ethnic health disparities? A review and conceptual model. Med Care Res Rev 2000;57 Suppl 1:181-217 [FREE Full text] [doi: 10.1177/1077558700057001S09] [Medline: 11092163]
44. Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ 2015 Jan 02;350:g7647 [FREE Full text] [doi: 10.1136/bmj.g7647] [Medline: 25555855]
45. Ageing. World Health Organization. URL: https://www.who.int/health-topics/ageing#tab=tab_1 [accessed 2022-05-31]
46. Foreign-born population. OECD iLibrary. URL: https://www.oecd-ilibrary.org/social-issues-migration-health/foreign-born-population/indicator/english_5a368e1b-en [accessed 2022-06-15]
47. About the foreign-born population. United States Census Bureau. 2021. URL: https://www.census.gov/topics/population/foreign-born/about.html [accessed 2022-06-14]
48. Racial discrimination. Ontario Human Rights Commission. URL: https://www.ohrc.on.ca/en/racial-discrimination-brochure [accessed 2022-05-31]
49. Covidence. URL: https://www.covidence.org/ [accessed 2021-06-30]
50. Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Med 2009 Jul 21;6(7):e1000097 [FREE Full text] [doi: 10.1371/journal.pmed.1000097] [Medline: 19621072]

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51. Noyes J, Lewin S. Chapter 5: extracting qualitative evidence. In: Noyes J, Booth A, Hannes K, Harden A, Harris J, Lewin S, editors. Supplementary Guidance for Inclusion of Qualitative Research in Cochrane Systematic Reviews of Interventions. Version 1 (updated August 2011). London, England: Cochrane Collaboration Qualitative Methods Group; 2011.
52. Munro SA, Lewin SA, Smith HJ, Engel ME, Fretheim A, Volmink J. Patient adherence to tuberculosis treatment: a systematic review of qualitative research. PLoS Med 2007 Jul 24;4(7):e238 [FREE Full text] [doi: 10.1371/journal.pmed.0040238] [Medline: 17676945]
53. Higgins J, Thomas J, Chandles J, Cumpston M, Li T, Page M, et al, editors. Cochrane Handbook for Systematic Reviews of Interventions version 6.3 (updated February 2022). London, England: Cochrane; 2022.
54. Bronfenbrenner U. Toward an experimental ecology of human development. Am Psychol 1977;32(7):513-531. [doi: 10.1037/0003-066x.32.7.513]
55. Sterne JAC, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. BMJ 2019 Aug 28;366:l4898. [doi: 10.1136/bmj.l4898] [Medline: 31462531]
56. Sterne JA, Hernán MA, Reeves BC, Savović J, Berkman ND, Viswanathan M, et al. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. BMJ 2016 Oct 12;355:i4919 [FREE Full text] [doi: 10.1136/bmj.i4919] [Medline: 27733354]
57. Thomas B, Ciliska D, Dobbins M, Micucci S. A process for systematically reviewing the literature: providing the research evidence for public health nursing interventions. Worldviews Evid Based Nurs 2004;1(3):176-184. [doi: 10.1111/j.1524-475X.2004.04006.x] [Medline: 17163895]
58. CASP Qualitative Checklist. Critical Appraisal Skills Programme. 2018. URL: https://casp-uk.net/wp-content/uploads/2018/01/CASP-Qualitative-Checklist-2018.pdf [accessed 2021-06-29]
59. Methodology for JBI mixed methods systematic reviews. Joanna Briggs Institute. 2014. URL: https://nursing.lsuhsc.edu/JBI/docs/ReviewersManuals/Mixed-Methods.pdf [accessed 2021-06-29]

Abbreviations

FBOA: foreign-born older adult
LGBT: lesbian, gay, bisexual, and transgender
LTC: long-term care
MeSH: Medical Subject Headings
PRISMA-P: Preferred Reporting Items for Systematic Reviews and Meta-Analyses–Protocols
ROB2: Risk of Bias 2
ROBINS-1: Risk of Bias In Non-randomized Studies of Interventions

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Protocol

Understanding Design Approaches and Evaluation Methods in mHealth Apps Targeting Substance Use: Protocol for a Systematic Review

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Abstract

Background: Substance use and use disorders in the United States have had significant and devastating impacts on individuals and communities. This escalating substance use crisis calls for urgent and innovative solutions to effectively detect and provide interventions for individuals in times of need. Recent mobile health (mHealth)–based approaches offer promising new opportunities to address these issues through ubiquitous devices. However, the design rationales, theoretical frameworks, and mechanisms through which users' perspectives and experiences guide the design and deployment of such systems have not been analyzed in any prior systematic reviews.

Objective: In this paper, we systematically review these approaches and apps for their feasibility, efficacy, and usability. Further, we evaluate whether human-centered research principles and techniques guide the design and development of these systems and examine how the current state-of-the-art systems apply to real-world contexts. In an effort to gauge the applicability of these systems, we also investigate whether these approaches consider the effects of stigma and privacy concerns related to collecting data on substance use. Lastly, we examine persistent challenges in the design and large-scale adoption of substance use intervention apps and draw inspiration from other domains of mHealth to suggest actionable reforms for the design and deployment of these apps.

Methods: Four databases (PubMed, IEEE Xplore, JMIR, and ACM Digital Library) were searched over a 5-year period (2016-2021) for articles evaluating mHealth approaches for substance use (alcohol use, marijuana use, opioid use, tobacco use, and substance co-use). Articles that will be included describe an mHealth detection or intervention targeting substance use, provide outcomes data, and include a discussion of design techniques and user perspectives. Independent evaluation will be conducted by one author, followed by secondary reviewer(s) who will check and validate themes and data.

Results: This is a protocol for a systematic review; therefore, results are not yet available. We are currently in the process of selecting the studies for inclusion in the final analysis.

Conclusions: To the best of our knowledge, this is the first systematic review to assess real-world applicability, scalability, and use of human-centered design and evaluation techniques in mHealth approaches targeting substance use. This study is expected to identify gaps and opportunities in current approaches used to develop and assess mHealth technologies for substance use detection and intervention. Further, this review also aims to highlight various design processes and components that result in engaging, usable, and effective systems for substance use, informing and motivating the future development of such systems.

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KEYWORDS

substance use; mHealth; human-centered design; use disorder; substance; design rationale; theoretical framing; protocol; systematic review; mobile health; smartphone; mobile phone; digital health

Introduction

More than 275 million people worldwide used substances in 2021, with problematic substance use costing the lives of half a million people globally in 2019 [1], an increase of more than 20% in the past 10 years. Further, substance use often has far-reaching consequences on human health and well-being, resulting in the loss of 18 million years of healthy life [1]. However, there remains a huge treatment gap—people with substance use concerns, especially in underserved populations (eg, ethnic and racial minorities, individuals experiencing homelessness, and sexual and gender minorities), often do not have access to appropriate diagnoses and care. As such, there has been an increasing focus on addressing this treatment gap by using technology to make substance use detection and intervention delivery more affordable and accessible to individuals and communities. Even with recent advances [2,3], a considerable amount of work remains to ensure that these technological approaches are scalable and usable for all, especially in underserved populations [4].

Earlier efforts to summarize the current research in this domain have primarily focused on efficacy and usability [2,3,5], but few have investigated the design and evaluation approaches that inform these systems and apps. The design principles these detection and intervention apps follow, the theoretical constructs that underlie these systems, and the mechanisms through which users' perspectives and experiences guide the design and deployment of such systems are individually reported in various works but have not been analyzed in any prior systematic reviews. Understanding these fundamental aspects of mobile health (mHealth) apps for substance use could guide researchers, designers, developers, and even policy makers and provide actionable insights for them in creating effective and usable technological systems for problematic substance use detection and interventions.

Further, an investigation of scalability and ethics, as well as stigma and privacy concerns of various stakeholders of these apps, could have broad implications not only for the domain of mHealth for substance use but also for the broader digital health domain. A few systematic reviews that focus on aspects of users' experiences with mHealth apps have generated useful findings such as recommendations about improving overall usability [6], capturing engagement in various settings [7,8], and ensuring the privacy and security of users' data [9,10]; however, all such evaluations have tended to focus on singular aspects of users' experiences (eg, only evaluating privacy, or only evaluating engagement or usability). So far, no systematic review offers a comprehensive evaluation of how these myriads of designs and considerations are associated with one another, and more importantly, with the intended health outcomes.

Toward the goal of identifying, analyzing, and summarizing these existing systems, we aim to systematically review approaches in the substance use domain of mHealth technologies for the following features: their design techniques; evaluation methodologies; resulting feasibility, efficacy, usability, and overall user experience; exploration of stigma, ethics, and privacy; and finally, the systems' applicability to real-world contexts. Specifically, we aim to (1) investigate whether these systems are designed using human-centered research methodologies and principles, as well as (2) generate concrete design guidelines to support the development of effective solutions in this context for future research. The following research questions will be addressed in our systematic review:

- Which measures of usability, engagement, and feasibility are currently used in substance use–centered mHealth studies? How is efficacy explicated in these studies?
- What key findings are reported in this literature, and to what extent do they apply to real-world contexts? Are the current approaches and systems scalable?
- Do these existing systems use human-centered design principles, and how is the presence or absence of human-computer interaction–based research methodologies associated with measures of usability and scalability?
- What are the common, persistent challenges faced by researchers and practitioners in developing mHealth systems for substance use, and how might they be addressed through robust, human-centered research techniques?
- How can we use findings, methods, and techniques from other areas of mHealth to inform future substance use detection and intervention work?

Methods

Study Design

To structure the design of this systematic review, we will use the PRISMA-P (Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols) guidelines [11]. This methodology consists of literature search, article selection and screening, data extraction and analysis, and an assessment of study quality and bias.

Search Strategy

We surveyed 4 large databases of digital health literature—ACM Digital Library, IEEE Xplore, JMIR, and PubMed—over a 5-year period (2016-2021), using keywords and terms extracted from an initial literature review. Search terms focused on 3 key areas: substance-related terms such as alcohol, cannabis, opioids, and tobacco; mHealth-related terms such as smartphone, smartwatch, and conversational agents; and design- and usability-related terms such as acceptability, user perspectives, engagement, and adoption. The full list of terms is provided in Table 1 and encompasses a broad survey of the existing literature on mHealth approaches for substance use that include some form of discussion on usability. Further, "similar articles" and citation networks were used to identify more relevant papers. This initial search yielded 3352 papers.

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Table 1. Search terms for literature review.

Domain	Keywords
Substances of interest (searched for in the abstract or title of the articles)	Alcohol OR opioid OR "substance use" OR tobacco OR cannabis OR marijuana OR "substance abuse" OR "drug use" OR cigarette OR vaping OR smoking
Relevant mHealth[a] platforms (searched for in all given metadata for an article)	mHealth OR mobile OR smartphone OR "mobile application" OR "smartphone application" OR wearable* OR smartwatch OR "conversational agent" OR "virtual coach" OR *bot OR smart-speaker OR "smart speaker"
Design techniques, evaluation methods, and user experience (searched for in the full text of the articles)	Usability OR "user centered" OR acceptability OR engagement OR "treatment adherence" OR adherence OR "user experience" OR acceptance OR "user acceptability" OR efficacy OR effectiveness OR "human-centered" OR "human centered" OR "user perspectives" OR "user perceptions" OR adoption OR feasibility

[a]mHealth: mobile health.

Substances of interest were searched for in the abstract or title of the articles, to maintain relevance with the aim of this work. Relevant mHealth platforms were searched for in all given metadata for an article, whereas terms related to design techniques, evaluation methods, and user experience were searched for in the full text of the article.

Inclusion and Exclusion Criteria

Given that mHealth technologies in this domain span an extensive set of target populations, methodologies, and devices, we established appropriate inclusion and exclusion criteria to define the scope of this protocol.

We included papers that meet all 4 following criteria:

- Papers describing an mHealth system or app with a reasonable degree of implementation and deployment, including generating results from a user study of any scale. We specifically included apps and systems that were implemented and tested out by users, as one of our main research questions was to analyze user perspectives—and their influence on the system design—through all stages of development.
- Papers presenting an app deployed on ubiquitous devices like smartphones, smartwatches, wearables, or smart speakers.
- Papers including a discussion of any depth about user perspectives, design approaches, usability, acceptability, feasibility, engagement, ethics, or privacy and stigma concerns, as this was an important variable in our literature analysis.
- Papers or articles in the English language.

We excluded papers that matched the following criteria:

- Papers describing machine learning approaches without system deployment and user testing, as this would not align with our primary aims of assessing mHealth approaches.
- Papers presenting social media–based detection and intervention approaches, since they do not include systems that are device-specific.
- Works targeting associated mental illnesses and treating substance use as a symptom, consequence, or a distal measure or outcome, as we wanted to only focus on papers that included or assessed substance use proximally.
- Papers presenting analyses without system implementation and deployment (eg, works examining associations between substance use and crime, economy, etc, without an app description).
- Telehealth or telemedicine (ie, telephone and video technologies) and web-based approaches (eg, patient portals), as we wanted to focus only on mHealth approaches, that is, systems that based their detection or intervention mechanisms on data collected through mobile devices such as smartphones or wearables (eg, self-report, biological samples, location data, sensor data, or physiologic data).

Data Extraction

All title- and abstract-screened articles were exported to a Zotero (version 5.0.96.3; Corporation for Digital Scholarship) library, and duplicate studies were removed. To extract relevant data from the selected list of papers, we will use standard Microsoft Excel forms that include the following variables: population targeted (eg, age group and existing health conditions), study type (eg, detection, data collection, feasibility or usability of the system or approach, intervention study, and app evaluation), study characteristics (eg, qualitative or quantitative methodology, number of participants, participant split, duration, and outcome domain), form of mHealth approach (eg, mobile phone, wearable, conversational agents, and combination), system description, targeted substance (eg, alcohol use, cannabis use, opioid use, tobacco use, and substance co-use), theoretical constructs used (eg, peer-based care facilitation or intervention, gamification, cognitive training, and behavioral theory), design approaches or the types of research that inform design (eg, focus groups, think-alouds, interviews, participatory design, observational studies, case studies, diaries, user testing, scenarios, or personas), rationale for design approach (eg, target population–based, behavior-based, or substance-based), design evaluation methods or how the efficacy of design was assessed (eg, through completion of tasks, usability ratings, interviews, usage duration data, or compliance data), design evaluation findings, privacy concerns and stigma-related findings, study outcomes or health and clinical outcomes (eg, frequency or intensity of substance use, mental health status, change in experiences or behaviors associated with substance use such as cravings, use of other substances, access to care, and change in consequences of substance use), and the cost of intervention.

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Study Quality Assessment

To assess the quality of the studies included in the final analyses, we will use the mHealth Evidence Reporting and Assessment [12] framework, which includes checklists consisting of numerous criteria deemed essential for reporting interventions and study design, such as intervention content, methods of delivery, usability testing, and user feedback, as well as other items such as discussions of population-level infrastructure availability and scalability limitations.

Data Analysis

A descriptive analysis using the aforementioned data extraction forms will be conducted after a final list of papers has been selected. We will organize themes identified in our analysis through subgroups to provide a succinct discussion of existing literature. In this discussion, we will aim to elaborate upon the following: how effectiveness of approach was explicated in various studies; what outcomes were deemed most important for the success of the approach; the various design approaches and evaluation techniques that were used and the subsequent findings; scope of the studies analyzed; how findings from these studies can inspire future work in substance use, as well as in mHealth; and finally, the features of successful mHealth approaches used in other domains that can positively impact the scalability and usability of current systems and apps in problematic substance use detection, prevention, and treatment.

Results

As of December 2021, we have identified 257 papers that met our initial screening. These papers will be further analyzed to remove those that do not exactly match the inclusion and exclusion criteria established above.

Discussion

In this protocol, we detailed the plan for a systematic analysis of design and evaluation approaches in mHealth systems with the aim to address, prevent, and treat problematic substance use. We anticipate that studies that invest in rigorous and iterative design or evaluation methods, incorporate theoretical framing, and consider issues such as accessibility, scalability, privacy concerns, and social stigma will result in systems that elicit positive health outcomes.

In this review, our principal findings will be organized into the following 3 main parts:

- First, we will present an analysis of the types of human-centered design and evaluation approaches used in the current state-of-the-art mHealth work in substance use. This analysis will allow us to highlight the most frequently used methods in this domain; the insights these approaches are capable of generating; and the challenges they pose with respect to feasibility, reliability, and generalizability.
- Second, we will establish the main constructs on which usability evaluations have been based in the selected studies and highlight those that have so far received less attention in this domain. Hence, we aim to explore whether each study conducts evaluations based on measures of privacy, scalability, and sustained usability, and whether ethical implications are considered in the proposed systems. This analysis of constructs will illustrate the opportunities and gaps in the use of human-centered techniques to improve health outcomes in this domain.
- Third, we examine the various components of the systems themselves: the theoretical foundations that guide them, the passive and self-reported data collected, detection and intervention methods, intervention content, design elements used in the interface (eg, notifications, gestures, and animations), and the platforms on which they are deployed. Extracting and analyzing these aspects will emphasize the characteristics that contribute to the overall user experience.

Through these multifaceted findings, our eventual goal is to establish best practices and guidelines for human-centered mHealth systems that target substance use detection and interventions. These guidelines will span several aspects across the system design flow, including suitable theoretical frameworks that address substance use in the population of interest, design elements and practices that can effectively be used to sustain user engagement and provide a rich user experience, approaches to responsibly collect data and ensure users' trust in the system, incorporation of evidence-based practices that improve health outcomes, and practices to ensure the system is accessible and operates on ethical principles. Future research into mHealth tools for substance use and subsequent implementations of apps can use these guidelines to develop systems that encourage meaningful use and support enduring impact.

Thus, this review will build on prior work in understanding the effectiveness of mHealth systems in this domain by broadening the scope from usability assessments to a more comprehensive understanding of user experience. Further, our work will also add to current literature in the human-computer intervention field by assessing the relative strengths of various design and evaluation approaches for mHealth systems.

There has been an increasing focus on developing novel mHealth systems to understand and address substance use due to their potential impact. This review aims to provide a comprehensive look at whether and how human-centered approaches are being used to create systems to address substance use; however, we are limited by the volume of new work constantly emerging in this domain. Thus, this review should not be treated as exhaustive but rather as a useful reference that can be used while considering various design and evaluation approaches in mHealth for a substance use context. Our work also has limitations due to its focus on ubiquitous devices, which means that other approaches such as social media and telehealth are not analyzed in this review. Lastly, we focus on works that assess substance use (and associated behaviors) as a primary outcome and exclude studies that assess substance use adjacent to other health issues, thus limiting the applicability of findings and generated guidelines to systems that solely target substance use. Future research could expand the scope of this work by including other modalities of mHealth that target a wide variety of physical and mental health issues related to substance use.

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Conflicts of Interest

None declared.

References

1. World Drug Report 2021. United Nations. URL: https://www.unodc.org/unodc/en/data-and-analysis/wdr2021.html [accessed 2022-06-14]
2. Kazemi DM, Borsari B, Levine MJ, Li S, Lamberson KA, Matta LA. A systematic review of the mHealth interventions to prevent alcohol and substance abuse. J Health Commun 2017 May;22(5):413-432 [FREE Full text] [doi: 10.1080/10810730.2017.1303556] [Medline: 28394729]
3. Marsch LA, Borodovsky JT. Technology-based interventions for preventing and treating substance use among youth. Child Adolesc Psychiatr Clin N Am 2016 Oct;25(4):755-768 [FREE Full text] [doi: 10.1016/j.chc.2016.06.005] [Medline: 27613350]
4. Schueller SM, Hunter JF, Figueroa C, Aguilera A. Use of digital mental health for marginalized and underserved populations. Curr Treat Options Psych 2019 Jul 5;6(3):243-255 [FREE Full text] [doi: 10.1007/s40501-019-00181-z]
5. Carreiro S, Newcomb M, Leach R, Ostrowski S, Boudreaux ED, Amante D. Current reporting of usability and impact of mHealth interventions for substance use disorder: A systematic review. Drug Alcohol Depend 2020 Oct 01;215:108201 [FREE Full text] [doi: 10.1016/j.drugalcdep.2020.108201] [Medline: 32777691]
6. Zapata BC, Fernández-Alemán JL, Idri A, Toval A. Empirical studies on usability of mHealth apps: a systematic literature review. J Med Syst 2015 Feb;39(2):1 [FREE Full text] [doi: 10.1007/s10916-014-0182-2] [Medline: 25600193]
7. Pham Q, Graham G, Carrion C, Morita PP, Seto E, Stinson JN, et al. A library of analytic indicators to evaluate effective engagement with consumer mHealth apps for chronic conditions: scoping review. JMIR mHealth uHealth 2019 Jan 18;7(1):e11941 [FREE Full text] [doi: 10.2196/11941] [Medline: 30664463]
8. Short CE, DeSmet A, Woods C, Williams SL, Maher C, Middelweerd A, et al. Measuring engagement in eHealth and mHealth behavior change interventions: viewpoint of methodologies. J Med Internet Res 2018 Nov 16;20(11):e292 [FREE Full text] [doi: 10.2196/jmir.9397] [Medline: 30446482]
9. Arora S, Yttri J, Nilsen W. Privacy and security in mobile health (mHealth) research. Alcohol Res 2014;36(1):143-151 [FREE Full text] [Medline: 26259009]
10. Nurgalieva L, O'Callaghan D, Doherty G. Security and privacy of mHealth applications: a scoping review. IEEE Access 2020;8:104247-104268 [FREE Full text] [doi: 10.1109/access.2020.2999934]
11. Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ 2015 Jan 02;350:g7647 [FREE Full text] [doi: 10.1136/bmj.g7647] [Medline: 25555855]
12. Agarwal S, LeFevre AE, Lee J, L'Engle K, Mehl G, Sinha C, WHO mHealth Technical Evidence Review Group. Guidelines for reporting of health interventions using mobile phones: mobile health (mHealth) evidence reporting and assessment (mERA) checklist. BMJ 2016 Mar 17;352:i1174. [doi: 10.1136/bmj.i1174] [Medline: 26988021]

Abbreviations

mHealth: mobile health
PRISMA-P: Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols

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Protocol

Effectiveness of Interventions to Promote Physical, Psychological, and Socioeconomic Well-being Outcomes of Parents of Children With Neurodevelopmental Disabilities: Protocol for a Systematic Review

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Abstract

Background: It is well recognized that parents of children with neurodevelopmental disabilities can experience a considerable burden of care associated with their child's disability, which can potentially impact their functioning and quality of life. Historically, the intervention efforts in pediatric rehabilitation have focused primarily on the child's development and well-being and much less on parental and family well-being. The impact that a child's diagnosis might have on parents remains unclear, and it is unknown how we can best support parents on their journey of childhood disability. It is, therefore, important to synthesize the published evidence on interventions for parents of children with neurodevelopmental disabilities so that clinicians can be better informed about the ways in which families they work with can be supported.

Objective: This manuscript presents the protocol for a systematic review of the effectiveness of interventions aiming to improve the physical, psychological, or socioeconomic well-being of parents of children with neurodevelopmental disabilities when compared to usual care or no care.

Methods: We will systematically search 4 databases (MEDLINE, Embase, PsycINFO, and CINAHL) from the year 2000 until the search date, for randomized controlled trials that evaluated the effectiveness of interventions to improve parental physical, psychological, or socioeconomic well-being. Two authors will independently screen the titles and abstracts, which will then be followed by full-text screening. After the eligibility assessment, two reviewers will independently extract data and conduct a risk of bias assessment using the Cochrane risk-of-bias tool. We will assess the quality of evidence using the Grading of Recommendations, Assessment, Development and Evaluation approach. If the data allow, we will perform a pairwise meta-analysis or network meta-analysis. We plan to evaluate the coherence of the network with a global test by using the node-splitting method.

Results: As of May 30, 2022, there have been two searches of data initiated: in September 2020 for articles published since 2000 and an updated search in January 2022 for articles published since 2020. We have screened all the titles and abstracts and performed eligibility assessment. However, the final number of references is still not available due to the additional information needed for some of the potentially eligible studies. The results from this systematic review will be published in an indexed journal within a year after this protocol is published.

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Conclusions: This study is expected to identify a variety of programs to address the well-being needs of parents of children with neurodevelopmental disabilities and provide directions on how parents can best be supported within health care. Such interventions might help professionals and stakeholders in creating service delivery models that can enhance parental well-being and minimize the risks to their physical, psychological, and socioeconomic functioning.

Trial Registration: PROSPERO CRD42021230706; https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=230706

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KEYWORDS

childhood disability; developmental disability; family; health; parent intervention; pediatric; children; parenting; rehabilitation; child development; health intervention; peer support; socioeconomic well-being; parent support; meta-analysis; quality of life

Introduction

Background

Becoming a parent of a child with a disability can be a life-altering experience, often accompanied by rearranging family life and functioning [1]. How parents adapt to this unexpected role and its associated caregiving demands is highly individual and influenced by many factors [2]. Caring for a child who has a disability often has an impact on caregiver health, functioning, and well-being. Despite the positive side of being a parent of a child with a disability [1,3-5], research consistently shows that these parents are more likely to experience challenges in their physical, psychological, financial, and social functioning [6-12]. Some of those challenges, such as the increased levels of stress and higher risk for depression (relative risk 1.75, 95% CI 1.55-1.97) and anxiety (1.40, 95% CI 1.18-1.67), have been extensively explored and are consistently found to be directly related to the increased burden of care for their child(ren) [7,8].

Furthermore, research shows that parenting a child with a disability does not only bring challenges and risks concerning psychological functioning and mental health; there is evidence that having a child with a disability might also affect parents' physical health and longevity. Research shows that parent caregivers of children who depend on medical technology are at risk of sleep deprivation, sleep disturbances, and excessive daytime sleepiness, which can all have serious consequences on health, daytime functioning, and quality of life [13,14]. Similar results were also found with parents of children with autism [7]. In addition, intensive physical demands of caregiving for children with physical disabilities can also lead to increased back pain [15-17]. A population-based cohort study by Cohen et al [9,10] showed that mothers of children with a congenital anomaly have increased cardiovascular risk and even increased risk of premature death when compared to other mothers.

In addition, parents of children with impairments have been found to experience more social marginalization, financial difficulties [18], under- or unemployment [7], and other disadvantages. We believe that parents' life circumstances can have serious impact on their overall well-being and prosperity. It is, therefore, important to identify which interventions effectively address parental needs and well-being, so that we can learn what, how, where, and for whom interventions have been explored.

Until recently, there has been no published model or framework that could guide professionals in considering parental well-being in the context of pediatric rehabilitation service delivery and research exploration. A recent scoping review by King et al [19] provided a framework that encompasses types of services that promote parent and family wellness. This study has been a significant contribution to the field by determining the types of services that parents and families need. It can be used as a cornerstone for mapping out and classifying existing services, as well as for guiding research exploration and implementation in day-to-day clinical practice. By building on this foundation, we want to expand on one of its domains, *addressing parent-specific needs*, and explore what interventions have focused specifically on parental health outcomes, functioning, needs, and well-being.

This paper presents the protocol for a systematic review of randomized controlled trials (RCTs) that aimed to evaluate the effectiveness of interventions addressing parental needs and well-being with a focus on physical, psychological, and socioeconomic outcomes. At the end of our proposed study, we will (1) report on the RCTs within the literature that explored the effectiveness of interventions aiming to support parents, and (2) inform about ways in which clinicians can better support the well-being and needs of parents of children with disabilities in everyday practice.

Objective

The objective of this study is to examine the effectiveness of interventions addressing parent-specific needs and the well-being of parents of children with disabilities. The following research question will be addressed:

> *What is the effectiveness of interventions focusing on parent-specific needs for parents of children with neurodevelopmental disabilities on physical, psychological, and socioeconomic well-being outcomes when compared to no care or usual care?*

Methods

Overview

This protocol was written according to the PRISMA-P (Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols) 2015 checklist [20] and the PRISMA for Network Meta-Analyses extension statement [21]. In accordance with the guidelines, this protocol was registered with PROSPERO

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(International Prospective Register of Systematic Reviews; 230706).

Ethical Considerations

Since this study will not involve contact with participants, we did not seek ethics approval.

Eligibility Criteria

Study Design

We will include RCTs, including feasibility RCTs, that investigated interventions that directly address physical, psychological, or socioeconomic well-being and needs of parents of children with disabilities. In the absence of RCTs (n<3), we will also include quasi-randomized studies. Only peer-reviewed studies will be eligible for inclusion (full-length reports only, not abstracts or conference proceedings).

Intervention

We will include studies that explored programs or interventions that were designed to address parent-specific physical, psychological, and/or socioeconomic needs, health, and well-being. We will exclude studies that were primarily child-focused but had a parent training, education, or assessment component. We will also exclude studies examining parent-mediated interventions for managing their child's symptoms or disability. Articles that did not describe the components of their intervention will be excluded. Additionally, studies that explored pharmacological or diet interventions will not qualify for this review. Studies will be eligible if the comparison interventions include no intervention, usual care, or wait-list control. Studies with multiple intervention arms (>2) will be considered only if there was a usual care, nonexposed, or wait-list control group.

Population

The population of interest in this study is parents of children (0-18 years) with lifelong neurodevelopmental disabilities (eg, cerebral palsy, Down syndrome, autism spectrum disorder, spina bifida, intellectual disabilities, multiple disabilities, genetic syndromes). This does not include parents of children who have mental illness (eg, depression, anxiety), eating disorders, behavioral problems (eg, oppositional defiant disorder, emotional disorders), or chronic diseases (eg, epilepsy, cancer, asthma) only. We will use the Institute of Medicine (US) Committee on Nervous System Disorders in Developing Countries [22] definition of developmental disabilities to guide our search strategy and define our target study population. According to the Institute of Medicine (US) Committee on Nervous System Disorders in Developing Countries, (neuro)developmental disabilities "include limitations in function resulting from disorders of the developing nervous system" [22], such as (1) cognitive (eg, intellectual disability, learning disability), (2) motor (eg, cerebral palsy, spina bifida), (3) vision (eg, blindness, visual impairment), (4) hearing and speech (eg, deafness, hearing impairment), and (5) behavior (eg, attention-deficit/hyperactivity disorder, autism spectrum disorder) disabilities [22]. We will include reports that focus primarily on parents and where parents of children with disabilities comprised 90% of the sample. In studies where there are multiple populations of interest (eg, parents, clinicians, teachers, grandparents), we will include them if at least 90% of parents were raising children with disabilities and will focus only on parent-specific data, analysis, and results. At least 90% of children of the parents included in the studies need to be children with lifelong disabilities who are aged ≤18 years.

Outcomes

We will consider parent-specific outcomes that fall under one of the following categories: physical well-being (eg, pain, fatigue), psychological functioning (eg, mental health, anxiety, depression, stress, self-efficacy, self-esteem, empowerment), and socioeconomic outcomes (eg, financial status, employment, friendships, sense of belonging, social support). Outcomes must be assessed by a validated tool or standardized measurement to be eligible for inclusion. We will extract data for individual outcomes, as reported in the original report.

Information Sources

We will search four electronic bibliographic databases: MEDLINE (1946-), PsycINFO (1987-), Embase (1984-), and CINAHL. We will also hand screen the reference lists of identified reviews and assess them for eligibility. Since the field of childhood disability has significantly changed in the last two decades due to advancements in health care thinking and societal changes, we will include only studies published since 2000. We will not apply any language or location criteria. Identified master's or doctoral dissertations that satisfy the eligibility criteria will also be considered for inclusion.

Search Strategy

Literature searches will include both subject headings and keywords with regard to the population, intervention, outcomes, and study design. The search strategy will be developed in collaboration with an experienced university librarian. A draft of the MEDLINE search strategy can be found in Table 1. The search might be rerun toward the end of the review.

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Table 1. MEDLINE search.

	Search terms
P (population): parents of children with developmental disabilities	• Parents/, Parent*.mp., Mothers/, mother*.mp., Fathers/, father*.mp. • (infant* or child* or teenage* or adolescen*).mp., Infant/ or child/ or adolescent/ • (disab* or disorder*).mp., Disabled Children/ • Child Development Disorders/, Pervasive/ or development* disorder*.mp. or Developmental Disabilities/, Neurodevelopmental Disorders/ or neurodevelopment* dis*.mp., Cerebral Palsy/ or cerebral palsy.mp., Spinal Dysraphism/ or spina bifida.mp. or spinal dysraphism.mp., Muscular Dystrophies/ or Muscular Dystrophy, Duchenne/ or muscular dystroph*.mp., Autistic Disorder/ or autis*.mp. or Autism Spectrum Disorder/, Asperger Syndrome/ or asperger syndrome*.mp., Attention Deficit Disorder with Hyperactivity/ or ADHD.mp. or attention deficit disorder*.mp., hyperactiv*.mp., Down Syndrome/ or Down syndrome*.mp., deaf*.mp. or Deafness/ or Deaf- Blind Disorders/ or blind*.mp. or Blindness/, Vision Disorders/ or vision disorder*.mp. or Visually Impaired Persons/ or visual impairment*.mp. or or deaf*blind*.mp., Intellectual Disability/ or intellectual dis*.mp.
I (intervention): any	• (intervention* or service* or program*).mp., (treatment* or therap*).mp., Mentoring/ or mentor*.mp., Counseling/ or counsel*.mp., support group*.mp., (peer-to-peer or peer to peer).mp.
O (outcomes): physical, psychological, and socioeconomic outcomes	• pain*.mp. or Pain/, discomfort.mp., Fatigue/ or fatigue.mp., (burnout or burn out or burn-out).mp. or Burnout, Psychological/, Anxi *.mp. or Anxiety/ or Anxiety Disorders/, Depression/ or depress*.mp., Stress, Psychological/ or stress*.mp., confiden*.mp., Self Efficacy/ or self*efficacy.mp., empower*.mp. Motivation/ or motivat*.mp., Mental Health/ or mental health.mp., worr*.mp., (wellbeing or well being or well- being).mp., Sick Leave/ or sick leave.mp., quality of life.mp. or “Quality of Life”/, productiv*.mp., Income/ or income.mp. or Poverty/, relationship*.mp., expense*.mp., Employment/ or employ*.mp., work.mp. or Work/, Job Satisfaction/ or Job Application/ or job*.mp., Social Support/ or social support.mp.
Study design: randomized controlled trials, quasi-randomized trials, mixed method trials	• (RCT* or randomized controlled trial*).mp. or (controlled trial* or controlled stud*).mp, (quasi-randomized or quasi-experimental*).mp., (quasi- randomized or quasi- experimental*)-.mp., (mixed-method* or mixed method*).mp.

Study Records

References yielded from the databases will be uploaded to Covidence Systematic Review Software [23]. We will use this web-based software program for deduplication and the first two levels of assessments: (1) title and abstract screening, and (2) full-text screening and eligibility assessment. Deduplication will be done automatically using Covidence and manually through the inspection of the reference list of identified reviews. The first author will manually upload the full-text reports after the first-level screening is completed. Data from the included studies will be extracted and stored in a Microsoft Excel spreadsheet [24]. Possible quantitative analysis will be done using the statistical software Stata (release 15.1; StataCorp LLC) [25] or R (R Foundation for Statistical Computing) [26].

Study Selection

Prior to starting to screen, a calibration exercise will be performed on at least 150 reference titles and abstracts to ensure consistency among the reviewers. Two reviewers (MNP and JY) will then independently screen titles and abstracts. Potentially eligible articles will move to the full-text screening phase. The two authors will then independently perform full-text screening for eligibility. Discrepancies in decisions between the reviewers will be resolved through discussion. If an agreement cannot be achieved, a third reviewer will be included. Additional information from study authors will be sought if critical information about the study is missing and the reviewers are unclear about its eligibility.

In cases where articles were published in languages that the two authors do not speak, we will consult with a native or bilingual colleague (researcher or graduate trainee) to determine its eligibility by looking at the full text. If a non-English full report is eligible, we will arrange an external translation service to create an English-language version before any data are extracted. Throughout the entire data extraction and interpretation process, we will continuously consult with colleagues fluent in that language to ensure accuracy.

Data extraction will be carried out in duplicate by two authors using a detailed data extraction manual. Any potential disagreements will be resolved through discussion. If further information about the study is required, we will contact the study authors directly (3 email attempts). If we identify multiple reports of a single study, we will treat them as one study.

Data Items

The following data will be extracted for the included articles:

- General information about the study (authors, year of publication, location, journal or other site where the record was published, study aim/research question)
- Study details (study design, unit of allocation, randomization/sampling strategy, number of groups)
- Information about the participants (population description, sample size, demographics, types of childhood disabilities, children’s age, control)
- Information about the intervention—modified Template for Intervention Description and Replication Checklist [27] (name and type of intervention, intervention description,

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materials/procedures, providers, setting in which the intervention occurred, duration, frequency, dose/intensity, format and mode of delivery, tailoring, modifications, fidelity, follow-up)
- Information about the parent-specific outcomes assessed (outcome name and definition, measures used, data collection time points, type of outcome [dichotomous, ordinal, continuous], baseline and first follow-up scores for continuous outcomes [mean, standard deviation, sample size] and number of events and sample size for dichotomous outcomes)
- Other information (key conclusions of study authors, adverse events, correspondence required)

Outcomes and Prioritization

Parents of children with disabilities can face challenges in multiple areas of life and functioning. In this study, we are interested to learn about the effects that interventions might have on three domains of well-being: *physical*, *psychological*, and/or *socioeconomic* well-being. We will extract data for outcomes that fit under one or more of these three categories.

For the purposes of this review, *physical outcomes* will be explicitly related to parents' physical health (eg, pain, muscle strength, cancer). An outcome will be considered *psychological* when it represents personal values, perceptions, judgments, feelings, or evaluations (eg, self-esteem, confidence, mental health, coping, self-efficacy). *Socioeconomic well-being outcomes* include various domains, such as social health and functioning and financial stability (eg, social support, relationships, employment). The judgment for inclusion of each outcome, and where it fits in the physical-psychological-socioeconomic map, will be done separately by two reviewers during the extraction phase. Potential discrepancies will be discussed.

Risk of Bias and Quality Assessment

The risk of bias will be assessed using the revised Cochrane risk-of-bias tool for randomized trials [28]. Each study will be evaluated with respect to sequence generation, allocation concealment, blinding, incomplete outcome data (≥20% missing data will be considered to be at high risk of bias), selective reporting, and other biases [28]. According to available information in the report, a judgment as to whether there is "high risk," "low risk," or "unclear risk" of bias will be made independently by two review authors. All potential disagreements in judgments will be discussed. The outcomes of the risk of bias assessment will be visually presented using RevMan [29] or Robvis [30].

The quality assessment of the outcomes of interest from the included studies will be done using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach [31]. We will first rate the importance of relevant outcomes in the literature as either *critical*, *important but not critical*, or *of limited importance* [32]. We will use the GRADE approach for rating the quality of evidence for each outcome or network estimate on an outcome-by-outcome basis. Network estimates quality will be rated based on the direct or indirect evidence that has contributed most to the network and will be rated as high, moderate, low, or very low quality based on the limitations in risk of bias, imprecision, inconsistency, indirectness, and publication bias. We will present the results of our quality assessment in a Summary of Findings table.

Data Synthesis

Data will be pooled if studies are homogeneous with respect to the intervention and outcomes measured. For each direct comparison, we will calculate standardized mean differences for the continuous outcomes or weighted mean differences if the outcomes are the same, and odds ratio for dichotomous outcomes with the associated 95% confidence intervals. Statistical heterogeneity will be assessed by visual inspection of forest plots and the I^2 statistic. I^2 of 0%-40% will be considered as "might not be important," 30%-60% as "moderate," 50%-90% as "substantial," and 75%-100% as "considerable" based on the Cochrane Handbook [33].

We will use the before and first follow-up measurements in cases of more than one assessment. We will perform a pairwise meta-analysis of the available direct comparisons using the DerSimonian–Laird random effects model for all outcomes. We will perform network meta-analysis to synthesize the available evidence from the entire network of trials by integrating direct and indirect estimates for each comparison into a single summary treatment effect. We will apply a frequentist random effects model using the methodology of multivariate meta-analysis to assess the comparative effectiveness of eligible interventions [34] in Stata [25].

We will perform a network meta-analysis to compare the effectiveness of identified interventions if the assumption of transitivity is met, meaning that "there are no systematic differences between the available comparisons other than the treatments being compared" [35]. The transitivity assumption will be assessed by investigating effect modifiers. If transitivity is not demonstrated, we will consider building separate networks for analysis. We will create network graphs to visualize the geometry of the networks and evaluate the networks' statistical incoherence with global design-by-treatment and local approaches using the node-splitting method. We will assume a common heterogeneity estimate across the network.

If conventional meta-analysis and network meta-analysis cannot be done for any methodological or data-related reason(s), the results will be presented qualitatively. We will use summary tables and figures to present our results.

Results

The first search of the literature of this systematic review commenced in September 2020 (from 2000). Due to the longevity of the process and limited resources, we ran an updated search on January 23, 2022 (from 2020). Data extraction for the first round of screening was initiated in June 2021. After the updated search was run and reference screening was completed in March 2022, we also started the data extraction for the remaining articles, a process that is currently underway. As of May 30, 2022, we have extracted the majority of data that were available in reports but are still in contact with the original authors of some of the studies for additional information. For

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example, we reached out to some authors to ask about the availability of a data subset or subgroup analysis, as well as some further details about the study execution that will confirm the studies' eligibility and direct our analytic approach. We plan to conduct the analysis in June and July 2022 and publish the results of this study within one year of publishing this protocol.

Discussion

Overview

This systematic review will provide a better understanding of the effectiveness of available programs that can be used to support the physical, psychological, and socioeconomic well-being of parents of children with neurodevelopmental disabilities. Based on the findings, we will determine the strength and quality of evidence for making recommendations for the implementation of evidence-based programs that support parents. Directions for future research will be discussed.

Research indicates that parents of children with neurodevelopmental disabilities face common challenges in their caregiving role across different types of childhood disability [36,37]. On the other hand, the realities of two families who both have, for example, a child on the autism spectrum might be hugely different. An approach that recognizes the commonalities of experiences of families of children with different types of disabilities, as well as the variations within the same disability category, is called *a noncategorical approach* [38]—an approach we have taken in this study. Despite the differences between families, evidence supports that parents value opportunities to connect with parents of children with different diagnoses and can greatly benefit from such opportunities [39]. Due to the expected heterogeneity of the population and interventions reported in eligible studies in this review, we anticipate that the statistical analysis will require multiple team discussions and careful consideration of all the factors (eg, study setting, population characteristics, type of intervention). Because of the breadth of our research question and lack of homogeneity of studies, we might be limited in our ability to conduct a robust statistical analysis and make strong clinical recommendations based on statistical findings. However, this study will provide a wide overview of the work that has been done to support parent-specific needs, with an aim of addressing their health and well-being. We also expect that this systematic review will identify gaps in the literature and provide direction for creating family-centered, needs-based, accessible solutions for supporting parent-caregivers.

Amendments

All the potential changes to this protocol will be published as amendments on our PROSPERO protocol webpage. We will share the date of each amendment, the changes we make, and the rationale for them.

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Authors' Contributions

MNP is the guarantor. MNP, PR, LM, BDR, and JY contributed to the idea and design of this study. LM, AN, and MNP developed the analysis plan. LM and AN provided statistical expertise. MNP developed the search strategy in collaboration with the university librarian. MNP wrote the initial draft of this manuscript and all the other authors revised it. All authors approved the final manuscript.

Conflicts of Interest

None declared.

References

1. Gupta A, Singhal N. Positive perceptions in parents of children with disabilities. Asia Pac Disabil Rehab J 2004;15(1):22-35 [FREE Full text]
2. Raina P, O'Donnell M, Schwellnus H, Rosenbaum P, King G, Brehaut J, et al. Caregiving process and caregiver burden: conceptual models to guide research and practice. BMC Pediatr 2004 Jan 14;4(1):1 [FREE Full text] [doi: 10.1186/1471-2431-4-1] [Medline: 14723791]
3. Hastings RP, Taunt HM. Positive perceptions in families of children with developmental disabilities. Am J Ment Retard 2002 Mar;107(2):116-127. [doi: 10.1352/0895-8017(2002)107<0116:PPIFOC>2.0.CO;2] [Medline: 11853529]
4. Scorgie K, Wilgosh L, McDonald L. Education and training in mental retardation and developmental disabilities. Div Autism Dev Disab 1999;34(4):395-405 [FREE Full text]
5. Stainton T, Besser H. The positive impact of children with an intellectual disability on the family. Journal of Intellectual & Developmental Disability 2009 Jul 10;23(1):57-70 [FREE Full text] [doi: 10.1080/13668259800033581]
6. Brehaut JC, Kohen DE, Garner RE, Miller AR, Lach LM, Klassen AF, et al. Health among caregivers of children with health problems: findings from a Canadian population-based study. Am J Public Health 2009 Jul;99(7):1254-1262. [doi: 10.2105/AJPH.2007.129817] [Medline: 19059861]
7. Bonis S. Stress and parents of children with autism: a review of literature. Issues Ment Health Nurs 2016 Mar 30;37(3):153-163. [doi: 10.3109/01612840.2015.1116030] [Medline: 27028741]

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8. Cohn LN, Pechlivanoglou P, Lee Y, Mahant S, Orkin J, Marson A, et al. Health outcomes of parents of children with chronic illness: a systematic review and meta-analysis. J Pediatr 2020 Mar;218:166-177.e2. [doi: 10.1016/j.jpeds.2019.10.068] [Medline: 31916997]
9. Cohen E, Horváth-Puhó E, Ray JG, Pedersen L, Adler N, Ording AG, et al. Association between the birth of an infant with major congenital anomalies and subsequent risk of mortality in their mothers. JAMA 2016 Dec 20;316(23):2515-2524. [doi: 10.1001/jama.2016.18425] [Medline: 27997654]
10. Cohen E, Horváth-Puhó E, Ray JG, Pedersen L, Ehrenstein V, Adler N, et al. Cardiovascular disease among women who gave birth to an infant with a major congenital anomaly. JAMA Netw Open 2018 Sep 07;1(5):e182320 [FREE Full text] [doi: 10.1001/jamanetworkopen.2018.2320] [Medline: 30646164]
11. Kuo DZ, Cohen E, Agrawal R, Berry JG, Casey PH. A national profile of caregiver challenges among more medically complex children with special health care needs. Arch Pediatr Adolesc Med 2011 Nov;165(11):1020-1026 [FREE Full text] [doi: 10.1001/archpediatrics.2011.172] [Medline: 22065182]
12. Lach LM, Kohen DE, Garner RE, Brehaut JC, Miller AR, Klassen AF, et al. The health and psychosocial functioning of caregivers of children with neurodevelopmental disorders. Disabil Rehabil 2009 Jul 07;31(8):607-618. [doi: 10.1080/09638280802242163] [Medline: 19360498]
13. Keilty K, Cohen E, Spalding K, Pullenayegum E, Stremler R. Sleep disturbance in family caregivers of children who depend on medical technology. Arch Dis Child 2018 Feb 26;103(2):137-142. [doi: 10.1136/archdischild-2016-312205] [Medline: 29074731]
14. Keilty K, Cohen E, Ho M, Spalding K, Stremler R. Sleep disturbance in family caregivers of children who depend on medical technology: A systematic review. J Pediatr Rehabil Med 2015;8(2):113-130. [doi: 10.3233/PRM-150325] [Medline: 26409865]
15. Czupryna K, Nowotny-Czupryna O, Nowotny J. Back pain in mothers of cerebral palsied children. Ortop Traumatol Rehabil 2014 Oct 3;16(5):497-505. [doi: 10.5604/15093492.1128840] [Medline: 25406923]
16. Tong HC, Haig AJ, Nelson VS, Yamakawa KS, Kandala G, Shin KY. Low back pain in adult female caregivers of children with physical disabilities. Arch Pediatr Adolesc Med 2003 Nov 01;157(11):1128-1133. [doi: 10.1001/archpedi.157.11.1128] [Medline: 14609905]
17. Tonga E, Düger T. Factors affecting low back pain in mothers who have disabled children. Journal of Back and Musculoskeletal Rehabilitation 2008 Dec 23;21(4):219-226. [doi: 10.3233/bmr-2008-21401]
18. Emerson E. Mothers of children and adolescents with intellectual disability: social and economic situation, mental health status, and the self-assessed social and psychological impact of the child's difficulties. J Intellect Disabil Res 2003 May;47(Pt 4-5):385-399. [doi: 10.1046/j.1365-2788.2003.00498.x] [Medline: 12787168]
19. King G, Williams L, Hahn Goldberg S. Family-oriented services in pediatric rehabilitation: a scoping review and framework to promote parent and family wellness. Child Care Health Dev 2017 May 12;43(3):334-347. [doi: 10.1111/cch.12435] [Medline: 28083952]
20. Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ 2015 Jan 02;350:g7647 [FREE Full text] [doi: 10.1136/bmj.g7647] [Medline: 25555855]
21. Hutton B, Salanti G, Caldwell DM, Chaimani A, Schmid CH, Cameron C, et al. The PRISMA extension statement for reporting of systematic reviews incorporating network meta-analyses of health care interventions: checklist and explanations. Ann Intern Med 2015 Jun 02;162(11):777-784 [FREE Full text] [doi: 10.7326/M14-2385] [Medline: 26030634]
22. Institute of Medicine (US) Committee on Nervous System Disorders in Developing Countries. Neurological, psychiatric, and developmental disorders: meeting the challenge in the developing world. In: Institute of Medicine (US) Committee on Nervous System Disorders in Developing Countries. Washington, DC: National Academies Press (US); 2001:113-115.
23. Covidence. URL: http://www.covidence.org/ [accessed 2022-06-27]
24. Microsoft Excel. Microsoft Corporation. URL: https://www.microsoft.com/en-us/microsoft-365/excel [accessed 2022-06-27]
25. Stata Statistical Software: Release 17. StataCorp LLC. 2017. URL: https://www.stata.com/ [accessed 2022-06-27]
26. R. R Core Team. URL: https://www.r-project.org/ [accessed 2022-06-27]
27. Hoffmann TC, Glasziou PP, Boutron I, Milne R, Perera R, Moher D, et al. Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide. BMJ 2014 Mar 07;348:g1687. [doi: 10.1136/bmj.g1687] [Medline: 24609605]
28. Sterne JAC, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. BMJ 2019 Aug 28;366:l4898. [doi: 10.1136/bmj.l4898] [Medline: 31462531]
29. Review Manager Web (RevMan Web). The Cochrane Collaboration. URL: https://training.cochrane.org/online-learning/core-software/revman [accessed 2022-06-27]
30. McGuinness LA, Higgins JPT. Risk-of-bias VISualization (robvis): An R package and Shiny web app for visualizing risk-of-bias assessments. Res Synth Methods 2021 Jan;12(1):55-61. [doi: 10.1002/jrsm.1411] [Medline: 32336025]
31. Schünemann H, Brożek J, Guyatt G, Oxman A. GRADE Handbook. URL: https://gdt.gradepro.org/app/handbook/handbook.html#h.svwngs6pm0f2 [accessed 2022-04-08]

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32. Puhan MA, Schünemann HJ, Murad MH, Li T, Brignardello-Petersen R, Singh JA, GRADE Working Group. A GRADE Working Group approach for rating the quality of treatment effect estimates from network meta-analysis. BMJ 2014 Sep 24;349:g5630. [doi: 10.1136/bmj.g5630] [Medline: 25252733]
33. Higgins JPT, Thomas J, Chandler J, Cumpston M. Cochrane Handbook for Systematic Reviews of Interventions. URL: https://training.cochrane.org/handbook/current [accessed 2022-04-08]
34. White IR. Multivariate random-effects meta-analysis. The Stata Journal 2009 Mar 01;9(1):40-56. [doi: 10.1177/1536867x0900900103]
35. Rouse B, Chaimani A, Li T. Network meta-analysis: an introduction for clinicians. Intern Emerg Med 2017 Feb;12(1):103-111 [FREE Full text] [doi: 10.1007/s11739-016-1583-7] [Medline: 27913917]
36. Nuri RP, Batorowicz B, Aldersey HM. Family support and family and child-related outcomes among families impacted by disability in low- and middle-income countries: A scoping review. J Child Health Care 2020 Dec;24(4):637-654. [doi: 10.1177/1367493519883456] [Medline: 31648535]
37. Hsiao Y. Parental stress in families of children with disabilities. Intervention in School and Clinic 2017 Jun 14;53(4):201-205. [doi: 10.1177/1053451217712956]
38. Nagel K, Robinson S, Rosenbaum P. Pediatric healthcare quality: A novel approach to lifelong child health research. J Healthc Qual 2008;30(2):31-36. [doi: 10.1111/j.1945-1474.2008.tb01132.x] [Medline: 18411890]
39. Shilling V, Morris C, Thompson-Coon J, Ukoumunne O, Rogers M, Logan S. Peer support for parents of children with chronic disabling conditions: a systematic review of quantitative and qualitative studies. Dev Med Child Neurol 2013 Jul;55(7):602-609 [FREE Full text] [doi: 10.1111/dmcn.12091] [Medline: 23421818]

Abbreviations

GRADE: Grading of Recommendations, Assessment, Development and Evaluation
PRISMA-P: Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols
PROSPERO: International Prospective Register of Systematic Reviews
RCT: randomized controlled trial

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Protocol

A Rapid-Learning Health System to Support Implementation of Early Intervention Services for Psychosis in Quebec, Canada: Protocol

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Abstract

Background: Given the strong evidence of their effectiveness, early intervention services (EIS) for psychosis are being widely implemented. However, heterogeneity in the implementation of essential components remains an ongoing challenge. Rapid-learning health systems (RLHSs) that embed data collection in clinical settings for real-time learning and continuous quality improvement can address this challenge. Therefore, we implemented an RLHS in 11 EIS in Quebec, Canada.

Objective: This project aims to determine the feasibility and acceptability of implementing an RLHS in EIS and assess its impact on compliance with standards for essential EIS components.

Methods: Funding for this project was secured in July 2019, and ethics approval was received in December 2019. The implementation of this RLHS involves 6 iterative phases: external and internal scan, design, implementation, evaluation, adjustment, and dissemination. Multiple stakeholder groups (service users, families, clinicians, researchers, decision makers, and provincial EIS associations) are involved in all phases. Meaningful EIS quality indicators (eg, satisfaction and timeliness of response to referrals) were selected based on a literature review, provincial guidelines, and stakeholder consensus on prioritization of indicators. A digital infrastructure was designed and deployed comprising a user-friendly interface for routinely collecting data from programs; a digital terminal and mobile app to collect feedback from service users and families regarding care received, health, and quality of life; and data analytic, visualization, and reporting functionalities to provide participating programs with real-time feedback on their ongoing performance in relation to standards and to other programs, including tailored recommendations. Our community of practice conducts activities, leveraging insights from data to build program capacity while continuously aligning their practices with standards and best practices. Guided by the RE-AIM (Reach, Effectiveness, Adoption, Implementation, Maintenance) framework, we are collecting quantitative and qualitative data on the reach, effectiveness, adoption, implementation, and maintenance of our RLHS for evaluating its impacts.

Results: Phase 1 (identifying RLHS indicators for EIS based on a literature synthesis, a survey, and consensus meetings with all stakeholder groups) and phase 2 (developing and implementing the RLHS digital infrastructure) are completed (September 2019 to May 2020). Phases 3 to 5 have been ongoing (June 2020 to June 2022). Continuous data collection through the RLHS data capture platforms and real-time feedback to all stakeholders are deployed. Phase 6 will be implemented in 2022 to assess

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the impact of the RLHS using the Reach, Effectiveness, Adoption, Implementation, and Maintenance framework with quantitative and qualitative data.

Conclusions: This project will yield valuable insights into the implementation of RLHS in EIS, offering preliminary evidence of its acceptability, feasibility, and impacts on program-level outcomes. The findings will refine our RLHS further and advance approaches that use data, stakeholder voices, and collaborative learning to improve outcomes and quality in services for psychosis.

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KEYWORDS

rapid-learning health system; early intervention for psychosis; measurement-based care; real-time electronic data capturing; patient-oriented research; knowledge translation; mobile phone

Introduction

Psychotic disorders, which include schizophrenia-spectrum and affective psychoses (bipolar and major depressive disorders with psychosis), have a lifetime prevalence of 3% to 3.5% [1,2] and typically emerge during a major neuro-sociodevelopmental period (age 15-30 years), posing further challenges in the early stages of illness management. Early intervention services (EIS) are now widely recognized as more effective than routine care for the treatment of psychosis [3-5] in the critical first 2- to 5-year period [6]. EIS aim to reduce the duration of untreated psychosis (ie, the delay between the first psychotic symptoms and initiation of adequate treatment), which negatively affects clinical and functional outcomes [7-10], and to positively affect longer-term outcome trajectories by maximizing symptomatic, functional, and recovery outcomes in this critical period. The EIS model was designed to address ubiquitous challenges in treating psychotic disorders, such as poor service engagement, medication nonadherence, and comorbid substance use, which are particularly salient in the early years [6,11]. This period is also associated with maximum risk of tragic outcomes such as violence, social and vocational impairment, long-term disability, and suicide [6,8,12-15].

Many countries [16,17], including Canada, have implemented the EIS model. On the basis of international and national guidelines for quality care, the model includes, among other essential components, an open referral process, timely access to treatment (reduced treatment delay), active engagement of service users and family members encouraged by a youth-friendly atmosphere, and comprehensive team-based care that combines pharmacological treatment using the lowest effective doses of antipsychotic medications with the provision of integrated, evidence-based psychosocial interventions [16,18,19]. Appropriate patient-staff ratios and continuous professional development are also recommended by the model [16,18,19].

In Canada, Ontario and British Columbia have taken the lead in developing EIS policies and creating provincial EIS networks [16,17]. In the late 1990s, clinicians supported by their institutions led the initial development of EIS in Quebec, where this research team is based. This was followed by the creation of the *Association québécoise des programmes pour premiers épisodes psychotiques* (AQPPEP), the Quebec association of EIS, in 2004. Support for the implementation of EIS across jurisdictions is enhanced by continuous professional development; networking; mentoring; communities of practice; and the promotion of evidence-based practices, use of clinical guidelines, and innovation. However, despite these efforts, EIS implementation in Canada [20-22] and internationally [23-25] has long been impeded by a lack of standards in some jurisdictions and implementation challenges related to delivering complex models of care in real-life settings [21,22,26]. Research has identified major challenges in relation to integrating essential organizational components (eg, open referral processes and appropriate patient-case manager ratios) [22] and insufficient funding and mentoring to ensure consistent implementation [22-25], as well as lack of systematic monitoring related to quality-of-care indicators and outcomes [21,22,26].

In 2017, the Quebec Ministry of Health and Social Services invested an additional CAD $10 million (US $7,905,200) to improve existing EIS and develop new services in underserved regions, adding approximately 16 new teams for a total of 33 EIS teams by 2020, which doubled EIS coverage across the province in <3 years. The Ministry of Health and Social Services also published the 2017 *Cadre de référence - Programmes d'interventions pour premiers épisodes psychotiques*, the Quebec guidelines for EIS, providing guidance on the essential components and related indicators for EIS. Although service improvements have been observed since the promulgation of this policy and related funding commitments, gaps remain in the implementation and real-time monitoring of practices related to EIS standards in Quebec [21]. Indeed, a survey conducted with 28 of the 33 Quebec EIS in 2020 revealed that administrative and organizational components such as clinical and administrative data collection, adherence to recommended patient to case manager ratios, and quality assurance monitoring were less widely implemented [21]. Moreover, many EIS were not able to offer some recommended specialized treatments such as cognitive behavioral therapy or peer support, often because of the lack of appropriately trained professionals.

In other fields of medicine, rapid-learning health systems (RLHSs) that embed data collection in clinical settings for real-time learning and continuous quality improvement have been deployed to improve service quality. We designed and piloted an RLHS to support Quebec EIS by systematically collecting real-time data for use in improving service quality and clinical practice.

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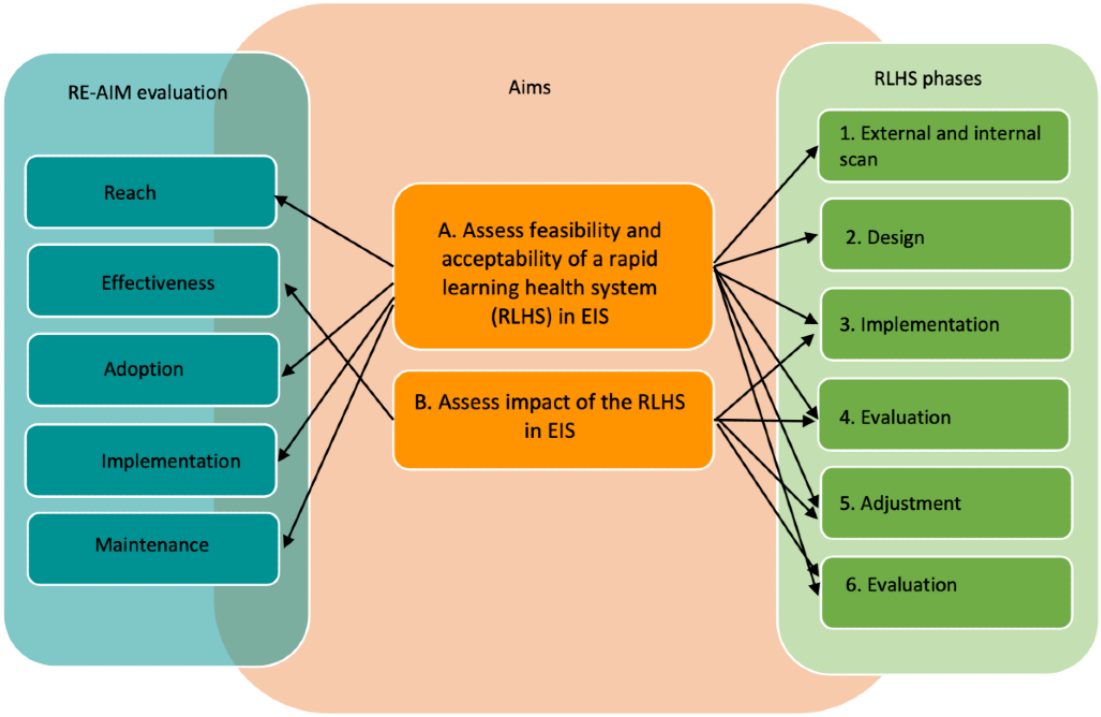
Methods

Objectives

The primary objective of this multiphase, mixed methods project is to determine the feasibility and acceptability of implementing an RLHS in EIS. The secondary objective is to evaluate the 2-year impact of the RLHS on patient-, family-, EIS-, and provincial-level outcomes (Figure 1).

More specifically, feasibility and acceptability were evaluated in terms of 2 objectives using the Reach, Effectiveness, Adoption, Implementation, and Maintenance (RE-AIM) framework. Objective 1 investigates the reach, adoption, implementation, and maintenance of (1) a user-friendly electronic platform that captures continuous data on selected service quality indicators from individual EIS, (2) continuous data-informed feedback to EIS, and (3) data-informed and capacity-building activities tailored to EIS members of our RLHS and the overall Quebec EIS community for improving service quality where EIS components are weaker. Objective 2 addresses *effectiveness* by evaluating improvements in (1) adherence to EIS components among participating EIS, (2) capacity of the EIS to collect data for monitoring quality of care, (3) key patient and family outcomes, and (4) program-level and provincial decision-making related to meeting quality-of-care standards in EIS.

Figure 1. Project conceptual framework. EIS: early intervention services; RE-AIM: Reach, Effectiveness, Adoption, Implementation, and Maintenance framework; RLHS: rapid-learning health system.



RLHS: A Novel Paradigm in EIS Implementation

The new RLHS health care paradigm [27] has been shown to promote innovation and responsiveness by bridging the gap between evidence and practice and improving efficiency, effectiveness, and quality in health care delivery, primarily in medical health care settings [28-32]. Among the various definitions of RLHS [28-31], the most frequently cited is the Institute of Medicine definition, which envisions "the development of a continuously learning health system in which science, informatics, incentives, and culture are aligned for continuous improvement and innovation, with best practices seamlessly embedded in the delivery process and new knowledge captured as an integral by-product of the delivery experience" [33]. According to the Institute of Medicine, an RLHS uses digital technologies to (1) generate and apply the best evidence to support collaborative health care choices by patients and providers; (2) drive the discovery process as a natural outgrowth of patient care; and (3) ensure quality, safety, value, and innovation in health care [33,34]. Digital technology, hardware, and software that process and transmit digital information (eg, electronic health records, databases, analytic tools, and visual dashboards) are at the core of the RLHS, providing data and information as catalysts for system *learning* and the transformation of clinical practice.

The RLHS addresses the knowledge-to-practice gap in medical care through the rapid and ethical transfer of knowledge produced by clinical research into routine clinical practice [35,36]. The RLHS can foster a culture of shared responsibility between clinicians and patients [37,38] and facilitate engagement by patients, clinical teams, and program managers for the production and dissemination of evidence to the public [39]. Thus, an RLHS was chosen as an innovative research paradigm to guide the transformation of the Quebec EIS system by addressing previously identified gaps such as lack of or inconsistent monitoring of quality and performance and gaps between standards, evidence, and actual practice.

This study, conducted in partnership with EIS and key stakeholders, is grounded in principles of patient-oriented

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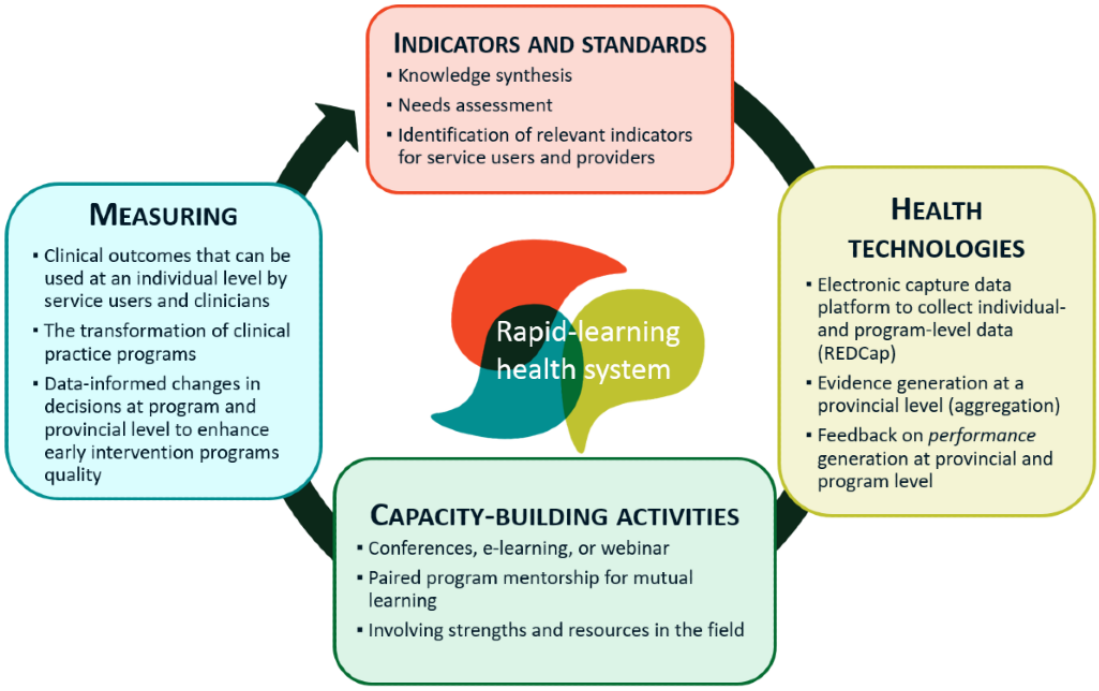
research that support meaningful and active engagement by patients and families. Adhering to this framework, we invited participation by patients, families, and knowledge users (eg, program administrators, clinicians, and representatives of the *Centre national d'excellence en santé mentale* of the Quebec Ministry of Health and Social Services mental health advisory branch) to develop the study (eg, study design and choice of outcomes), and we will continue this practice in the implementation and dissemination of the study findings.

Guided by the literature [27,33,34], the implementation of our RLHS involves 6 iterative phases (objective 1), as shown in Figure 2. These phases are outlined in Textbox 1.

Guided by the RE-AIM framework, we are in the process of collecting quantitative and qualitative data on the reach, effectiveness, adoption, implementation, and maintenance of the RLHS. These RE-AIM data will be analyzed to evaluate the impact of the RLHS and address the 2 study objectives.

Figure 2. Rapid-learning health system for early intervention for psychosis.



Textbox 1. The 6 iterative phases of implementation in our rapid-learning health system (RLHS).

Implementation phases

1. Identification of indicators in the RLHS for early intervention services (EIS) through an external and internal scan and building of the RLHS community. This involves a knowledge synthesis of relevant peer-reviewed literature and EIS guidelines (external scan) and an environmental scan in the form of a survey with selected EIS (internal scan), followed by the selection of meaningful indicators for quality care in EIS.
2. Design and setup of a digital infrastructure for our RLHS to collect data routinely and iteratively regarding selected indicators of quality care in EIS.
3. Implementation of the RLHS data capture platform in real-life settings while systematically and continuously analyzing data to generate new evidence and recommendations for improvement of the RLHS.
4. Use of RLHS digital technologies to collect data, perform analysis, and propose recommendations for subsequent clinical care as well as capacity-building activities tailored to evolving needs in individual EIS as identified by the data collected.
5. Evaluation of outcomes related to clinical practice and program-level changes.
6. Evaluation of overall outcomes of the RLHS and dissemination of findings to key stakeholders.

Study Settings

The RLHS literature recommends small-scale pilot-testing of digital technologies to build knowledge and confidence regarding complex digital systems as such innovations are often viewed skeptically by health care clinicians and managers [27,33,34]. For this reason, we purposefully selected a maximum variation sample of 11 EIS among the 33 existing EIS in Quebec based on various characteristics: environment (academic and nonacademic), setting (urban, semiurban, and rural), years of operation (<5 years vs >10 years), and patient age range covered by admission criteria (adolescents only, young adults only, or both; Table 1). EIS were also selected for their willingness to improve services and to represent diversity in relation to the previously identified implementation challenges they have faced [21]. All 11 EIS invited to the study agreed to participate, although 18% (2/11) mentioned staffing problems as a potential barrier to full participation in the project. These EIS were

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retained as staffing is an important issue in real-world implementation. As *early adopters*, these EIS will guide implementation and future scale-up of the RLHS. Representatives of the 11 selected EIS participated in activities leading to the development of this protocol and in project implementation activities.

Table 1. Characteristics of the selected sites.

EIS[a] for psychosis	Location of the EIS: urban, semirural, or rural	Years of operation	Active service users, N	Full-time staff, N
1	Urban	>10	290	16
2	Urban	>10	220	10
3	Urban	>10	150	12
4	Urban	>10	45	2
5	Urban	>10	270	14
6	Urban	>10	180	3
7	Urban-semirural	<5	190	10
8	Semirural	>10	30	4
9	Semirural	<5	130	10
10	Semiurban and rural	>10	60	3
11	Urban and semirural	<5	130	7

[a]EIS: early intervention services.

Objective 1: Assess Feasibility and Acceptability of an RLHS in EIS

Phase 1: Identifying Indicators for the RLHS for EIS Through an External and Internal Scan and Building the RLHS Community (Completed)

Quality indicators are measures or metrics based on guidelines or health organization directives used in monitoring the quality of patient care [40,41]. The research team identified indicators based on extensive literature reviews, including an external environmental scan of published national and international EIS guidelines and fidelity scales, and the peer-reviewed literature on program evaluation and outcomes in EIS [20,22,42]. The team then conducted an internal environmental scan using an email survey (unpublished data) inviting clinicians, team leaders, local decision makers and managers from participating EIS, and other key stakeholders (service users, caregivers, researchers, and representatives from the *Centre national d'excellence en santé mentale*, Quebec Ministry of Health and Social Services) to prioritize the indicators by importance, document the degree of implementation for each indicator in their respective EIS, estimate the capacity to improve implementation with the available resources, and determine the availability and level of data already collected for each indicator. We also assessed what resources would be needed in each EIS for measurement of the designated indicators. In total, 2 group discussions were convened by videoconference with representatives of the stakeholder groups representing the various EIS to gather input, as shown in Figure 3.

Table 2 provides the final list of evidence-based indicators and corresponding data collection procedures. In keeping with the RLHS requirements, we chose measurable indicators (eg, delay between referral and initial evaluation; a scale for self-rated clinical outcomes). These indicators were also chosen to balance maximum impact on program quality and patient outcomes with minimal burden related to data collection for the participating EIS.

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Figure 3. Involvement of stakeholders in our rapid-learning health system for early intervention for psychosis.

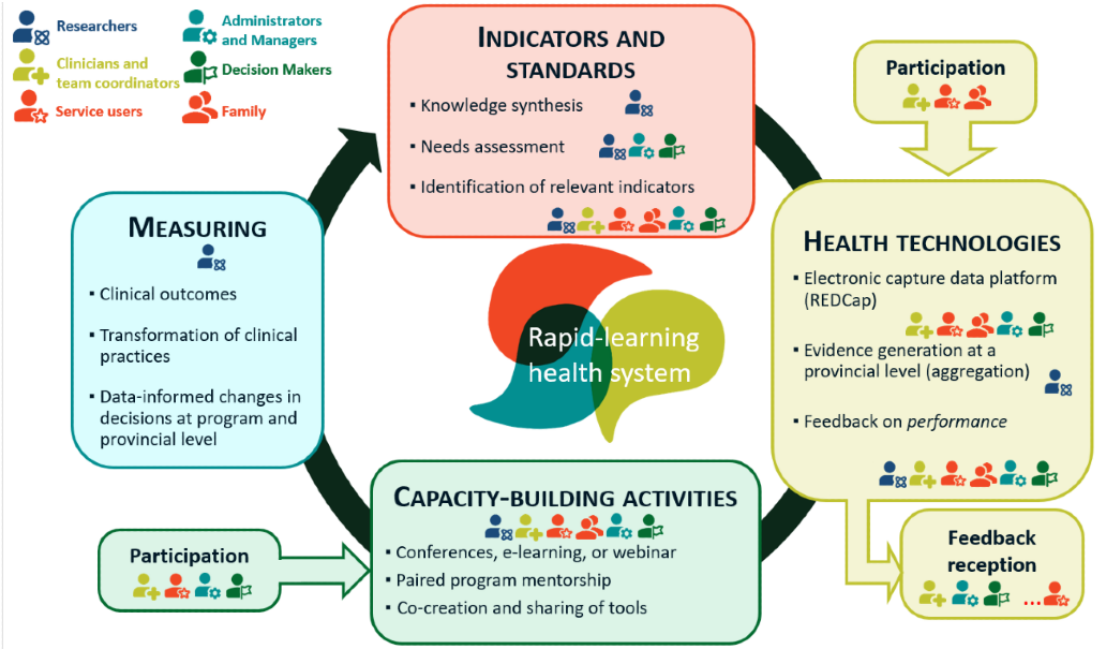

Table 2. List of indicators and examples of data collected for each indicator.

Indicators	Examples of data collected
Service user engagement and satisfaction with services	• Services adapted to the needs of young people • Youth-friendly environment • Disengagement • Outreach practices • Youth satisfaction
Family engagement	• Type of intervention offered • Percentage of families reached • Number of visits • Satisfaction of family members
Access to care—pathways	• Direct access • Referral sources, including self and the community • Inclusion and exclusion criteria • Number of contacts before access

Access to care—systemic delays	• Time between referral and
	  • First contact
	  • First assessment
	  • Start of treatment

Continuous education	• Number and type of continuing education events attended by workers • Supervision and mentoring
Provider-to-patient ratios	• Patient: Mental professional ratio • Patient: Psychitriest ratio
Evidence-based practices and recovery-oriented practices	• Cognitive behavioral therapy, family intervention, employment or study programs, integrated treatment for substance use disorders, and peer support • Type of specialists who offer the interventions • Percentage of patients receiving long acting injectable antipsychotics • Percentage of patients receiving clozapine
Self-reported outcomes by the patient	• Patient's evaluation of their health, recovery, and quality of life

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Phase 2: Designing the RLHS by Building Digital Infrastructure (Completed)

Program-level indicator data are collected using the REDCap (Research Electronic Data Capture; Vanderbilt University) digital platform, which provides an open-access, user-friendly, secure electronic health data capture platform for routinely collecting real-time clinical data. Hosted by the *Centre de Recherche du Centre Hospitalier de l'Université de Montréal*, REDCap allows the team leader of each participating EIS to collect program-level data. The platform is accessible from any electronic device (eg, computer, tablet, or smartphone) through a secure, open-access website. Each EIS can independently import data by answering specific multiple-choice and open-ended questions on selected indicators.

Data from service users and family members on the quality of services, an often-neglected indicator in the literature, are collected during on-site, web-based, or outreach clinical appointments. Each participating EIS collects information on service user satisfaction using the *Happy or Not* wireless digital terminals conveniently located on the walls of waiting rooms. Alternatively, service users can access the questionnaire on the web using any electronic device through a bar code scan. The questionnaire includes 3 questions. The first asks the following: *Are you satisfied with the service you received today?* Using 4 smiley-face emoticon buttons on the terminals, service users respond by choosing a face indicating whether they are *very happy*, *happy*, *unhappy*, or *very unhappy* with the service they received. The second question asks the following: *Among the following items, which one did you appreciate the most/least: quality of care and services, being welcomed with respect, feeling listened to, waiting time, respect for my opinion, something else?* These items were selected based on a literature review of youth-friendly mental health services and prioritized by consensus with service user representatives. Finally, comments are solicited using an open textbox.

A second REDCap-supported digital questionnaire for a more comprehensive evaluation of service quality and self-evaluation of personal recovery dimensions may be completed on the web or with any electronic device using a bar code scan or weblink. This quality-of-service digital questionnaire provides service users and family members with access to either the same questionnaire as the one on the service user feedback terminal with the 4 smiley-face emoticons (1-2–minute duration) or a more detailed version (10-minute duration). Satisfaction with the most recent on-site, web-based, or outreach clinical appointment may be evaluated, as well as service users' perceptions dating from the beginning of the EIS. Finally, service users can rate their satisfaction with their health situation, quality of life and recovery, and the impact of services on their recovery journey.

Phase 3: Implementing the RLHS Data Capture Platforms (Completed) and Feedback Development (Ongoing)

New digital technologies (eg, the REDCap digital platform for EIS clinicians, smiley-face emoticon feedback terminals, bar code scans, and REDCap satisfaction with services questionnaire) were presented to key stakeholders for comments, and adjustments were made before deployment. The technologies were then tested with at least two representatives from each stakeholder group (service users, family members, EIS coordinators, and managers) to ensure clarity of content and effectiveness of the digital tools. Learning from these usability testing activities was compiled and used by the RLHS project coordinator during web-based or on-site meetings with EIS managers, coordinators, or leaders to support easy, safe, and effective uptake of the RLHS. This implementation strategy leads to high program engagement and strengthens partnerships between researchers, experts, clinical staff, managers, and EIS leaders.

Phase 4: Using RLHS Digital Technologies to Collect Data, Perform Analysis, and Share Results and Feedback With EIS and All Stakeholders (Ongoing)

Data Collection and Support

The RLHS collects data on selected indicators from each participating EIS at 4-month intervals using the REDCap platform (Table 2). Maintaining regular or as-needed contact with each EIS via web conferencing, telephone, email, or in person, the project coordinator supports participating EIS with data collection, use of the REDCap platform, and integration of the collected data into clinical routines. EIS leaders and coordinators enter data on organizational indicators (eg, number of clinical staff, caseload, and referral sources) and evidence-based interventions offered (eg, cognitive behavioral therapy, supported employment, and family interventions) directly into the REDCap digital platform.

Continuous, Real-Time Feedback to the EIS on Quality Indicators for Essential Components

After completion of the quarterly data collection cycle by the clinical team leader, the RLHS provides feedback to each EIS in the form of an individualized, user-friendly graphic report generated quarterly. Progress on specific program-level indicators can be tracked by each EIS over time, and its implementation level can be compared with the aggregated data from other participating EIS and with provincial standards. This feedback indicates whether the EIS meets or does not meet the provincial benchmarks for each specific indicator, providing the rationale for each essential component and guidance on how to improve implementation. The RLHS then uses the feedback system to guide subsequent actions toward better-informed and evidence-based implementation [28]. Moreover, the aggregated data on service user and family perceptions of quality and satisfaction with services, including their self-assessments of progress toward clinical recovery, are integrated into the REDCap digital platform, allowing the RLHS to provide regular service user feedback to the individual EIS.

The EIS may receive feedback reports on services and the service user or family satisfaction *happy or not* questionnaire by email or through a website, selecting a preferred frequency (eg, daily, weekly, or monthly). The EIS may also monitor their overall progress for selected periods (eg, daily, weekly, monthly, or quarterly). These 2 reports may be used for administrative reporting; advocacy work to secure resources; guidance; support

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for quality improvement in services; or descriptions of clinical services tailored to service users, families, or other audiences.

Phase 5: Evaluating Outcomes Related to Change at the Program Level Based on Capacity-Building Activities (Ongoing)

Capacity building is understood as an evidence-driven process for strengthening the abilities of individuals, organizations, and systems to perform core functions effectively, efficiently, and sustainably, continuously improving and developing them over time [43]. Capacity-building activities are geared toward helping program managers, clinical team leaders, and clinicians use data effectively to improve the quality of clinical practices, aligning them with guidelines and tailoring practices to data-identified program needs. These activities take the form of knowledge exchange events for improving knowledge and clinical skills while providing program representatives and stakeholders with opportunities to share their experiences, increase self-assessment skills, and participate more fully in the RLHS.

The AQPPEP and the *Centre national d'excellence en santé mentale* of the Quebec Ministry of Health and Social Services have been partners in designing this project. Project-related webinars and web-based training with participating EIS occur roughly 3 times a year and are conducted with program leaders, coordinators, or managers of each participating EIS. Clinical teams from participating EIS are met by the RLHS research team or representatives from the *Centre national d'excellence en santé mentale*, who explain the project, examine the EIS feedback reports in further detail highlighting strengths and challenges of the EIS, and discuss the rationale behind essential components and alternative ways of reaching goals. In addition to these meetings involving all participating EIS, we are partnering with the *Centre national d'excellence en santé mentale* to provide individualized digital training and coaching to improve EIS performance on specific indicators and developing a web-based media library for asynchronous training on related themes. Programs demonstrating high performance on certain indicators (positive deviance) may be partnered with programs needing help. The *Centre national d'excellence en santé mentale*, the Ministry of Health and Social Services, and AQPPEP already use this type of system for peer mentorship. These approaches have proven effective for use in knowledge translation and implementation science [43-45]. A continuous back-and-forth between digital data capture, continuous feedback on performance, and capacity-building activities will facilitate positive evolution in aligning participating Quebec EIS with best practices.

Phase 6: Evaluating and Disseminating RLHS Outcomes to Stakeholders (to Be Implemented)

The RLHS project and its outcomes will be presented at AQPPEP events, which are attended by most staff from the Quebec EIS, and at Quebec, Canadian, and international scientific conferences. We plan to adapt the RLHS based on lessons learned from this pilot project in terms of successes, weaknesses, facilitators, and challenges. The anticipated longer-term structural impact of the project will be the adoption and integration of the RLHS by EIS across the province, ideally with support from the Ministry of Health and Social Services. The project will positively affect decision-making at the local and provincial levels to become more data-informed and responsive in real time. Institutional bodies housing many of the EIS will be better able to monitor their implementation, targeting areas for improvement and resources needed. The Ministry of Health and Social Services will be able to follow the progress of EIS implementation across the province in relation to changes in sociopolitical measures and context (eg, investments, provision of new guidelines, or revisions to existing guidelines). The AQPPEP, the *Centre national d'excellence en santé mentale* of the Ministry of Health and Social Services, and similar organizations currently structured to train and support EIS will become more resource-efficient and effective after using the RLHS by tailoring their offerings to EIS, selecting appropriate target groups for training, and adopting data-driven evaluation and modification in capacity-building activities.

Objective 2: Assess the Impact of the RLHS in EIS

The RLHS will further provide us with valuable information and data suggesting whether this paradigm does indeed lead to improved quality of care in EIS. The RE-AIM framework, used to assess the feasibility and impact of our project, was developed specifically to evaluate the implementation of interventions in real-world settings and sensitize researchers, knowledge users, and stakeholders to the essential elements involved in the sustainable adoption and implementation of targeted interventions. For our RLHS, we will assess *reach* (proportion of the targeted population that participates in the RLHS), *effectiveness* (impact of the RLHS on outcomes), *adoption* (extent and ease of adoption of the RLHS and degree of change), *implementation* (in-depth analyses of RLHS process data to determine which facilitators and barriers are associated with better implementation of the RLHS), and *maintenance* (extent to which the RLHS and its impact can be maintained), as shown in Figure 1.

To gain a qualitative perspective, we will invite all stakeholder groups (clinicians, managers, service users, and family members), advisory committee members, and representatives from the selected EIS (clinical staff, program leaders, managers, and decision makers) to participate in focus groups. Before the end of the project, a total of 6 remote focus groups (8-10 participants per group and 1.5-hour duration) will be implemented as follows: 1 (20%) for clinicians, 2 (40%) for program leaders (one for medical professionals and the other for professional team leaders), 1 (20%) for managers and decision makers, 1 (20%) for service users, and 1 (20%) for family members. The focus groups will be held by videoconference with a trained moderator and a research staff member acting as cofacilitators. Focus group questions will be designed following Krueger and Casey [46] and structured to explore the 5 key dimensions of learning health systems by Lessard [37] that capture the nature of an RLHS: the *goals* pursued by an RLHS to promote evidence-based and quality care; the *social dimension*, focused on building a community; the *technical dimension*, addressing digital data integration into routine care; the *scientific dimension*, enabling learning, innovation, and discovery; and the *ethics dimension*, ensuring that an RLHS pursues its learning and innovation

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activities in a manner that protects patient rights and privacy. Focus group participants will provide information on their experiences and perceptions related to the RLHS; the impact of the RLHS on them; their willingness to change and maintain use of the RLHS; attitudes about data collection; and the facilitators and barriers to implementation encountered, including their impact on decision-making at both the clinical and administrative levels. A research assistant will transcribe the focus group audio files and prepare them for analysis. Informed by the Braun and Clark analytic procedure [47], we will (1) familiarize ourselves with the data (reviewing transcriptions for accuracy), (2) generate initial codes using the dimensions of learning health systems by Lessard [37], (3) review and redefine themes, and (4) further unpack the analysis through the writing process.

For a quantitative and qualitative picture of EIS evolution along the RE-AIM parameters, we will track the uptake of the RLHS and extract data on all indicators from the REDCap platform, monitoring performance for each EIS on each indicator (Table 2) and comparing data from baseline to project completion to assess effectiveness. The components of the RE-AIM framework will be assessed as outlined in Textbox 2.

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Textbox 2. Assessment guidelines for each component of the Reach, Effectiveness, Adoption, Implementation, and Maintenance framework.

Reach

- Proportion of invited early intervention services (EIS) that participate in the project
- Proportion of invited EIS representatives (eg, clinicians, team leaders, or managers) and invited service users and family members who participate in capacity-building activities, knowledge exchange events, and implementation meetings
- Proportion of participating EIS who adopt our electronic data capture platform and ask service users and family members to provide information on satisfaction with services, self-evaluation of recovery dimensions, and the impact of services on recovery
- Proportion of invited people from each stakeholder group (clinicians, managers, service users, and family members) who participate in research focus groups

Effectiveness

- Improvement over time in indicators (eg, reduction of delays in access, increase in service user and family member engagement in services, satisfaction with services, and recovery outcomes such as employment)
- Increase over time in provision of evidence-based care as required by Ministry guidelines—the *cadre de référence* (eg, proportion of EIS offering cognitive behavioral therapy, family interventions, supported employment or education, integrated interventions for substance use disorder, peer support, and pharmacological interventions)
- Accuracy of data obtained from each EIS throughout the project using the rapid-learning health system (RLHS) electronic platform based on a comparison of the program-reported data from REDCap (Research Electronic Data Capture; Vanderbilt University) surveys in our RLHS with data collected by chart review on a selection of charts from each participating EIS. Deidentified data on *access to care* (eg, referral sources and delay from referral to initial evaluation), interventions offered (eg, cognitive behavioral therapy and family psychoeducation), and indicators of user engagement will be collected by research participants from the charts of 20 randomly selected service users at baseline and an additional 10 service users at all other time points (4 months preceding study onset and every 4 months subsequently until study completion). This step will ensure the trustworthiness of self-report data from the EIS by comparing self-report data with objective data from the files (eg, delays in evaluation and percentages of service users offered family interventions). If trustworthy, data reported by the programs themselves, as in our RLHS, may enable the creation of large, ecologically valid data sets that may be used to draw inferences about program performance and its relationship with patient outcomes on different recovery dimensions
- Perceptions of each stakeholder group (clinicians, managers, service users, and family members) regarding the ability of the RLHS to promote evidence-based and quality care in the EIS

Adoption

- Proportion of programs represented and proportion of each invited stakeholder group (clinicians, team leaders, managers, service users, and family members) in attendance at the various training sessions offered by the project
- Number of programs not involved in the research project whose representatives express interest in adopting the RLHS after attending presentations at the *Association québécoise des programmes pour premiers épisodes psychotiques* (Quebec Association of Programs for First-Episode Psychosis) or other events
- Progression over time in the proportion of data collected by program staff and service users as well as completion rates
- Proportion of participating EIS that continuously engage service users and family members to provide information on satisfaction with services, self-evaluation of recovery dimensions, and the impact of services on recovery using our electronic data capture platform
- Perceptions of each stakeholder group (researchers, clinicians, managers, service users, and family members) regarding the ability of the RLHS to foster a learning community
- Perceptions of each stakeholder group (clinicians, managers, service users, and family members) on whether it was feasible for the EIS to integrate indicators and digital data into routine care

Implementation

- Extent to which capacity-building strategies (eg, training) are implemented (at least one targeted after each 4-month data collection period)
- Proportion of participating programs using RLHS health technologies regularly until the end of the project
- Barriers, facilitators, and overall burden related to implementation of the RLHS as assessed qualitatively in focus groups
- Perceptions of each stakeholder group (clinicians, managers, service users, and family members) regarding the feasibility of implementing the RLHS in EIS
- Perceptions of each stakeholder group (clinicians, managers, service users, and family members) regarding the extent to which the RLHS protects patient rights and privacy

Maintenance

Maintenance is defined as the use of health technologies over time, with regular data collection by programs estimated in terms of the extent to which data collection is sustained by the participating programs over the course of the project

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- Program commitment (e-survey) to continue using the electronic data capture system beyond the project
- Proportion of EIS attending advisory committee meetings over the entire duration of the project
- Proportion of EIS attending capacity-building and knowledge exchange events over the entire duration of the project
- Perceptions of each stakeholder group (clinicians, managers, service users, and family members) on how the RLHS enables learning, innovation, and discovery

Ethics Approval

In August 2019, this proposal was accepted by the *Fonds de recherche du Québec-Santé*. Research ethics approval was received from the ethics board of the *Centre de Recherche du Centre Hospitalier de l'Université de Montréal* in December 2019 (reference 19-282 and MP-02-2020-8627), followed by institutional ethics approval from each of the 11 participating sites. Any important modifications to the protocol were reported to the ethics board of the *Centre Hospitalier de l'Université de Montréal* as well as the institutional research ethics boards overseeing the participating sites.

At all sites, youth, family members, and professionals provided web-based or written consent to participate in the study according to the protocol and to the regulations governing informed consent procedures.

Results

Phase 1 was implemented between September 2018 and December 2018 to inform the project proposal, which was submitted to a Quebec government granting agency, the *Fonds de recherche du Québec-Santé*, in December 2018. On the basis of a previous descriptive study by our group characterizing all Quebec EIS [21], we selected 11 EIS representing the different contexts in which EIS services are delivered (Table 1). They all agreed to participate in the RLHS project. In phase 1, the authors first performed a knowledge synthesis of relevant peer-reviewed literature on essential EIS components, guidelines, and performance indicators. On the basis of this knowledge synthesis, 8 meaningful indicators for quality care in EIS (Table 2) were chosen through a survey and consensus meetings with representatives of each stakeholder group, including those from each of the 11 participating sites. An environmental scan in the form of a survey was then sent to the clinical leaders of the 11 selected sites to estimate capacity and assess their support needs regarding implementation of the RLHS, especially the capacity for data collection.

Phase 2 was implemented between September 2019 and May 2020. It involved the creation (with the collaboration of service users, team leaders, and researchers) and setup of the RLHS digital infrastructure using the REDCap platform and digital terminals that allowed service users and clinical team leaders to collect data routinely and iteratively on the selected indicators of quality care.

Phases 3 to 5 are ongoing and will continue for the first 6 months of 2022. The RLHS data capture platforms were first made available to the 11 EIS in June 2020, allowing for data collection on the selected indicators. These data are systematically and continuously analyzed to generate new evidence and recommendations for improving the RLHS as well as user-friendly illustrated feedback on a few indicators for the participating EIS and all stakeholder groups. The collected data also inform capacity-building activities tailored to the evolving needs of individual EIS and those of the 11 EIS as a group.

Phase 6, which assesses the impact of the RLHS (objective 2) and the dissemination of our findings, will be implemented in 2022. Using the RE-AIM framework, we will evaluate the outcomes related to clinical practice and program-level changes to assess the overall impact of the RLHS in EIS. In this regard, quantitative and qualitative data will be analyzed.

Discussion

At the completion of the project, we should have developed the first province-wide database for real-time, clinically relevant data on quality indicators from representative EIS. We also expect that clinical practices at participating EIS will be better aligned with provincial and international EIS guidelines. Program capacity for continuous data collection and quality improvement in services and care provision will increase. Importantly, access to services by users and families and satisfaction with services should also improve, leading to better recovery outcomes for individual patients.

Should results of the RLHS project prove effective, we will have the potential to immediately scale up this RLHS across the province given the strong links between this project and Quebec EIS and the credibility of the project with the AQPPEP. We will also count on government support as a financial partner on the grant, including our ongoing support from the Quebec Ministry of Health and Social Services dating from the beginning of the grant submission process. Our decision to develop free, open-access instruments and platforms is another advantage. Further dissemination of the RLHS will result in population-level improvements in outcomes for psychosis. Over the longer term, should the type of RLHS we propose take root across the province, Quebec may rapidly advance to become both a national and international exemplar in EIS.

This project will also have multiple structural impacts. The first is an increase in the provision of patient-centered care, using individual-level data to tailor treatments while offering program-level data to improve patient and family experiences bearing on the accessibility, quality, and responsiveness of EIS. The second area of impact will affect the overall system of care across Quebec EIS, creating, most importantly, a system that continuously *learns*. The system as a whole and each individual EIS will have developed an increased capacity for providing evidence-based care, monitoring its own performance, setting improvement targets, using data to make program-level decisions, using aggregated data to make provincial-level

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decisions, and generating greater capacity for collaborative learning and multistakeholder interactions. By the end of this pilot project, the RLHS for EIS will be ready for deployment to all the remaining EIS in Quebec.

Finally, lessons from this project may support provincial decision-making regarding health informatics solutions, health care monitoring, system integration, the creation of communities of practice, and multicenter research. Most importantly, this project can contribute to a better understanding and operationalization of the RLHS approach in mental health and health services. Moreover, this project will lay the foundation for extending the RLHS paradigm to other Canadian provinces and to other countries where EIS for psychosis programs are currently available.

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Authors' Contributions

MF wrote the first version of the main manuscript, prepared the figures and annexes all of which were reviewed and revised by SI and AAB. SI, AAB, MAR, and AL reviewed, revised, and improved the original text. All the authors approved the final manuscript.

Conflicts of Interest

None declared.

References

1. Castle DJ, Murray RM. The epidemiology of late-onset schizophrenia. Schizophr Bull 1993;19(4):691-700. [doi: 10.1093/schbul/19.4.691] [Medline: 8303220]
2. Copeland JR, Dewey ME, Scott A, Gilmore C, Larkin BA, Cleave N, et al. Schizophrenia and delusional disorder in older age: community prevalence, incidence, comorbidity, and outcome. Schizophr Bull 1998;24(1):153-161. [doi: 10.1093/oxfordjournals.schbul.a033307] [Medline: 9502553]
3. Bertelsen M, Jeppesen P, Petersen L, Thorup A, Øhlenschlaeger J, le Quach P, et al. Five-year follow-up of a randomized multicenter trial of intensive early intervention vs standard treatment for patients with a first episode of psychotic illness: the OPUS trial. Arch Gen Psychiatry 2008 Jul;65(7):762-771. [doi: 10.1001/archpsyc.65.7.762] [Medline: 18606949]
4. Harvey P, Lepage M, Malla A. Benefits of enriched intervention compared with standard care for patients with recent-onset psychosis: a metaanalytic approach. Can J Psychiatry 2007 Jul;52(7):464-472. [doi: 10.1177/070674370705200709] [Medline: 17688011]
5. Craig TK, Garety P, Power P, Rahaman N, Colbert S, Fornells-Ambrojo M, et al. The Lambeth Early Onset (LEO) Team: randomised controlled trial of the effectiveness of specialised care for early psychosis. BMJ 2004 Nov 06;329(7474):1067 [FREE Full text] [doi: 10.1136/bmj.38246.594873.7C] [Medline: 15485934]
6. Birchwood M, Todd P, Jackson C. Early intervention in psychosis. The critical period hypothesis. Br J Psychiatry Suppl 1998;172(33):53-59. [Medline: 9764127]
7. Albert N, Melau M, Jensen H, Hastrup LH, Hjorthøj C, Nordentoft M. The effect of duration of untreated psychosis and treatment delay on the outcomes of prolonged early intervention in psychotic disorders. NPJ Schizophr 2017 Sep 26;3(1):34 [FREE Full text] [doi: 10.1038/s41537-017-0034-4] [Medline: 28951544]
8. Norman RM, Malla AK. Duration of untreated psychosis: a critical examination of the concept and its importance. Psychol Med 2001 Apr;31(3):381-400. [doi: 10.1017/s0033291701003488] [Medline: 11305847]
9. Penttilä M, Jääskeläinen E, Hirvonen N, Isohanni M, Miettunen J. Duration of untreated psychosis as predictor of long-term outcome in schizophrenia: systematic review and meta-analysis. Br J Psychiatry 2014 Aug;205(2):88-94. [doi: 10.1192/bjp.bp.113.127753] [Medline: 25252316]
10. Perkins DO, Gu H, Boteva K, Lieberman JA. Relationship between duration of untreated psychosis and outcome in first-episode schizophrenia: a critical review and meta-analysis. Am J Psychiatry 2005 Oct;162(10):1785-1804. [doi: 10.1176/appi.ajp.162.10.1785] [Medline: 16199825]

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11. Ouellet-Plamondon C, Abdel-Baki A, Salvat E, Potvin S. Specific impact of stimulant, alcohol and cannabis use disorders on first-episode psychosis: 2-year functional and symptomatic outcomes. Psychol Med 2017 Oct;47(14):2461-2471. [doi: 10.1017/S0033291717000976] [Medline: 28424105]
12. Doyle R, Turner N, Fanning F, Brennan D, Renwick L, Lawlor E, et al. First-episode psychosis and disengagement from treatment: a systematic review. Psychiatr Serv 2014 May 01;65(5):603-611. [doi: 10.1176/appi.ps.201200570] [Medline: 24535333]
13. Insel TR. RAISE-ing our expectations for first-episode psychosis. Am J Psychiatry 2016 Apr 01;173(4):311-312. [doi: 10.1176/appi.ajp.2015.15091204] [Medline: 26481175]
14. Petersen L, Thorup A, Øqhlenschlaeger J, Christensen T, Jeppesen P, Krarup G, et al. Predictors of remission and recovery in a first-episode schizophrenia spectrum disorder sample: 2-year follow-up of the OPUS trial. Can J Psychiatry 2008 Oct;53(10):660-670. [doi: 10.1177/070674370805301005] [Medline: 18940034]
15. Winsper C, Singh SP, Marwaha S, Amos T, Lester H, Everard L, et al. Pathways to violent behavior during first-episode psychosis: a report from the UK National EDEN Study. JAMA Psychiatry 2013 Dec;70(12):1287-1293. [doi: 10.1001/jamapsychiatry.2013.2445] [Medline: 24089149]
16. Iyer S, Jordan G, MacDonald K, Joober R, Malla A. Early intervention for psychosis: a Canadian perspective. J Nerv Ment Dis 2015 May;203(5):356-364. [doi: 10.1097/NMD.0000000000000288] [Medline: 25900548]
17. McGorry P, Bates T, Birchwood M. Designing youth mental health services for the 21st century: examples from Australia, Ireland and the UK. Br J Psychiatry Suppl 2013 Jan;54:s30-s35. [doi: 10.1192/bjp.bp.112.119214] [Medline: 23288499]
18. Malla AK, Norman RM, Joober R. First-episode psychosis, early intervention, and outcome: what have we learned? Can J Psychiatry 2005 Dec;50(14):881-891. [doi: 10.1177/070674370505001402] [Medline: 16494257]
19. McGorry PD. Early intervention in psychosis: obvious, effective, overdue. J Nerv Ment Dis 2015 May;203(5):310-318 [FREE Full text] [doi: 10.1097/NMD.0000000000000284] [Medline: 25919380]
20. Addington DE, McKenzie E, Norman R, Wang J, Bond GR. Essential evidence-based components of first-episode psychosis services. Psychiatr Serv 2013 May 01;64(5):452-457. [doi: 10.1176/appi.ps.201200156] [Medline: 23370444]
21. Bertulies-Esposito B, Iyer S, Abdel-Baki A. The impact of policy changes, dedicated funding and implementation support on early intervention programs for psychosis. Can J Psychiatry 2022 Jan 11:7067437211065726 [FREE Full text] [doi: 10.1177/07067437211065726] [Medline: 35014891]
22. Nolin M, Malla A, Tibbo P, Norman R, Abdel-Baki A. Early intervention for psychosis in Canada: what is the state of affairs? Can J Psychiatry 2016 Mar;61(3):186-194 [FREE Full text] [doi: 10.1177/0706743716632516] [Medline: 27254094]
23. Csillag C, Nordentoft M, Mizuno M, Jones PB, Killackey E, Taylor M, et al. Early intervention services in psychosis: from evidence to wide implementation. Early Interv Psychiatry 2016 Dec;10(6):540-546. [doi: 10.1111/eip.12279] [Medline: 26362703]
24. Csillag C, Nordentoft M, Mizuno M, McDaid D, Arango C, Smith J, et al. Early intervention in psychosis: from clinical intervention to health system implementation. Early Interv Psychiatry 2018 Aug;12(4):757-764. [doi: 10.1111/eip.12514] [Medline: 29143456]
25. Cocchi A, Cavicchini A, Collavo M, Ghio L, Macchi S, Meneghelli A, et al. Implementation and development of early intervention in psychosis services in Italy: a national survey promoted by the Associazione Italiana Interventi Precoci nelle Psicosi. Early Interv Psychiatry 2018 Feb;12(1):37-44. [doi: 10.1111/eip.12277] [Medline: 26416725]
26. Durbin J, Selick A, Hierlihy D, Moss S, Cheng C. A first step in system improvement: a survey of Early Psychosis Intervention Programmes in Ontario. Early Interv Psychiatry 2016 Dec;10(6):485-493. [doi: 10.1111/eip.12201] [Medline: 25366518]
27. Greene SM, Reid RJ, Larson EB. Implementing the learning health system: from concept to action. Ann Intern Med 2012 Aug 07;157(3):207-210. [doi: 10.7326/0003-4819-157-3-201208070-00012] [Medline: 22868839]
28. Abernethy AP, Etheredge LM, Ganz PA, Wallace P, German RR, Neti C, et al. Rapid-learning system for cancer care. J Clin Oncol 2010 Sep 20;28(27):4268-4274 [FREE Full text] [doi: 10.1200/JCO.2010.28.5478] [Medline: 20585094]
29. ASCO's CancerLinQ: building a transformation in cancer care. The ASCO Post. URL: https://ascopost.com/issues/july-1-2012/asco-s-cancerlinq-building-a-transformation-in-cancer-care/ [accessed 2022-06-02]
30. Platt R, Wilson M, Chan KA, Benner JS, Marchibroda J, McClellan M. The new Sentinel Network--improving the evidence of medical-product safety. N Engl J Med 2009 Aug 13;361(7):645-647. [doi: 10.1056/NEJMp0905338] [Medline: 19635947]
31. Wallace PJ. Reshaping cancer learning through the use of health information technology. Health Aff (Millwood) 2007;26(2):w169-w177. [doi: 10.1377/hlthaff.26.2.w169] [Medline: 17259200]
32. Delaney BC, Curcin V, Andreasson A, Arvanitis TN, Bastiaens H, Corrigan D, et al. Translational medicine and patient safety in Europe: TRANSFoRm--Architecture for the learning health system in Europe. Biomed Res Int 2015;2015:961526 [FREE Full text] [doi: 10.1155/2015/961526] [Medline: 26539547]
33. Value in Health Care Accounting for Cost, Quality, Safety, Outcomes, and Innovation. Washington, D.C., United States: National Academies Press (US); 2010.
34. Institute of Medicine (US) Roundtable on Evidence-Based Medicine. The Learning Healthcare System Workshop Summary. Washington, DC: National Academies Press; 2007.
35. Abernethy AP. Demonstrating the learning health system through practical use cases. Pediatrics 2014 Jul;134(1):171-172. [doi: 10.1542/peds.2014-1182] [Medline: 24935998]

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36. Morain SR, Kass NE. Ethics issues arising in the transition to learning health care systems: results from interviews with leaders from 25 health systems. EGEMS (Wash DC) 2016;4(2):1212 [FREE Full text] [doi: 10.13063/2327-9214.1212] [Medline: 27141521]
37. Lessard L, Michalowski W, Fung-Kee-Fung M, Jones L, Grudniewicz A. Architectural frameworks: defining the structures for implementing learning health systems. Implement Sci 2017 Jun 23;12(1):78 [FREE Full text] [doi: 10.1186/s13012-017-0607-7] [Medline: 28645319]
38. Riley WT, Glasgow RE, Etheredge L, Abernethy AP. Rapid, responsive, relevant (R3) research: a call for a rapid learning health research enterprise. Clin Transl Med 2013 May 10;2(1):10 [FREE Full text] [doi: 10.1186/2001-1326-2-10] [Medline: 23663660]
39. Lowes LP, Noritz GH, Newmeyer A, Embi PJ, Yin H, Smoyer WE, 'Learn from Every Patient' Study Group. 'Learn From Every Patient': implementation and early results of a learning health system. Dev Med Child Neurol 2017 Feb;59(2):183-191 [FREE Full text] [doi: 10.1111/dmcn.13227] [Medline: 27545839]
40. Mainz J. Defining and classifying clinical indicators for quality improvement. Int J Qual Health Care 2003 Dec;15(6):523-530. [doi: 10.1093/intqhc/mzg081] [Medline: 14660535]
41. Valiani S, Rigal R, Stelfox HT, Muscedere J, Martin CM, Dodek P, et al. An environmental scan of quality indicators in critical care. CMAJ Open 2017 Jun 21;5(2):E488-E495 [FREE Full text] [doi: 10.9778/cmajo.20150139] [Medline: 28637683]
42. Cadre de référence - Programmes d'interventions pour premiers épisodes psychotiques. Quebec: ministère de la Santé et des Services sociaux; 2017.
43. Thornicroft G, Cooper S, Bortel TV, Kakuma R, Lund C. Capacity building in global mental health research. Harv Rev Psychiatry 2012;20(1):13-24 [FREE Full text] [doi: 10.3109/10673229.2012.649117] [Medline: 22335179]
44. Hawk M, Nimgaonkar V, Bhatia T, Brar JS, Elbahaey WA, Egan JE, et al. A 'Grantathon' model to mentor new investigators in mental health research. Health Res Policy Syst 2017 Oct 24;15(1):92 [FREE Full text] [doi: 10.1186/s12961-017-0254-0] [Medline: 29065894]
45. Keynejad R, Semrau M, Toynbee M, Evans-Lacko S, Lund C, Gureje O, et al. Building the capacity of policy-makers and planners to strengthen mental health systems in low- and middle-income countries: a systematic review. BMC Health Serv Res 2016 Oct 21;16(1):601 [FREE Full text] [doi: 10.1186/s12913-016-1853-0] [Medline: 27769270]
46. McQuarrie EF, Krueger RA. Focus groups: a practical guide for applied research. J Marketing Res 1989 Aug;26(3):371. [doi: 10.2307/3172912]
47. Braun V, Clarke V. Using thematic analysis in psychology. Qual Res Psychol 2006 Jan;3(2):77-101. [doi: 10.1191/1478088706qp063oa]
48. Équipe. URL: https://sarpep.ca/equipe/ [accessed 2022-06-17]

Abbreviations

AQPPEP: Association québécoise des programmes pour premiers épisodes psychotiques (Quebec Association of Programs for First-Episode Psychosis)
EIS: early intervention services
RE-AIM: Reach, Effectiveness, Adoption, Implementation, and Maintenance model
RLHS: rapid-learning health system

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Proposal

Sickle Cell Transplantation Evaluation of Long-term and Late Effects Registry (STELLAR) to Compare Long-term Outcomes After Hematopoietic Cell Transplantation to Those in Siblings Without Sickle Cell Disease and in Nontransplanted Individuals With Sickle Cell Disease: Design and Feasibility Study

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Abstract

Background: There are sparse data on the long-term and late effects of hematopoietic cell transplantation (HCT) for sickle cell disease (SCD).

Objective: This study aims to establish an international registry of long-term outcomes post-HCT for SCD and demonstrate the feasibility of recruitment at a single site in the United States.

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Methods: The Sickle Cell Transplantation Evaluation of Long-Term and Late Effects Registry (STELLAR) was designed to enroll patients with SCD ≥1 year post-HCT, their siblings without SCD, and nontransplanted controls with SCD to collect web-based participant self-reports of health status and practices by using the Bone Marrow Transplant Survivor Study (BMTSS) surveys, health-related quality of life (HRQOL) using the Patient-Reported Outcomes Measurement Information System (PROMIS) Pediatric Profile-25 or Pediatric Profile-29 survey, chronic graft-versus-host disease (cGVHD) using the symptom scale survey, daily pain using an electronic pain diary, the economic impact of HCT using the financial hardship survey, sexual function using the PROMIS Sexual Function SexFSv2.0 survey, and economic productivity using the American Time Use Survey (ATUS). We also piloted retrieval of clinical data previously submitted to the Center for International Blood and Marrow Transplant Research (CIBMTR); recorded demographics, height, weight, blood pressure, waist and hip circumferences, timed up and go (TUG) test, and handgrip test; and obtained blood for metabolic screening, gonadal function, fertility potential, and biorepository of plasma, serum, RNA, and DNA.

Results: Of 100 eligible post-HCT patients, we enrolled 72 (72%) participants aged 9-38 (median 17) years. We also enrolled 19 siblings aged 5-32 (median 10) years and 28 nontransplanted controls with SCD aged 4-46 (median 22) years. Of the total 119 participants, 73 (61%) completed 85 sets of surveys and 41 (35%) contributed samples to the biorepository. We completed ATUS interviews of 28 (24%) participants. We successfully piloted retrieval of data submitted to the CIBMTR and expanded recruitment to multiple sites in the United States, Canada, the United Kingdom, and Nigeria.

Conclusions: It is feasible to recruit subjects and conduct study procedures for STELLAR in order to determine the long-term and late effects of HCT for SCD.

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KEYWORDS

anemia; sickle cell; late effect; hematopoietic cell transplantation; web-based registry; sickle cell disease; transplant; protocol

Introduction

Hematopoietic cell transplantation (HCT) remains the only treatment undertaken with curative intent for sickle cell disease (SCD). HCT has the possibility of alleviating disease-related morbidity, improving physical function, stabilizing organ function, and improving the quality of life [1,2]. The results of HCT for SCD from human leukocyte antigen (HLA)-identical sibling donors are excellent, with over 94% overall survival and 91% event-free survival [3-8]. Alternative donor HCT [5,9-13] and autologous gene therapy (GT) can further increase the applicability of HCT for SCD [9,14-16]. Observational case series, clinical trials, and research registries have typically captured the short- and intermediate-term outcomes of engraftment, graft-versus-host disease (GVHD), and survival 1-3 years post-HCT. However, the late effects of HCT, including detailed patient-reported outcomes (PROs), physical function, health status, health behaviors, and health outcomes, have not been captured. In addition, approximately 10% of post-HCT mortality after HCT for SCD occurs beyond 5 years after HCT [6]. Therefore, there is potential for persistent or new late morbidity following HCT for SCD. These observations provide a rationale for the systematic study of long-term and late effects to understand the impact of allogeneic HCT and autologous GT on patients' life course and outcomes.

The impact of HCT in SCD can be better understood by comparing the long-term outcomes in the post-HCT group with those in their siblings without SCD and in nontransplanted persons with SCD matched for age, genotype, and disease characteristics that define the propensity to undergo HCT. Siblings share social, psychological, and environmental exposures and may share genetic predispositions. Thus, this comparison group provides the best approximation of how the participants may have fared had they not been born with SCD. In contrast, nontransplanted individuals with SCD matched for age, gender, and propensity to undergo HCT provide the best estimate of what may have been the outcomes of post-HCT patients had they not undergone HCT. Unfortunately, no such contemporaneous comparison cohort has been established to date, despite the awareness of this knowledge gap.

We designed the Sickle Cell Transplantation Evaluation of Long-Term and Late Effects Registry (STELLAR) to address this knowledge gap and track and compare the long-term outcomes and late effects of HCT for SCD compared to unaffected sibling controls and nontransplanted patients with SCD. We implemented the registry in collaboration with the Center for International Blood and Marrow Transplant Research (CIBMTR) and core centers experienced in the conduct of HCT for SCD. Our overarching hypothesis is that *HCT for SCD improves the health-related quality of life (HRQOL) and immune function but is associated with gonadal damage and impaired fertility potential compared to nontransplanted controls with SCD and sibling controls without SCD*. Our objectives were to (1) compare the long-term HRQOL, pain, financial hardship, physical function, health status, health behaviors, and economic productivity; (2) compare gonadal function and fertility status in adults post-HCT for SCD with these contemporaneous comparison groups; and (3) leverage current data collected through the CIBMTR to harmonize data collection and avoid duplication of effort in the field. This report describes STELLAR's design and development and its pilot testing and implementation in participating pediatric and adult programs in Atlanta, GA, USA.

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Methods

Study Design

STELLAR is a prospective, longitudinal, observational tool comparing health outcomes in study participants post-HCT for SCD, siblings without SCD, and a contemporary group of nontransplanted subjects with SCD.

Ethics

The study was approved by the Western Institutional Review Board (IRB), which served as the single IRB for the study (approval number WIRB 20200372). All the study procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Declaration of Helsinki of 1975, as revised in 2000.

Participants

The inclusion criteria were (1) patients with SCD of any age >1 year post-HCT or autologous GT; (2) HLA-matched donor siblings for post-HCT participants or a sibling without SCD of the recipient who is closest in age for the recipient of the transplant from an HLA-matched unrelated donor, HLA-haploidentical related donor, or autologous GT; and (3) patients with SCD (Hemoglobin SS [HbSS] or Hemoglobin S/β0 Thalassemia [HbSβ^0]) who have not undergone HCT.

The exclusion criterion was non-English-speaking individuals.

Setting

The study was designed as a collaboration among several sites with substantial experience and expertise in performing HCT for SCD (Textbox 1) for the recruitment of subjects through direct contact and in clinic settings.

Textbox 1. Participating sites.

- Emory University, Aflac Cancer and Blood Disorders Center, Children's Healthcare of Atlanta, GA, USA
- Emory University Department of Hematology, Grady Hospital, Atlanta, GA, USA
- Children's National Health Systems, Washington, DC, USA
- Columbia University Medical Center, NY, USA
- Cook Children's Medical Center, TX, USA
- Alberta Children's Hospital, Calgary, Canada
- Children's Hospital of Los Angeles, CA, USA
- Imperial College Healthcare, London
- National Heart, Lung, and Blood Institute, Bethesda, MD, USA
- University of North Carolina, NC, USA
- Lagos University Teaching Hospital, Lagos, Nigeria
- Duke University, NC, USA
- Washington University School of Medicine, MO, USA
- Baylor College of Medicine, TX, USA

Recruitment of Individuals Post-HCT for SCD

We reviewed electronic medical records to identify individuals who underwent allogeneic HCT or autologous GT or follow-up care in the participating centers. Then, using the last-known contact information, we approached potential participants by mail, email, and telephone. For participants currently <18 years old, we approached their parents/legal guardians for participation. In the case of potential study participants ≥18 years old, we contacted them directly. When we did not have the correct contact information for potential participants, we used social media and people-finding software to establish contact with those individuals. In addition, we organized annual reunions of survivors and their families to raise awareness of the study. Participants aged ≥18 years were also offered participation in the reproductive health substudy to assess sexual function and reproductive health. Individuals post-HCT for SCD were also approached when they attended an ex-sickle clinic, a clinic designated for long-term follow-ups of patients with successful HCT for SCD.

Recruitment of Nontransplanted Controls With SCD

After establishing procedures for enrollment of transplant recipients, we sequentially expanded enrollment to siblings without SCD and nontransplanted participants with SCD. Nontransplanted patients with SCD were approached for study in a comprehensive sickle cell clinic. Patients and siblings were also approached in annual post-HCT reunions and through social media. In the case of minor siblings, we contacted their parents to obtain informed consent. In the case of adult siblings, we received permission from HCT survivors or their parents to contact the siblings.

We piloted the enrollment of pediatric and adult nontransplanted patients with SCD in the pediatric and adult sickle cell programs in Atlanta, GA, USA. Since registration is ongoing and participants are of a wide age range, we enrolled control subjects regardless of age to establish a pool of control patients. For matching post-HCT participants to nontransplanted individuals, we will select age, gender, and the propensity score matched to post-HCT patients. We will use logistic regression for propensity

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score calculation from the following variables: (1) the number of episodes of acute chest syndrome, (2) the frequency of hospitalization for a vaso-occlusive crisis in the 2 years pre-HCT, and (3) a history of stroke. A 1:1 propensity score matching will be performed using the nearest-neighbor-matching method with a caliper width fixed at 0.2. Propensity score matching will be performed using JMP Pro 13.2.0 (SAS Institute Japan, Co, Ltd, Tokyo, Japan).

Study Procedures

The study procedures included medical record review, data retrieval from the CIBMTR, participant-completed surveys and electronic pain diaries, fertility evaluation, clinical parameters, vital measurements, physical function tests, and blood samples for metabolic screening, gonadal and fertility potential, and biobanking specimens.

Clinical Parameters and Vital Measurements

We recorded clinical parameters, including vital signs, and measurements, including height, weight, and waist and hip circumferences. In addition, we performed a handgrip test, a measure of the maximum isometric strength of hand and forearm muscles and the widely used general muscle strength [17-20], a timed up and go (TUG) test [21,22], and a test of mobility and balance as assessments of physical function [17-19]. We will repeat these procedures annually.

Surveys

We used a set of validated surveys to capture patient reports of health outcomes, health practices, and the HRQOL (Table 1). The Bone Marrow Transplant Survivor Study (BMTSS) survey [23,24] is a measure that has been extensively validated for use in long-term survivors of BMT to capture patient reports of health, health practices, health interventions, and complications [23-25].

The patient report on this survey was validated against medical records and was found to be accurate. The BMTSS surveys contain 130 items that ask questions on health status regarding hearing, vision, speech, and urinary tract; hormonal, heart and circulatory, respiratory, digestive, and brain and nervous systems; cancer; offspring; and pregnancy. The surveys also address health habits and practices related to alcohol or substance abuse, school history, employment history, and insurance. We reduced the burden of completing BMTSS surveys by using branching logic, also known as skip logic, which creates a custom pathway based on a user's response and accordingly presents subsequent questions, thus allowing the user to skip a question that does not apply to them.

Patients <18 years old completed the Patient-Reported Outcomes Measurement Information System (PROMIS) Pediatric Profile-25 survey. This survey assesses 6 HRQOL domains (ie, mobility, anxiety, depression, fatigue, peer relationships, and pain interference) by asking 4 questions per domain [26-30]. There is a single item on pain intensity. Patients >18 years old completed the PROMIS Pediatric Profile-29 v2.0 survey [31,32], which assesses pain intensity by a single question on a 0-10 rating scale and 6 health domains (ie, physical function, fatigue, pain interference, depressive symptoms, anxiety, and ability to participate in social roles and activities) and sleep disturbance using 4 questions per domain. Adults also completed the stiffness subscale of the Adult Sickle Cell Quality of Life Measurement Information System (ASCQ-Me) [29,33-35].

All patients with SCD completed the sickle cell self-efficacy survey [26-30,36] containing 9 questions relating to participants' perceptions of their ability to function daily and manage SCD symptomatology [36,37]. In addition, transplant recipients completed the chronic graft-versus-host disease (cGVHD) symptom survey and financial hardship assessments. The cGVHD symptom scale is a 30-item scale with 7 subscales to capture the cGVHD-specific burden [38,39].

To determine the impact of HCT on financial hardship, including income, employment, and insurance status, we adapted a 43-item measure developed at the Dana Farber Cancer Institute (DFCI) and used in stem cell transplant economic impact studies [40,41]. We modified the survey to a 38-question patient-reported financial hardship assessment tool. In addition, we adapted the survey for use in a pediatric population with parent proxy and age-appropriate patient surveys.

Study participants completed surveys electronically. The application is adaptable for use on smartphones, tablets, or computers and is platform “agnostic.” Participants can start, stop, and save completion of surveys at will. To further minimize the burden of survey completion, we split the surveys into 4 parts and gave participants the option of completing these surveys quarterly over the year. To reduce the burden for completion in subsequent years, the response fields are automatically populated with draft responses from previous years. Participants are prompted to accept or change the response to proceed to the next screen. We incorporated a page timer in the surveys to track the amount of time spent by participants in each survey.

Our hypothesis was that those with SCD have lower rates of participation in economic activity and spend more time in health-related activities than the African American population in general as well as patients with SCD who are long-term survivors of HCT for SCD. To test this hypothesis, we piloted the American Time Use Survey (ATUS), a structured computer-assisted telephone interview.

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Table 1. Surveys completed and average time taken to complete them.

Description of scale	Average time to complete
Health and health practice surveys for all age groups (total time for the first quarter: 11 min 31 s)	
Demographics	1 min 17 s
School history	1 min 7 s
Employment history	1 min 2 s
Insurance	51 s
PROMIS[a] Adult Profile v2.0 or PROMIS Pediatric Profile-25 v2.0	6 min 36 s
ASCQ-Me[b] stiffness	26 s
Health and health practice surveys for all age groups (total time for the second quarter: 8 min 13 s)	
cGVHD[c]	1 min 38 s
Previous encounters	45 s
Family history	4 min 46 s
Marital status	52 s
Religion	7 s
Health and health practice surveys for all age groups (total time for the third quarter: 5 min)	
Hearing and speech	41 s
Urinary system	13 s
Hormonal system	35 s
Health and circulatory system	40 s
Respiratory system	29 s
Digestive system	31 s
Brain and nervous system	1 min 53 s
Health and health practice surveys for all age groups (>total time for the fourth quarter: 11 min 6 s)	
Financial survey	5 min 26 s
Health habits	1 min 32 s
Surgical procedures	59 s
Medical care	1 min 19 s
Other issues (SCD[d] SEQ-C[e])	22 s
Financial survey	2 min
Reproductive Health Survey (HCT[f] recipients and controls with SCD aged >18 years only)	
PROMIS Sexual Function SEXFSv2.0	7 min
Service utilization and cost (transplant recipients and controls with SCD)	
GAIN[g] Scale	3 min
Financial burden of HCT	
DFCI[h] finances and employment scale	3 min
ATUS[i]	
Economic productivity	30-45 min interview

[a]PROMIS: Patient-Reported Outcomes Measurement Information System.

[b]ASCQ-Me: Adult Sickle Cell Quality of Life Measurement Information System.

[c]cGVHD: chronic graft-versus-host disease.

[d]SCD: sickle cell disease.

[e]SCD SEQ-C: Sickle Cell Disease Self-Efficacy Questionnaire for Children.

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[f]HCT: hematopoietic cell transplantation.

[g]GAIN: Global Assessment of Individual Needs.

[h]DFCI: Dana Farber Cancer Institute.

[i]ATUS: American Time Use Survey.

Assessment of Reproductive Potential and Hormonal and Sexual Function

For post-HCT patients and nontransplanted controls with SCD who were ≥18 years old, we administered offspring and pregnancy history surveys, reproductive health from the BMTSS, and PROMIS sexual function and satisfaction surveys v2.0 [7,8]. Blood samples were collected for assay of reproductive hormones, including anti-Mullerian hormone (AMH), luteinizing hormone (LH), follicle-stimulating hormone (FSH), and estradiol in females and LH, FSH, and testosterone in males. In addition, fertility potential was assessed by semen analysis in males and the antral follicle count in females. A STELLAR study fertility specialist interpreted reproductive hormone labs, semen analysis, and antral follicle counts.

Data Retrieval From the CIBMTR

We collaborated closely with the CIBMTR to develop a process for retrieving clinical data submitted by centers to the CIBMTR before and after HCT. The CIBMTR has now established mechanisms by which centers can recover their own submitted data, either on an individual patient level or with data visualizations. The CIBMTR has also collaborated with the CureSC initiative to prepare a deidentified publicly available data set of patients with SCD undergoing HCT. This data set includes variables relevant to late effects, approved by a large group of stakeholders, and standard pre-, peri-, and post-HCT patient, disease, and demographic variables. The CIBMTR leveraged the CureSC data set to identify patients transplanted at the Atlanta site, and data have already been successfully retrieved. The CIBMTR will facilitate a process to offer participating STELLAR locations their center code to identify their patients within the publicly available data set and merge those data with other data at their center.

Medical Record Data Abstraction

The clinical data unavailable or not collected by the CIBMTR and relevant to this study were abstracted from the patients' medical charts. We reviewed the medical records and collected data from the clinical assessment to determine health care utilization, disease complications, and outcomes in post-HCT patients, non-HCT patients with SCD, donors, and healthy sibling controls.

Pain Diary

We used a validated web-based electronic multidimensional pain diary for collecting ecological momentary assessment (EMA) pain data [42]. Post-HCT participants with SCD and nontransplanted controls with SCD completed an electronic pain diary, as described earlier, twice a day for 2 weeks each year. Participants were asked to use the pain diary if they were ≥8 years old, had undergone HCT or autologous GT, or had SCD. Participants were asked to begin survey completion at their convenience and as soon as possible after study enrollment. The items on the pain diary include pain intensity, pain location, pain quality description, interference with sleep, mood, work/school, daily life, interactions with friends and family, and medications and nonpharmacological treatments for pain. There are 5 items for morning data collection and 14 items for evening data collection, which take approximately 5 min to complete.

Biological Specimen Collection

Blood samples of subjects who consented were collected by phlebotomy during the visit. The timing of blood and urine sample collection and other study procedures is described in Table 2. Metabolic screening was implemented with fasting blood sugar levels, urinalysis, the complete blood count, and the lipid profile.

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Table 2. Specimen collection: blood work and procedures.

Labs and procedures	Enrollment	Annual
Biorepository[a]	✓	N/A[b]
C-reactive protein	✓	N/A
Fibrinogen	✓	N/A
Troponin-I	✓	N/A
Brain natriuretic peptide (BNP)	✓	N/A
Immunoglobulin G (IgG)	✓	N/A
Fasting blood glucose	✓	✓
Glucose fructosamine	✓	✓
Insulin level	✓	✓
Urinalysis	✓	✓
Urine for microalbuminuria	✓	✓
Complete blood count with differential	✓	✓
Urine creatinine	✓	✓
Lipoprotein, serum lipids after 12 h fast	✓	✓
Immunophenotype of T, B, and natural killer (NK) cells	✓	N/A
Pneumococcal-23 serotype IgG	✓	N/A
D-dimer	✓	N/A
FSH[c] (≥11 years old)	✓	✓
LH[d] (≥11 years old)	✓	✓
AMH[e] (females ≥11 years old)	✓	✓
Testosterone (males ≥11 years old)	✓	✓
Estradiol (females ≥11 years old)	✓	✓
Blood urea nitrogen (BUN)	✓	✓
Creatinine	✓	✓
Thyroid panel	✓	✓
Lactate dehydrogenase (LDH)	✓	N/A
Hemoglobin electrophoresis	✓	✓
Chimerism study (HCT[f] patients only; fluorescent in situ hybridization [FISH] or variable number of tandem repeats [VNTR]; not paid for by study funds)	✓	✓
Semen analysis (males enrolled in reproductive health aim)	✓	N/A
Antral follicle count by vaginal ultrasound (females enrolled in the reproductive health aim	✓	N/A
Height/weight[g]	✓	✓
Hip/waist circumference[g]	✓	✓
Handgrip[h]	✓	N/A
TUG[h,i]	✓	N/A
Pain diary[j]	✓	N/A
Surveys[k]	✓	✓

[a]Biorepository specimen tests include testing of soluble urokinase plasminogen activator receptor (suPAR) and metabolomics to identify untargeted and global small-molecule metabolites, functional opsonophagocytic activity, and splenic function assay with flow cytometric enumeration of Howell-Jolly micronuclei. The biorepository specimens will be shipped to the Children's Healthcare of Atlanta lab.

[b]N/A: not applicable.

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[c]FSH: follicle-stimulating hormone.

[d]LH: luteinizing hormone.

[e]AMH: anti-Mullerian hormone.

[f]HCT: hematopoietic cell transplantation.

[g]All participants will complete height/weight and hip/waist circumference measurements.

[h]TUG: timed up and go.

[i]Participants ≥4 years old will complete handgrip and TUG testing.

[j]The pain diary will only be used over a 2-week period for individuals ≥8 years old who underwent HCT or autologous GT[l] or have SCD[m]. Please see the Pain Diary section for additional details.

[k]Refer to Textbox 1 and Table 1 surveys for additional information.

[l]GT: gene therapy.

[m]SCD: sickle cell disease.

Participant Tracking/Monitoring

Participants receive automated reminders for study procedures. In addition, research coordinators monitor the status of completing surveys, reach out directly to participants, and offer reminders and technical support, as needed. We will also continue the engagement of study participants through relevant educational messages on the study website, personal messages on birthdays and HCT anniversaries, and social reunions of individuals who have undergone HCT.

Power Calculation and Analysis Plan

For adequate power to capture a range of effect sizes in the final registry, we targeted a sample size that would be feasible to recruit and provide adequate statistical power to detect smaller effect sizes (eg, standardized mean difference [SMD]<0.3). To determine whether HCT survivors differ from matched nontransplanted patients with respect to pain, physical functioning, and HRQoL, we would need approximately 1000 patients (500 per group) to have at least 85% power to detect a 0.20 SMD in these outcome measures among the 2 groups using a 2-sided 2-sample *t* test with a type I error rate of 0.025. The primary analysis strategy relies on the use of a propensity score. It is possible that some patients may be missing important baseline data, restricting their inclusion in the propensity score analysis. However, even with 20% missing data without any imputation, our sample size would still achieve at least 80% power to detect a minimum effect size of 0.22 with a 0.025 type I error rate.

Power was calculated using a 2-sample *t* test using Power Analysis & Sample Size (PASS) version 14.0.8 (NCSS, LLC, Kaysville, UT, USA). To recruit an adequate sibling cohort for post-HCT patients with SCD, we will enroll 500 HCT survivors, with nontransplanted patients with SCD recruited at a 1:1 ratio. Assuming at least 75% of patients with HCT will have a sibling control, 375 post-HCT patients with SCD with 375 sibling controls would provide at least 80% and 85% power to detect minimum effect sizes of 0.23 and 0.24, respectively, in the sibling cohort samples using a 2-sided 2-sample *t* test with a 0.025 significance level.

An estimated 996 cases of HCT for SCD were reported between 2008 and 2017, and annually over 140 new cases are reported to the CIBMTR [5,43]. The centers participating in this study reported nearly half of all HCT procedures reported to the CIBMTR to date. Further, since reporting of HCT to the CIBMTR was not mandatory before 2008, and some of the participating centers do not currently report data to the CIBMTR, there may be additional patients available for study. Thus, for this study of the feasibility of the registry, we estimated that if we can enroll and capture outcomes on 50% of the eligible individuals, we would have demonstrated the feasibility of adequate enrollment of post-HCT participants.

Results

Participant Details

We attempted to contact 100 eligible post-HCT individuals with SCD, identified from a review of medical records at a single center. We enrolled 72 (72%) post-HCT individuals who were 9-38 (median 17) years old and 1-29 (median 3) years old, and 63 (87%) of them had received the transplant from an HLA-identical sibling donor. After optimizing study procedures for transplant recipients, we sequentially opened the study to enroll siblings without SCD and nontransplanted patients with SCD. To date, we have enrolled 19 siblings aged 5-32 (median 10) years and have also enrolled 28 nontransplanted controls with SCD, aged 4-46 (median 22) years. Of the 119 participants enrolled in the study so far, 85 sets of surveys have been completed by 73 (61%) nonduplicated participants (51 [70%] post-HCT, 11 [15%] siblings, 11 [15%] controls), including 80 completed PROMIS HRQOL surveys. Although there was variability in the numbers who started each of the different surveys, there were few missing data fields overall and they appeared random for the completed surveys. A total of 44 (61%) post-HCT subjects with SCD (26 [59%] females, 18 [41%] men), 10 (53%) sibling donors, and 10 (36%) nontransplanted controls with SCD have completed the fertility-screening surveys. In addition, hormone surveys have been completed by 63 (53%) individuals, offspring surveys by 22 (19%) individuals, and surveys on PROMIS satisfaction with sexual function by 21 (18%) participants. Measurements of height and weight were available on 72 (61%) individuals. To date, 41 (34%) participants have provided research blood samples, and 20 (17%) participants have also submitted samples on subsequent time points. We piloted data retrieval from the CIBMTR for post-HCT subjects with SCD enrolled in Atlanta, GA, USA. We requested data on 52 post-HCT participants in this study on whom data had previously been submitted to the CIBMTR; 11 (21%) subjects had not signed consent for research at the original data submission to the CIBMTR, so no data could be shared. Of 41 participants who had provided consent to the

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CIBMTR for using their data for research, 14 (34%) had limited essential transplant data collected, while 27 (66%) had been randomized to gather detailed research case report forms. The missing data from the CIBMTR were completed by abstracting data from electronic medical records. The study is now opening at centers in the U.S., U.K., Nigeria, and Canada, and enrollment at other centers has commenced. We have completed 28 (24%) American Time Use Survey (ATUS) interviews.

Discussion

Principal Findings

We described the design and implementation of an international registry designed to capture long-term and late effects of HCT for SCD. Although the importance of long-term and late effects of HCT for SCD is well recognized and consensus guidelines for follow-up have been published, there is still a lack of data on the subject [44-47].

Initial implementation of STELLAR at the pilot site in Atlanta, GA, USA, suggests that such a study is feasible on a large scale. We recruited 72 (72%) of 100 eligible post-HCT patients with SCD at a single site even as we iteratively implemented optimization of our methodology. Enrollment continues, although it is impacted by interruptions in routine clinic attendance during the COVID-19 pandemic. Nevertheless, this invitation response rate for recruitment is comparable to the recruitment experience of long-term survivors of HCT in the BMTSS [48], although the participants are predominantly African Americans and may be disadvantaged by health disparities. Further, although several consenting patients did not complete surveys, those who started surveys completed them with minimal missing data.

Comparison With Previous Studies

This study was modeled on the extensively validated methodology of the Childhood Cancer Survivor Study and the BMTSS [24,49,50]. These studies have refined, validated, and implemented approaches to studying of late effects of treatment. Therefore, we adopted the best practices in the field for this study and adapted them for electronic data capture by patients using a computer, tablet, or smartphone. In addition, we added validated measures of PROs, physical function, and vital measurements.

Strengths

The CIBMTR captures data on the survival of transplant recipients through the HCT center lifelong. The CIBMTR has also demonstrated that centralized PRO data collection in HCT is feasible and clinically meaningful [51]. However, individuals with stable donor-derived erythropoiesis post-HCT are typically no longer followed at the HCT center or to the center. This is likely because they are no longer perceived as needing any specialized services, are not eligible for Medicaid because they do not have the diagnosis of SCD (for US participants), live far from the center, or have difficulty obtaining health insurance as adults. Thus, the HCT center may not be able to provide data or subject access to the CIBMTR. In addition, their primary care provider may or may not be aware of current guidelines on monitoring for the late effects of HCT and may not be performing the screening procedures.

Further, since PROs are not captured during routine clinical encounters, they cannot be retrieved by mining electronic medical records. STELLAR is thus designed to supplement the efforts of the CIBMTR by directly engaging post-HCT and control study participants and enrolling and prospectively following participants in the long term. Such an approach can provide granular information about the health status, health behaviors, and health outcomes throughout the life course.

Another major strength of this study is the detailed follow-up of sexual function and fertility potential. Ovarian and testicular dysfunction are significant concerns for patients facing gonadotoxic therapies. The strong likelihood of loss of reproductive potential is a substantial consideration of patients and their caregivers considering HCT [52]. In addition, sexual dysfunction is a concern in patients post-HCT [53], especially females with failure to produce sex hormones. Males with SCD who have had recurrent priapism are at risk for sexual dysfunction. Therefore, it is crucial to understand the prevalence of infertility, low sex hormone production, and sexual dysfunction in all patients with SCD, including after HCT and autologous GT. These understudied outcomes will aid in counseling patients about expectations around reproductive health with or without curative therapy. In addition, assessing patient perceptions of risk for infertility or sexual dysfunction will assist in adapting communication about reproductive health to avoid inaccurate patient perceptions of reproductive health risks secondary to HCT. An accurate understanding of patient perceptions will help decision-making and promote decisional satisfaction.

Key Lessons Learned in Implementation

In implementing STELLAR at the coordinating site in Atlanta, GA, USA, we learned several vital lessons about recruiting and retaining participants that helped us refine our approach. First, after trying various strategies to reach out to post-HCT patients, we found that the ex-sickle clinic, a clinic focused on the long-term follow-up of survivors of HCT, provides the best opportunity to approach potential participants. The majority of the HCT and sibling participants were enrolled and study procedures were carried out in the setting of an ex-sickle clinic. Such a clinic allows study data to be collected contemporaneously to deliver clinical care and, thus, minimizes participant burden. Further, a sizable majority of post-HCT patients have undergone the procedure within the past 8 years [5]. Therefore, they are likely to retain connections to the HCT center. Thus, they could potentially be reached at such a clinic.

Second, in piloting the study, it became apparent that completing several surveys and repeating them annually may pose a substantial participant burden. Therefore, we have successfully implemented several measures to reduce participant burden, including using branching logic, splitting surveys into multiple parts, and allowing survey data to be carried over from year to year, with the participant being able to review and accept or edit the responses. Several patients who consented to participate in the study still did not complete PROs, which underscores the difficulties inherent in understanding what motivates participants

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to consent and remain in a registry in the long term, how to optimize their experience, and how to communicate information derived from the study that is of interest to them.

Limitations

There are several limitations to this study. First, we recruited participants who remained connected to a single HCT center with a well-established long-term follow-up in an ex-sickle clinic. Expanding this study to the other US and international centers with different institutional and cultural settings with various health care models may require overcoming barriers that may not have been foreseen. Even at this single center, we were only able to offer the study to those patients for whom we had a current address and who were responsive to our efforts to reach them. Thus, our sample does not include any patients unwilling to or unable to connect to the HCT center. Second, we have available PROs only from participants who completed them. Thus, we do not know the impact of selection bias and missing data on STELLAR. To minimize this potential bias and reach a more significant proportion of transplant recipients, we have refined our approach to recruiting subjects directly through internet and social media advertisements. An emerging body of literature will guide our efforts to implement and refine web-based recruitment and address the ethical, regulatory, and logistical issues related to the recruitment and retention of study participants online [54-57]. Once we enroll subjects online, we will also seek their consent to contact their HCT center and obtain additional, detailed, and accurate clinical information relevant to the study.

Conclusion

We described the design of STELLAR and the feasibility of capturing outcomes in patients with SCD who have undergone HCT or GT, their siblings without SCD, and nontransplanted patients with SCD. We also reported the critical lessons learned from refining the study design and optimizing study processes at the lead site in Atlanta, GA, USA. In addition, we have taken essential steps to establish methods for retrieving data submitted to the CIBMTR and harmonizing data collection. Thus, STELLAR provides a model for the longitudinal collection of critical data on the long-term outcomes of HCT and contemporaneous comparison cohorts, which are vital for future studies of allogeneic HCT and autologous GT. The necessary next steps will be the participation of sites worldwide, with ongoing feasibility evaluation of multisite participation.

Conflicts of Interest

None declared.

Multimedia Appendix 1
Peer review summary statement from National Insttutes of Health (NIH).
[PDF File (Adobe PDF File), 160 KB - resprot_v11i7e36780_app1.pdf]

References

1. Badawy SM, Beg U, Liem RI, Chaudhury S, Thompson AA. A systematic review of quality of life in sickle cell disease and thalassemia after stem cell transplant or gene therapy. Blood Adv 2021 Jan 26;5(2):570-583 [FREE Full text] [doi: 10.1182/bloodadvances.2020002948] [Medline: 33496753]
2. Walters MC, Hardy K, Edwards S, Adamkiewicz T, Barkovich J, Bernaudin F, Multicenter Study of Bone Marrow Transplantation for Sickle Cell Disease. Pulmonary, gonadal, and central nervous system status after bone marrow transplantation for sickle cell disease. Biol Blood Marrow Transplant 2010 Feb;16(2):263-272 [FREE Full text] [doi: 10.1016/j.bbmt.2009.10.005] [Medline: 19822218]
3. Bernaudin F, Dalle J, Bories D, de Latour RP, Robin M, Bertrand Y, Société Française de Greffe de Moelle et de Thérapie Cellulaire. Long-term event-free survival, chimerism and fertility outcomes in 234 patients with sickle-cell anemia younger than 30 years after myeloablative conditioning and matched-sibling transplantation in France. Haematologica 2020 Jan;105(1):91-101 [FREE Full text] [doi: 10.3324/haematol.2018.213207] [Medline: 31097628]
4. Cappelli B, Volt F, Tozatto-Maio K, Scigliuolo GM, Ferster A, Dupont S, Eurocord, the Cellular TherapyImmunobiology Working Party (CTIWP) and the Paediatric Diseases Working Party (PDWP) of the EBMT. Risk factors and outcomes according to age at transplantation with an HLA-identical sibling for sickle cell disease. Haematologica 2019 Dec 24;104(12):e543-e546 [FREE Full text] [doi: 10.3324/haematol.2019.216788] [Medline: 31018975]
5. Eapen M, Brazauskas R, Walters MC, Bernaudin F, Bo-Subait K, Fitzhugh CD, et al. Effect of donor type and conditioning regimen intensity on allogeneic transplantation outcomes in patients with sickle cell disease: a retrospective multicentre, cohort study. Lancet Haematol 2019 Nov;6(11):e585-e596. [doi: 10.1016/s2352-3026(19)30154-1]
6. Gluckman E, Cappelli B, Bernaudin F, Labopin M, Volt F, Carreras J, Eurocord, the Pediatric Working Party of the European Society for Blood and Marrow Transplantation,the Center for International Blood and Marrow Transplant Research. Sickle cell disease: an international survey of results of HLA-identical sibling hematopoietic stem cell transplantation. Blood 2017 Mar 16;129(11):1548-1556 [FREE Full text] [doi: 10.1182/blood-2016-10-745711] [Medline: 27965196]
7. Reeve BB, Wang M, Weinfurt K, Flynn KE, Usinger DS, Chen RC. Psychometric evaluation of PROMIS sexual function and satisfaction measures in a longitudinal population-based cohort of men with localized prostate cancer. J Sex Med 2018 Dec;15(12):1792-1810 [FREE Full text] [doi: 10.1016/j.jsxm.2018.09.015] [Medline: 30539735]

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8. Weinfurt KP, Lin L, Bruner DW, Cyranowski JM, Dombeck CB, Hahn EA, et al. Development and initial validation of the PROMIS(®) sexual function and satisfaction measures version 2.0. J Sex Med 2015 Sep;12(9):1961-1974. [doi: 10.1111/jsm.12966] [Medline: 26346418]
9. Gluckman E, Cappelli B, Scigliuolo GM, De la Fuente J, Corbacioglu S. Alternative donor hematopoietic stem cell transplantation for sickle cell disease in Europe. Hematol Oncol Stem Cell Ther 2020 Dec;13(4):181-188 [FREE Full text] [doi: 10.1016/j.hemonc.2019.12.011] [Medline: 32201153]
10. Patel DA, Akinsete AM, de la Fuente J, Kassim AA. Haploidentical bone marrow transplant with posttransplant cyclophosphamide for sickle cell disease: an update. Hematol Oncol Stem Cell Ther 2020 Jun;13(2):91-97 [FREE Full text] [doi: 10.1016/j.hemonc.2020.01.002] [Medline: 32202252]
11. Bolaños-Meade J, Cooke KR, Gamper CJ, Ali SA, Ambinder RF, Borrello IM, et al. Effect of increased dose of total body irradiation on graft failure associated with HLA-haploidentical transplantation in patients with severe haemoglobinopathies: a prospective clinical trial. Lancet Haematol 2019 Apr;6(4):e183-e193 [FREE Full text] [doi: 10.1016/S2352-3026(19)30031-6] [Medline: 30878319]
12. Abraham A, Cluster A, Jacobsohn D, Delgado D, Hulbert ML, Kukadiya D, et al. Unrelated umbilical cord blood transplantation for sickle cell disease following reduced-intensity conditioning: results of a phase I trial. Biol Blood Marrow Transplant 2017 Sep;23(9):1587-1592 [FREE Full text] [doi: 10.1016/j.bbmt.2017.05.027] [Medline: 28578010]
13. Cairo MS, Talano J, Moore TB, Shi Q, Weinberg RS, Grossman B, et al. Familial haploidentical stem cell transplant in children and adolescents with high-risk sickle cell disease: a phase 2 clinical trial. JAMA Pediatr 2020 Feb 01;174(2):195-197 [FREE Full text] [doi: 10.1001/jamapediatrics.2019.4715] [Medline: 31816036]
14. de la Fuente J, Gluckman E, Makani J, Telfer P, Faulkner L, Corbacioglu S, et al. The role of haematopoietic stem cell transplantation for sickle cell disease in the era of targeted disease-modifying therapies and gene editing. Lancet Haematol 2020 Dec;7(12):e902-e911. [doi: 10.1016/S2352-3026(20)30283-0] [Medline: 33242447]
15. Esrick EB, Lehmann LE, Biffi A, Achebe M, Brendel C, Ciuculescu MF, et al. Post-transcriptional genetic silencing of BCL11A to treat sickle cell disease. N Engl J Med 2021 Jan 21;384(3):205-215 [FREE Full text] [doi: 10.1056/NEJMoa2029392] [Medline: 33283990]
16. Frangoul H, Ho TW, Corbacioglu S. CRISPR-Cas9 gene editing for sickle cell disease and β-thalassemia. Reply. N Engl J Med 2021 Jun 10;384(23):e91. [doi: 10.1056/NEJMc2103481] [Medline: 34107197]
17. Artero EG, España-Romero V, Castro-Piñero J, Ortega FB, Suni J, Castillo-Garzon MJ, et al. Reliability of field-based fitness tests in youth. Int J Sports Med 2011 Mar;32(3):159-169. [doi: 10.1055/s-0030-1268488] [Medline: 21165805]
18. Bianco A, Jemni M, Thomas E, Patti A, Paoli A, Ramos Roque J, et al. A systematic review to determine reliability and usefulness of the field-based test batteries for the assessment of physical fitness in adolescents: the ASSO Project. Int J Occup Med Environ Health 2015;28(3):445-478 [FREE Full text] [doi: 10.13075/ijomeh.1896.00393] [Medline: 26190724]
19. Ortega FB, Cadenas-Sánchez C, Sánchez-Delgado G, Mora-González J, Martínez-Téllez B, Artero EG, et al. Systematic review and proposal of a field-based physical fitness-test battery in preschool children: the PREFIT battery. Sports Med 2015 Apr;45(4):533-555. [doi: 10.1007/s40279-014-0281-8] [Medline: 25370201]
20. Slater ME, Steinberger J, Ross JA, Kelly AS, Chow EJ, Koves IH, et al. Physical activity, fitness, and cardiometabolic risk factors in adult survivors of childhood cancer with a history of hematopoietic cell transplantation. Biol Blood Marrow Transplant 2015 Jul;21(7):1278-1283 [FREE Full text] [doi: 10.1016/j.bbmt.2015.04.007] [Medline: 25865649]
21. Morishita S, Kaida K, Aoki O, Yamauchi S, Wakasugi T, Ikegame K, et al. Balance function in patients who had undergone allogeneic hematopoietic stem cell transplantation. Gait Posture 2015 Sep;42(3):406-408. [doi: 10.1016/j.gaitpost.2015.07.011] [Medline: 26233580]
22. Salas MQ, Atenafu EG, Bascom O, Wilson L, Lam W, Law AD, et al. Pilot prospective study of frailty and functionality in routine clinical assessment in allogeneic hematopoietic cell transplantation. Bone Marrow Transplant 2021 Jan;56(1):60-69. [doi: 10.1038/s41409-020-0979-1] [Medline: 32606454]
23. Armenian SH, Sun C, Francisco L, Baker KS, Weisdorf DJ, Forman SJ, et al. Health behaviors and cancer screening practices in long-term survivors of hematopoietic cell transplantation (HCT): a report from the BMT Survivor Study. Bone Marrow Transplant 2012 Feb;47(2):283-290 [FREE Full text] [doi: 10.1038/bmt.2011.60] [Medline: 21423125]
24. Louie AD, Robison LL, Bogue M, Hyde S, Forman SJ, Bhatia S. Validation of self-reported complications by bone marrow transplantation survivors. Bone Marrow Transplant 2000 Jun;25(11):1191-1196. [doi: 10.1038/sj.bmt.1702419] [Medline: 10849532]
25. Baker F, Zabora J, Polland A, Wingard J. Reintegration after bone marrow transplantation. Cancer Pract 1999;7(4):190-197. [doi: 10.1046/j.1523-5394.1999.74005.x] [Medline: 10687584]
26. Badawy SM, Thompson AA, Lai J, Penedo FJ, Rychlik K, Liem RI. Adherence to hydroxyurea, health-related quality of life domains, and patients' perceptions of sickle cell disease and hydroxyurea: a cross-sectional study in adolescents and young adults. Health Qual Life Outcomes 2017 Jul 05;15(1):136 [FREE Full text] [doi: 10.1186/s12955-017-0713-x] [Medline: 28679417]
27. Curtis S, Brandow AM. Responsiveness of Patient-Reported Outcome Measurement Information System (PROMIS) pain domains and disease-specific patient-reported outcome measures in children and adults with sickle cell disease. Hematology

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Am Soc Hematol Educ Program 2017 Dec 08;2017(1):542-545 [FREE Full text] [doi: 10.1182/asheducation-2017.1.542] [Medline: 29222303]
28. Dampier C, Barry V, Gross HE, Lui Y, Thornburg CD, DeWalt DA, et al. Initial evaluation of the pediatric PROMIS® health domains in children and adolescents with sickle cell disease. Pediatr Blood Cancer 2016 Jun;63(6):1031-1037 [FREE Full text] [doi: 10.1002/pbc.25944] [Medline: 26895143]
29. Keller S, Yang M, Treadwell MJ, Hassell KL. Sensitivity of alternative measures of functioning and wellbeing for adults with sickle cell disease: comparison of PROMIS® to ASCQ-Me . Health Qual Life Outcomes 2017 Jun 02;15(1):117 [FREE Full text] [doi: 10.1186/s12955-017-0661-5] [Medline: 28577358]
30. Reeve BB, Edwards LJ, Jaeger BC, Hinds PS, Dampier C, Gipson DS, et al. Assessing responsiveness over time of the PROMIS pediatric symptom and function measures in cancer, nephrotic syndrome, and sickle cell disease. Qual Life Res 2018 Jan;27(1):249-257 [FREE Full text] [doi: 10.1007/s11136-017-1697-z] [Medline: 28884421]
31. Cella D, Choi SW, Condon DM, Schalet B, Hays RD, Rothrock NE, et al. PROMIS adult health profiles: efficient short-form measures of seven health domains. Value Health 2019 May;22(5):537-544 [FREE Full text] [doi: 10.1016/j.jval.2019.02.004] [Medline: 31104731]
32. Hays RD, Spritzer KL, Schalet BD, Cella D. PROMIS-29 v2.0 profile physical and mental health summary scores. Qual Life Res 2018 Jul;27(7):1885-1891 [FREE Full text] [doi: 10.1007/s11136-018-1842-3] [Medline: 29569016]
33. Cooper O, McBain H, Tangayi S, Telfer P, Tsitsikas D, Yardumian A, et al. Psychometric analysis of the adult sickle cell quality of life measurement information system (ACSQ-Me) in a UK population. Health Qual Life Outcomes 2019 Apr 29;17(1):74 [FREE Full text] [doi: 10.1186/s12955-019-1136-7] [Medline: 31036017]
34. Keller SD, Yang M, Treadwell MJ, Werner EM, Hassell KL. Patient reports of health outcome for adults living with sickle cell disease: development and testing of the ASCQ-Me item banks. Health Qual Life Outcomes 2014 Aug 22;12:125 [FREE Full text] [doi: 10.1186/s12955-014-0125-0] [Medline: 25146160]
35. Treadwell MJ, Hassell K, Levine R, Keller S. Adult sickle cell quality-of-life measurement information system (ASCQ-Me): conceptual model based on review of the literature and formative research. Clin J Pain 2014 Oct;30(10):902-914 [FREE Full text] [doi: 10.1097/AJP.0000000000000054] [Medline: 24300219]
36. Edwards R, Telfair J, Cecil H, Lenoci J. Reliability and validity of a self-efficacy instrument specific to sickle cell disease. Behav Res Ther 2000 Sep;38(9):951-963. [doi: 10.1016/s0005-7967(99)00140-0] [Medline: 10957829]
37. Clay OJ, Telfair J. Evaluation of a disease-specific self-efficacy instrument in adolescents with sickle cell disease and its relationship to adjustment. Child Neuropsychol 2007 Mar;13(2):188-203. [doi: 10.1080/09297040600770746] [Medline: 17364574]
38. Lee SK, Cook EF, Soiffer R, Antin JH. Development and validation of a scale to measure symptoms of chronic graft-versus-host disease. Biol Blood Marrow Transplant 2002;8(8):444-452 [FREE Full text] [doi: 10.1053/bbmt.2002.v8.pm12234170] [Medline: 12234170]
39. Merkel EC, Mitchell SA, Lee SJ. Content validity of the Lee Chronic Graft-versus-Host Disease Symptom Scale as assessed by cognitive interviews. Biol Blood Marrow Transplant 2016 Apr;22(4):752-758 [FREE Full text] [doi: 10.1016/j.bbmt.2015.12.026] [Medline: 26751003]
40. Abel GA, Albelda R, Khera N, Hahn T, Salas Coronado DY, Odejide OO, et al. Financial hardship and patient-reported outcomes after hematopoietic cell transplantation. Biol Blood Marrow Transplant 2016 Aug;22(8):1504-1510 [FREE Full text] [doi: 10.1016/j.bbmt.2016.05.008] [Medline: 27184627]
41. Bona K, London WB, Guo D, Abel G, Lehmann L, Wolfe J. Prevalence and impact of financial hardship among New England pediatric stem cell transplantation families. Biol Blood Marrow Transplant 2015 Feb;21(2):312-318 [FREE Full text] [doi: 10.1016/j.bbmt.2014.10.016] [Medline: 25445021]
42. Bakshi N, Stinson JN, Ross D, Lukombo I, Mittal N, Joshi SV, et al. Development, content validity, and user review of a web-based multidimensional pain diary for adolescent and young adults with sickle cell disease. Clin J Pain 2015 Jun;31(6):580-590. [doi: 10.1097/AJP.0000000000000195] [Medline: 25565585]
43. Transplant Activity Report. URL: https://bloodstemcell.hrsa.gov/data/donation-and-transplantation-statistics/transplant-activity-report#year [accessed 2022-04-21]
44. Elchuri SV, Williamson Lewis R, Quarmyne M, Haight AE, Cottrell HN, Meacham LR. Longitudinal description of gonadal function in sickle-cell patients treated with hematopoietic stem cell transplant using alkylator-based conditioning regimens. J Pediatr Hematol Oncol 2020 Oct;42(7):e575-e582. [doi: 10.1097/MPH.0000000000001782] [Medline: 32205784]
45. Fitzhugh CD, Perl S, Hsieh MM. Late effects of myeloablative bone marrow transplantation (BMT) in sickle cell disease (SCD); author reply 1744. Blood 2008 Feb 01;111(3):1742-1743 [FREE Full text] [doi: 10.1182/blood-2007-10-118257] [Medline: 18223176]
46. Shenoy S, Angelucci E, Arnold SD, Baker KS, Bhatia M, Bresters D, et al. Current results and future research priorities in late effects after hematopoietic stem cell transplantation for children with sickle cell disease and thalassemia: a consensus statement from the Second Pediatric Blood and Marrow Transplant Consortium International Conference on Late Effects after Pediatric Hematopoietic Stem Cell Transplantation. Biol Blood Marrow Transplant 2017 Apr;23(4):552-561 [FREE Full text] [doi: 10.1016/j.bbmt.2017.01.009] [Medline: 28065838]

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47. Shenoy S, Gaziev J, Angelucci E, King A, Bhatia M, Smith A, et al. Late effects screening guidelines after hematopoietic cell transplantation (hct) for hemoglobinopathy: consensus statement from the Second Pediatric Blood and Marrow Transplant Consortium International Conference on Late Effects after Pediatric HCT. Biol Blood Marrow Transplant 2018 Jul;24(7):1313-1321 [FREE Full text] [doi: 10.1016/j.bbmt.2018.04.002] [Medline: 29653206]
48. Shankar SM, Carter A, Sun C, Francisco L, Baker KS, Gurney JG, et al. Health care utilization by adult long-term survivors of hematopoietic cell transplant: report from the Bone Marrow Transplant Survivor Study. Cancer Epidemiol Biomarkers Prev 2007 Apr;16(4):834-839. [doi: 10.1158/1055-9965.EPI-06-0714] [Medline: 17416780]
49. Holmqvist AS, Chen Y, Wu J, Battles K, Bhatia R, Francisco L, et al. Late mortality after autologous blood or marrow transplantation in childhood: a Blood or Marrow Transplant Survivor Study-2 report. Blood 2018 Jun 14;131(24):2720-2729 [FREE Full text] [doi: 10.1182/blood-2018-02-831156] [Medline: 29661789]
50. Murdaugh DL, Bosworth A, Patel SK, Sharafeldin N, Chen Y, Francisco L, et al. Self-endorsed cognitive problems versus objectively assessed cognitive impairment in blood or bone marrow transplantation recipients: a longitudinal study. Cancer 2020 May 15;126(10):2174-2182 [FREE Full text] [doi: 10.1002/cncr.32773] [Medline: 32097508]
51. Shaw BE, Brazauskas R, Millard HR, Fonstad R, Flynn KE, Abernethy A, et al. Centralized patient-reported outcome data collection in transplantation is feasible and clinically meaningful. Cancer 2017 Dec 01;123(23):4687-4700 [FREE Full text] [doi: 10.1002/cncr.30936] [Medline: 28817182]
52. Sinha CB, Bakshi N, Ross D, Loewenstein G, Krishnamurti L. Primary caregiver decision-making in hematopoietic cell transplantation and gene therapy for sickle cell disease. Pediatr Blood Cancer 2021 Jan 08;68(1):e28749 [FREE Full text] [doi: 10.1002/pbc.28749] [Medline: 33034129]
53. Noerskov KH, Schjødt I, Syrjala KL, Jarden M. Sexual function 1-year after allogeneic hematopoietic stem cell transplantation. Bone Marrow Transplant 2016 Jun;51(6):833-840 [FREE Full text] [doi: 10.1038/bmt.2015.342] [Medline: 26878660]
54. Frandsen M, Thow M, Ferguson SG. The effectiveness of social media (Facebook) compared with more traditional advertising methods for recruiting eligible participants to health research studies: a randomized, controlled clinical trial. JMIR Res Protoc 2016 Aug 10;5(3):e161 [FREE Full text] [doi: 10.2196/resprot.5747] [Medline: 27511829]
55. Koziol-McLain J, McLean C, Rohan M, Sisk R, Dobbs T, Nada-Raja S, et al. Participant recruitment and engagement in automated eHealth trial registration: challenges and opportunities for recruiting women who experience violence. J Med Internet Res 2016 Oct 25;18(10):e281 [FREE Full text] [doi: 10.2196/jmir.6515] [Medline: 27780796]
56. Lattie EG, Kaiser SM, Alam N, Tomasino KN, Sargent E, Rubanovich CK, et al. A practical do-it-yourself recruitment framework for concurrent ehealth clinical trials: identification of efficient and cost-effective methods for decision making (part 2). J Med Internet Res 2018 Nov 29;20(11):e11050 [FREE Full text] [doi: 10.2196/11050] [Medline: 30497997]
57. Pang PC, Chang S, Verspoor K, Clavisi O. The use of web-based technologies in health research participation: qualitative study of consumer and researcher experiences. J Med Internet Res 2018 Oct 30;20(10):e12094 [FREE Full text] [doi: 10.2196/12094] [Medline: 30377139]

Abbreviations

AMH: anti-Mullerian hormone
ASCQ-Me: Adult Sickle Cell Quality of Life Measurement Information System
ATUS: American Time Use Survey
BMTSS: Bone Marrow Transplant Survivor Study
cGVHD: chronic graft-versus-host disease
CIBMTR: Center for International Blood and Marrow Transplant Research
DFCI: Dana Farber Cancer Institute.
EMA: ecological momentary assessment
FSH: follicle-stimulating hormone
GT: gene therapy
GVHD: graft-versus-host disease
HCT: hematopoietic cell transplantation
HLA: human leukocyte antigen
HRQOL: health-related quality of life
IRB: Institutional Review Board
LH: luteinizing hormone
PROMIS: Patient-Reported Outcomes Measurement Information System
SCD: sickle cell disease
SCD SEQ-C: Sickle Cell Disease Self-Efficacy Questionnaire for Children
SMD: standardized mean difference
STELLAR: Sickle Cell Transplantation Evaluation of Long-Term and Late Effects Registry
TUG: timed up and go

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Protocol

Proximal Risk for Suicide: Protocol for an Ecological Momentary Assessment Study

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Abstract

Background: Suicide is a prevalent public health concern in the United States across all age groups. Research has emphasized the need to identify risk markers that prevent suicide along shorter timeframes, such as days to weeks. Furthermore, little has been done to explore the relative significance of factors that can predict short-term suicide risk or to evaluate how daily variability in these factors impacts suicidal ideation or behavior. This proposed project aims to identify risk factors that best predict near-time changes in suicidal ideation and examine potential interactions between these factors to predict transitions into suicidal thinking or behaviors.

Objective: The aim of this proposed study is threefold: (1) To identify which psychological risk factors are most strongly associated with proximal changes in suicide risk across days and weeks. (2) To evaluate theoretical assumptions of the Integrative-Motivational-Volitional Theory of Suicide. (3) To determine how disruptions in physiological arousal interact with theoretical mechanisms of risk to predict concurrent and short-term prospective increase in suicidal thoughts and behaviors.

Methods: A daily diary or ecological momentary assessment design will be utilized with 200 participants. Participants will complete 2 in-person visits separated by 3 weeks during which they will complete 3 brief daily assessments within their natural environments using the ilumivu research app on a smart device. Research will occur at the Mayo Clinic Health System (MCHS) Eau Claire site. Participants will be recruited through chart review and standard care delivery assessment.

Results: This manuscript outlines the protocol that will guide the conduct of the forthcoming study.

Conclusions: The proposed project aims to lead efforts using technological advances to capture microchanges in suicidal thinking/behavior over shorter timeframes and thereby guide future clinical assessment and management of suicidal patients. Results of this study will generate robust evidence to evaluate which risk factors predict proximal changes in suicidal ideation and behaviors. They will also provide the ability to examine potential interactions with multiple theoretically derived risk factors to predict proximal transitions into worsening suicidal thinking or behaviors. Such information will provide new targets for intervention that could ultimately reduce suicide-related morbidity and mortality.

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KEYWORDS

suicide; suicide risk; suicide ideation; suicide prevention; diary; ecological momentary assessment; Integrative-Volitional-Motivational Theory

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Introduction

Background

Deaths from suicide continue to rise within the United States across all age groups [1]. Despite it being a significant public health concern, little progress has been made over the past 50 years in our ability to differentiate those at risk of suicidal thoughts versus attempts [2]. While many risk factors, warning signs, and predictors have been identified for suicidal risk broadly, most research has focused on factors that predict suicide within the next year [2]. This is of minimal utility for the clinician trying to evaluate whether a patient may attempt suicide in the coming hours and days. Researchers emphasize the need to identify risk markers that predict suicide in days to weeks [3,4], but this work remains scarce. Even within this inquiry into shorter-term risk, most studies focus on single psychiatric or demographic risk factors, which is problematic given that suicide is a complex phenomenon involving multiple interacting factors [5,6]. Major advances in the prevention of suicide require studies that examine interacting processes that covary with and immediately precede changes in suicidal behavior [2,7].

Some of the factors that appear to predict short-term risk for escalation in suicidal thinking or attempts include specific hopelessness about life concerns [8,9], engagement in nonsuicidal self-injury (NSSI; [10]), interpersonal stressors including perceived burdensomeness and lack of belonging [11], substance use [2], poor sleep quality/insomnia [12,13], agitation [14], and self-criticism/self-hate [15]. However, only few of these factors have been examined simultaneously to determine the most important ones to discerning suicide risk; besides, none have been studied to evaluate how daily variability in these factors impacts daily changes in suicidal thinking or behavior. This study begins to address these scientific and clinical questions by identifying which of the noted factors hold the strongest association with short-term suicide-related crisis escalation within and across days, in addition to examining potential interactions among the variables.

Recent theoretical models of suicide acknowledge the volatile nature of suicidal thinking/risk across hours and days, stressing the importance of identifying how changes in theorized risk factors interact to facilitate transitions from suicidal thinking to suicidal actions. The Integrative-Motivational-Volitional (IMV) Theory of Suicide [16] specifies that transitions to suicidal thinking and behavior are determined by different state-specific processes that interact with preexisting states of distress (eg, entrapment, hopelessness) to either facilitate or hinder movement between thinking and acting. Motivational factors (eg, loneliness, burdensomeness, specific hopelessness) are theorized to impact the development of suicidal ideation, whereas volitional factors (eg, self-hate, agitation, reduced fears of death, engagement in NSSI) impact transition to suicidal behavior. While there is support for the IMV, almost all the research has been cross sectional, exploring single motivational moderators impacting the emergence of suicidal ideation (eg, [17,18]). To date, there are only 2 known studies [19,20] that have evaluated the daily or weekly relationship between motivational or volitional factors and the transition to suicidal behavior. One study evaluated the motivational factors of hopelessness, thwarted belonging, and perceived belongingness within 74 patients who completed a 6-day ecological momentary assessment (EMA) protocol [20]. They found that hopelessness and perceived burdensomeness prospectively predicted both passive and active suicidal ideation, and the interaction between thwarted belonging and perceived burdensomeness also predicted active ideation. These results were similar to those reported by Al-Dajani and Czyz [19] in a sample of 78 adolescents hospitalized for suicide risk. The limited research examining proximal changes in motivational and volitional factors for suicide ideation and behavior represents a major gap in the field and is essential to evaluating the clinical validity of the IMV theory. In addition, studies have yet to explore how motivational and volitional factors interact among themselves to influence risk escalation and how other psychological processes (eg, sleep quality) may impact these factors and their temporal variability in risk transition. The proposed project will be the first to provide data testing these theoretical assumptions.

Recent studies of acute risk for suicide have identified that forms of physiological arousal such as agitation [21] and sleep difficulties [22] are linked to risk for suicidal behavior [23]. Meta-analyses consistently identify that insomnia, disrupted sleep patterns, and especially nightmares are linked to increased suicide risk [12,13,22,24]. Studies evaluating interactions between variability in sleep disturbances and other psychological processes (eg, agitation, self-hate, burdensomeness) believed to impact suicide risk are lacking. This study will advance scientific knowledge and potentially improve the utility of suicide theories, such as the IMV for clinical practice, by examining how sleep disturbances impact psychological processes, such as agitation, to predict near-term changes in suicidal thinking or behaviors.

We know that suicidal ideation and behavior are fluid across hours and days, and that suicidal crises are typically brief [3,25,26]. Most of the existing research relies on long-term retrospective recall; little research uses prospective designs and many use hospital records, which provide limited details of individual experiences. EMA studies have participants respond to brief surveys multiple times daily, providing an avenue to identify acute precursors of problematic behavior and contribute new insights into the factors impacting the fluid nature of suicidal ideation and behavior. Assessing components of ideation-to-action transitions through an EMA methodology has the advantage of relying on recall from the past hours rather than recall over days, weeks, and months. Numerous experts have called for an increase in the use of micro-longitudinal methods such as EMA to study suicide [27,28], yet these studies remain rare [29].

To date, there are a few known studies that have utilized EMA research designs to obtain data about the within- and between-day changes in suicidal thinking (our study will be among the first to also examine suicidal behaviors). The first study was conducted by Kleiman and colleagues [26]. They enrolled 90 adults with a recent suicide attempt recruited from the social media platform Reddit or inpatients hospitalized for suicide attempts. These participants completed up to 28 days of EMA data collection that included 4 randomly signaled

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assessment prompts separated by 4-8 hours. Results revealed that suicidal ideation severity fluctuated markedly across hours, as did the risk factors assessed. The variability in the risk factors experienced was significantly correlated with concurrent changes in suicidal thinking. Three similar studies, all conducted with adolescents discharged from acute psychiatric care [30-32], found similar results in that suicidal ideation significantly fluctuated across hours and covaried with similar fluctuations in assessed risk factors. Relevant to the current proposal, a recent EMA study (1-week duration; 6 assessment prompts/day) of 51 adults with current suicidal ideation found that a shorter sleep duration predicted higher severity of suicidal ideation the next day. Furthermore, Hallensleben and colleagues [20] reported that both passive and active ideation demonstrated significant within- and moment-to-moment variability, which was associated with momentary variability in hopelessness and perceived burdensomeness. These studies provide some of the first and much needed, fine-grained data to better understand how suicide risk varies across short intervals. They provide proof of concept and feasibility of using EMA to study suicide safely but remain primarily descriptive and fail to test prominent theoretical assumptions detailing transitions to increased suicidal thinking and behaviors.

This proposed project will be one of the first to better define which risk factors predict near-time changes in suicidal ideation and provide data on potential interactions among multiple theoretically derived risk factors to predict proximal transitions into worsening suicidal thinking or behaviors. The ability to provide data capable of identifying proximal indicators of risk and temporal sequencing of risk factors to suicidal behaviors addresses a suicide research priority [29,33], and the data to be collected will also enable a variety of additional exploratory aims related to the IMV theory to be evaluated. To truly advance the field of suicide research and prevention, researchers must begin to use innovative methodologies, such as EMA, to assess patients at frequent intervals to understand the acute evolution of suicidal crises. This study will fill a gap in the existing research on suicide, providing a fine-grain assessment of theoretical risk factors believed to impact the processes that influence suicidal crisis and provide clinicians with more ecologically valid risk indicators to monitor with their patients.

Study Aims and Objectives

The purpose of this study is to better understand suicide risk among patients by identifying the daily markers/factors associated with near-term (proximal) escalation in suicide thinking and behaviors among patients so that clinicians can be better prepared to monitor risk and intervene.

The aims of this study are as follows:

1. To identify which psychological risk factors are most strongly associated with proximal changes in suicide risk across days and weeks to enhance clinical risk monitoring.
   - Hypothesis 1a: Based on the IMV theory predictions [16] as well as recently published work (eg, [19,20]), within-day variability of hopelessness, self-hate, agitation, entrapment, burdensomeness, and connectedness will be associated with same-day moment-to-moment variability in suicidal ideation and behaviors.
   - Hypothesis 1b: Participants will be more likely to report increases in suicidal ideation on days when they experience increases in hopelessness, burdensomeness, entrapment, and decreases in connectedness (see [19,34]).
   - Hypothesis 1c: Given recent work demonstrating that poor sleep quality predicted next-day increases in suicidal ideation (eg, [35]), we also hypothesize that participants will be more likely to report engagement in suicidal behaviors on days when sleep quality is poor, and self-hate and agitation are high.
2. To evaluate theoretical assumptions of the IMV [16] theory describing transitional processes from suicidal ideation to behavior:
   - Hypothesis 2a: According to the IMV theoretical predictions and cross-sectional studies (eg, [17]), we hypothesize that changes in entrapment and hopelessness will produce changes in suicidal ideation and the strength of the association will be moderated by variability in burdensomeness, connectedness, and self-hate (eg, motivational moderators).
   - Hypothesis 2b: Changes in suicidal ideation will co-occur with changes in suicidal behavior and the strength of the association will be moderated by variability in NSSI engagement/urges, self-hate, and agitation (eg, volitional moderators; [10,16]).
3. To determine how disruptions in physiological arousal (sleep problems/substance use) interact with theoretical mechanisms of risk [16] to predict concurrent and short-term prospective increases in suicidal thoughts and behaviors.

   Drawing from empirical studies showing that disruptions in sleep (eg, [35,36]) and increases in substance abuse (eg, [37]) are related to increased suicidal thoughts and behaviors, we hypothesize that:
   - Hypothesis 3a: Daily (weekly) changes in sleep quality (and substance use) will be associated with next day (week) changes in hopelessness, self-hate, burdensomeness, entrapment, and agitation to predict changes in suicidal ideation and behaviors (also see [38]).
   - Hypothesis 3b: Daily (weekly) variability in sleep quality (substance use) will interact with entrapment, hopelessness, and the motivational moderators of connectedness and burdensomeness to predict concurrent and next day (week) increases in suicidal ideation.
   - Hypothesis 3c: Daily (weekly) variability in sleep quality (substance use) will interact with suicidal ideation, self-hate, and agitation to predict concurrent and next-day (week) engagement in suicidal behaviors.

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Methods

Study Design

This study uses a micro-longitudinal study design, also known as a daily diary or EMA. We will use EMA to refer to this study design throughout this proposal. The general study procedure includes participants completing 2 in-person visits, separated by 3 weeks, during which they will complete 3 brief (approximately 5 minutes) daily assessments within their natural environments through the ilumivu research app downloaded onto their smartphone or a similar device (total daily time commitment required is approximately 15 minutes). The first in-person visit will be used to enroll participants into the study and begin active data collection, including training participants to use the EMA study app. After the 3 weeks, participants will return for a final in-person visit to conclude their participation.

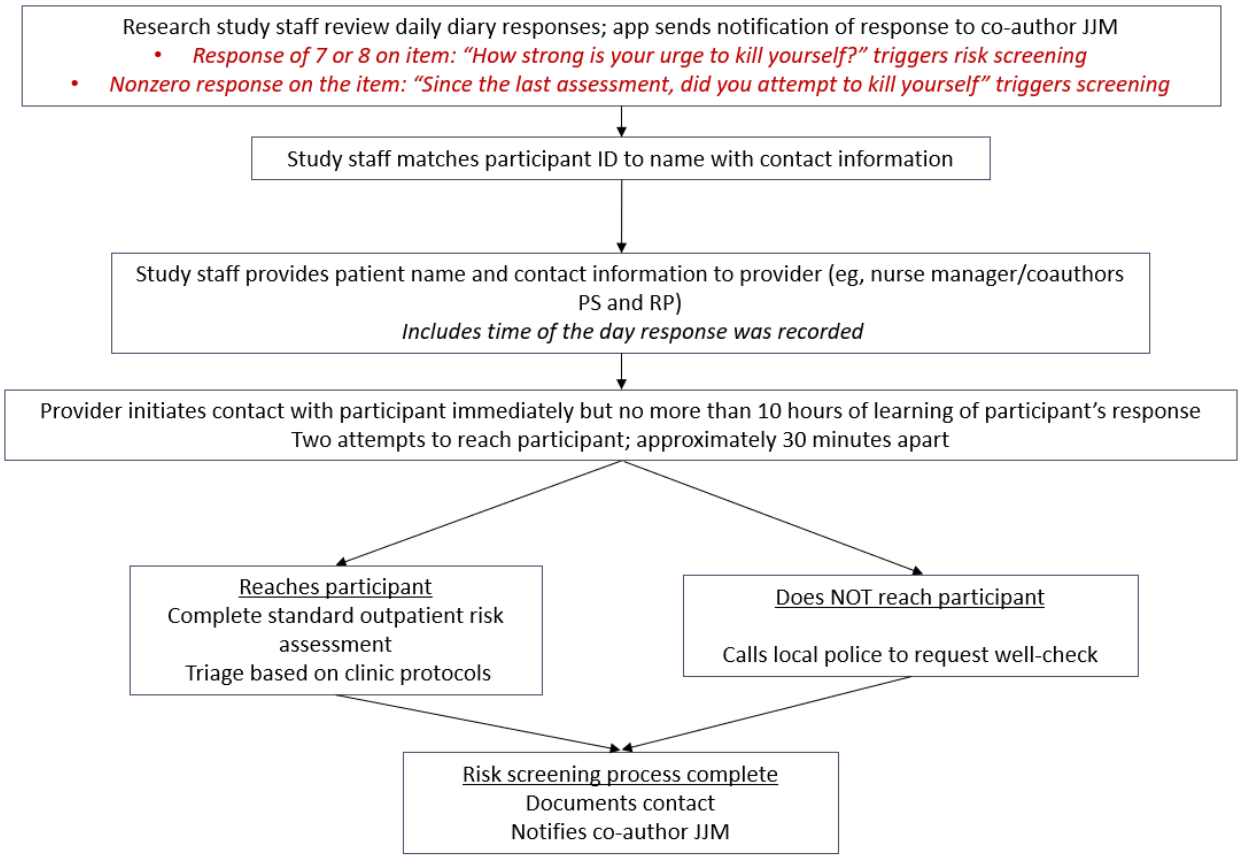
Recruitment

This research will occur at the Mayo Clinic Health System Eau Claire site. Study staff will identify potential participants through chart review and standard care delivery assessment processes. Patients who meet inclusion criteria for suicidal thinking (ie, a score of ≥1 in item 9 of the Patient Health Questionnaire or a "yes" response to item 2 in the Columbia-Suicide Severity Rating Scale [C-SSRS] screening tool and are patients involved with behavioral health services) will be recruited for the study. Eligible patients will be contacted through their patient portal with information about the study and invited to participate in the study by reaching out to study staff via email or phone. Treating clinicians may also identify potential participants who will briefly inform the patient about the study, stating that the study staff will contact them if the patient expresses interest in participating. The referring clinician would then provide the patient's name to the research study coordinator. Study staff will contact potential participants, provide additional study information, and schedule a 1:1 meeting to obtain consent/collect baseline data.

Baseline Data Collection Visit (Visit 1)

Study staff will meet with a potential participant in a private room within the outpatient behavioral health clinic to gather participant consent to participate in the study. Study staff will verbally review the informed consent form with participants, including a careful review of the study safety protocol (Figure 1), answering questions and concerns. Patients agreeing to participate will sign the informed consent form and be given a copy for their records.

Figure 1. Safety screening process flowchart.



Following the consenting process, participants will complete the baseline data collection protocol consisting of self-report questionnaires and behavioral reaction time tasks on an iPad provided by the study staff. The baseline questionnaires will be accessed through a hyperlink to a study-specific survey housed on Inquisit, a secure online survey administration tool. The baseline assessments include psychometrically validated comprehensive measures of the primary variables of interest to the study that will be presented in a random order across participants to reduce ordering effects on the data quality. The

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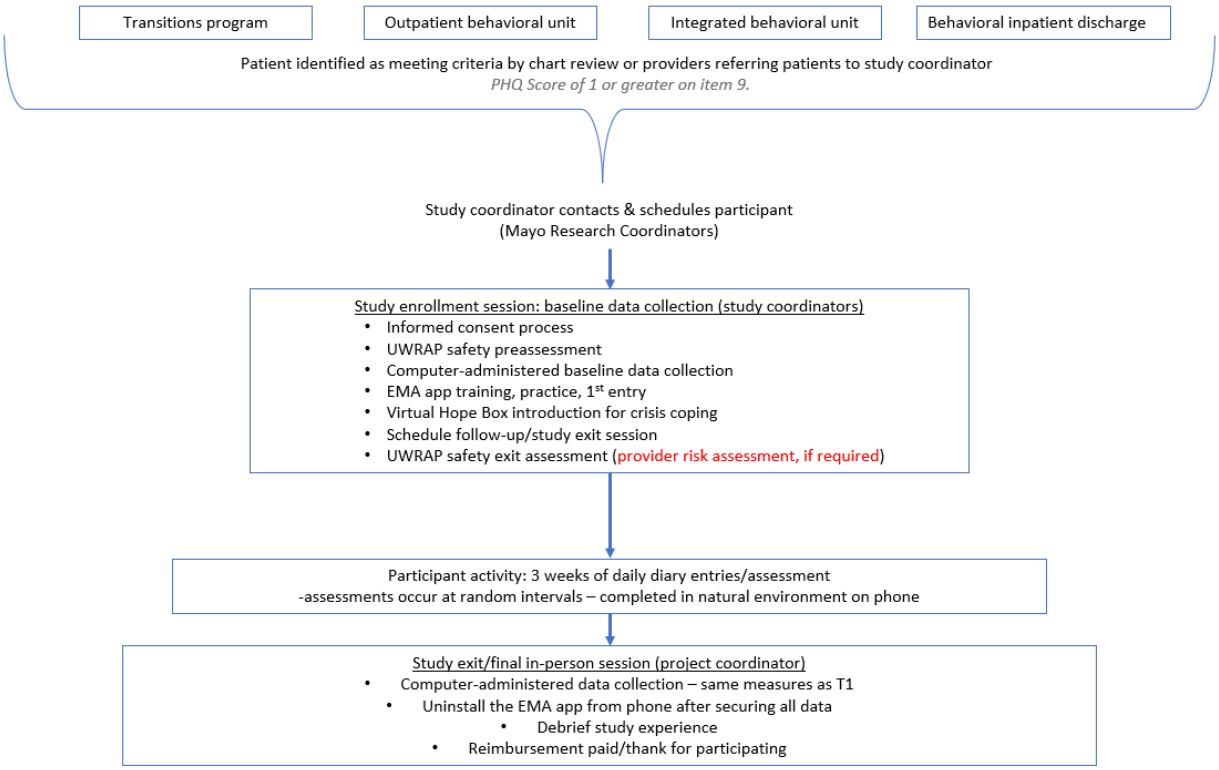
content of the baseline assessment can be seen in Multimedia Appendix 1. Following baseline data collection, participants will be introduced to the ilumivu EMA app. Study staff will assist participants with downloading the required apps onto their smartphone device. Participants will be trained on using the EMA app for data collection and complete their first EMA entry.

After completing their first EMA data entry on their smartphone, participants will be introduced to the Virtual Hope Box app, which is a freely accessible app that has demonstrated effectiveness as a tool to manage and cope with suicidal urges [39,40]. Participants will be encouraged to download this app to help manage future suicidal impulses as part of the study safety protocol, in addition to being provided local and national crisis response resources. At the end of this session, participants will be compensated for their initial visit (US $30.00) and schedule their final session visit appointment (Figure 2).

Figure 2. Study process workflow. EMA: ecological momentary assessment; PHQ: Patient Health Questionnaire; UWRAP: University of Washington Risk Assessment Protocol.



Three-Week EMA Data Collection

Starting on the day of the study enrollment, participants will begin the EMA data collection phase of the study. On each day for a 3-week period, participants will be notified to log into the EMA app on their smartphone 3 times throughout the day (7-10 AM, 1-4 PM, and 6-9 PM). Each assessment will include single-item questions evaluating the study variables and should take approximately 5 minutes to complete. Questions about sleep quality will only be asked during the first daily assessment and questions about substance use and medication adherence will only be asked during the third/final assessment of each day. The content for each daily diary assessment can be accessed through Multimedia Appendix 2. Participants who have not responded during a survey window will receive a push notification to remind them to complete their survey before it closes (within 30 minutes of the timeframe).

Study Completion (Final Visit)

Study staff will contact participants before their scheduled study completion visit to confirm the appointment or reschedule if necessary. At this visit, participants will complete the same set of computer-administered questionnaires that were completed during the enrollment visit, allowing for longitudinal data analysis with comprehensive measures of the study variables. Study staff will ensure participants safely uninstall the ilumivu EMA software app from their smartphones and will debrief the study experience. Questions will be answered, and participants will receive their prorated compensation based on visits/daily assessments completed.

Analysis

Research aim 1 focuses on testing the coupled associations between within-day variability of psychological risk factors and within-day variability of suicidal thoughts and behaviors. For Hypothesis 1a, the root mean square of successive differences (RMSSDs) can be used to quantify within-person variability in clinical indicators while accounting for temporal dependency, amplitude, and frequency [41]. We will calculate the within-day RMSSD of each psychological risk factor (ie, hopelessness, self-hate, agitation, entrapment, burdensomeness, and connectedness) and each outcome (ie, suicidal ideation and suicidal behaviors). The RMSSD of each risk factor will then be used as a level 1 predictor of same-day RMSSD of each

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outcome in a multilevel linear model. We will include any demographic covariates in the level 2 model. A lagged model will assess whether variability in risk factors on day *t* predicts suicide outcomes on day *t* + 1, controlling for variability in risk factor at *t* + 1. To test hypothesis 1b, we will examine the within-day coupled association between the average level of suicidal ideation in each assessment and the average level of each psychological risk factor (ie, hopelessness, self-hate, agitation, entrapment, burdensomeness, and connectedness). Risk factors will be entered as level 1 predictors in separate multivariate linear models (MLMs), with suicidal ideation as the dependent variable. To test hypothesis 1c, we will first create a daily average of self-hate and agitation (each measured 3 times per day) using the mean score of available reports. We will then run separate MLMs with sleep quality, average self-hate, and average agitation as level 1 predictors of daily suicidal behavior. As noted earlier, we expect that suicidal behavior will be infrequent even in this clinical sample. Thus, we anticipate that zero-inflated or binomial models may fit the data better than a linear model.

Research aim 2 focuses on testing moderators of the coupled relationships tested in aim 1 and hypotheses 2 and 3. We will again use multilevel linear models to test these relationships. To test hypothesis 2a, we will manually calculate the interaction between each person-centered focal predictor (ie, entrapment, hopelessness) and each person-centered moderator (ie, burdensomeness, connectedness, and self-hate). Each combination of focal predictor, moderator, and interaction will be entered as level 1 effects in an MLM predicting suicidal ideation. To test hypothesis 2b, we will again manually calculate the interactions between the person-centered focal predictor (ie, suicidal ideation) and moderators (ie, NSSI urge/engagement, self-hate, and agitation), and then enter combinations of each into separate MLMs predicting suicidal behavior.

Research aim 3 focuses on examining psychological risk factors as potential mediators of the relationship between physiological arousal (ie, sleep problems, substance use) and suicidal ideation or behavior. Unlike the previous contemporaneous models, which focus on within-day effects, these models also include lagged effects, with predictors on day *j* predicting changes in the outcome on day *j*+1. To account for these additional complexities, we will use multilevel structural equation modeling, which offers a number of advantages when testing multilevel mediation (see [42]), including an autoregressive mediation model appropriate to these hypotheses.

To test hypothesis 3a, each model will include direct paths between one of the focal predictors (ie, daily sleep or substance use) and next-day suicidal ideation or behavior as well as indirect paths through each of the 5 hypothesized mediators (ie, daily averages of hopelessness, self-hate, burdensomeness, entrapment, and agitation) lagged by 1 period (ie, *j*+1), controlling for the autocorrelations of each predictor on days *j* and *j*+1.

To test hypothesis 3b, we will examine (1) the main effect of variability (ie, RMSSD) in daily sleep quality; (2) the main effects of daily entrapment, hopelessness, and burdensomeness; and (3) the interactions of (1) and (2) in predicting same-day suicidal ideation. We will then extend this model to predict next-day suicidal ideation, controlling for the autocorrelation of suicidal ideation on the previous day. Similarly, to test hypothesis 3.3, we will examine whether variability in sleep quality interacts with average daily suicidal ideation, self-hate, or agitation to predict same-day or next-day (lagged) suicidal behavior. These models will again use standard MLM, with level 1 interactions manually computed from the person-centered variables and entered as predictors along with the main effects of each focal predictor and moderator.

Power Statement

To determine our planned sample size, we conducted power analyses using the ema.pcurve function of the EMAtools package [43]. With 200 participants responding to as few as 75% of survey requests, we will obtain 47.25 data points per participant (200 × 47.25 responses = 9450 datapoints), which is sufficient to detect medium to large effects (Cohen $d > 0.5$) at over 90% power and small effects (Cohen $d > 0.2$) with at least 30% power. This sample will be larger than many of the existing suicide-focused EMA studies to date (eg, [20,26]). Thus, the sample size is adequate for a preliminary study.

Ethics Approval

The study was approved by the Mayo Clinic Institutional Review Board (ID: 20-005229) after obtaining and implementing expert peer review comments from the Psychiatry and Psychology Research Committee.

Results

While the methodologies used to conduct this study pose minimal risk to participants, this study does include self-report questions about suicidal thoughts and is recruiting participants with some level of suicidal thinking; therefore, it requires participant safety monitoring. This study will utilize the Research Protocols and Risk of Suicide guidelines [44] published by the UCLA (University of California at Los Angeles) Office of the Human Research Protection Program (2012), as recommended by the National Institutes of Health (NIH), to ensure the safety of participants as well as the expert consensus recommendations for conducting EMA studies of suicide [45]. The guidelines note that studies that identify participants who may have current suicidal ideation through direct questions about suicidal thoughts and plans, or through direct questions regarding known risk factors for suicide need a patient safety monitoring system in place. Based on the guidelines, we will have multiple risk management procedures in place (Figure 1).

Discussion

This project will generate robust evidence to evaluate which risk factors predict proximal changes in suicidal ideation and behaviors. It also provides an innovative ability to examine potential interactions with multiple theoretically derived risk factors to predict proximal transitions into worsening suicidal thinking or behaviors. In sum, the study has practical and clinical implications and will inform clinicians of a better understanding of the real-world, daily events that can lead to escalations in

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suicidal crises, and is expected to contribute to advancements in clinical care of suicidal patients. In addition, the project has the potential to theoretically enhance the understanding of the elements that elevate suicide risk and will demonstrate the feasibility of app-based real-time monitoring of suicide risk factors that will have a huge impact on advancing innovative suicide prevention and treatment.

This proposed project will join and help lead a paradigm shift in the scientific study of suicide using technological advances (ie, EMA) to capture microchanges in psychological processes to predict acute changes in suicidal thinking and behavior. The information obtained from this study has excellent potential to guide clinical assessment and care of suicidal patients.

Acknowledgments

We acknowledge financial support from the Mayo Clinic–UW-Eau Claire Research Innovation Collaboration.

Data Availability

The data sets that will be generated during or analyzed during the study can be obtained from the corresponding author on reasonable request.

Conflicts of Interest

None declared.

Multimedia Appendix 1
Baseline data collection visit.
[DOCX File , 27 KB - resprot_v11i7e37583_app1.docx]

Multimedia Appendix 2
Ecological momentary assessment data collection.
[DOCX File , 120 KB - resprot_v11i7e37583_app2.docx]

References

1. Center for Disease Control and Prevention (CDC). Suicide Prevention: Facts About Suicide. CDC. 2021. URL: https://www.cdc.gov/suicide/facts/index.html [accessed 2022-06-13]
2. Franklin JC, Ribeiro JD, Fox KR, Bentley KH, Kleiman EM, Huang X, et al. Risk factors for suicidal thoughts and behaviors: A meta-analysis of 50 years of research. Psychol Bull 2017 Feb;143(2):187-232. [doi: 10.1037/bul0000084] [Medline: 27841450]
3. Galynker I. Clinical guide to the assessment of imminent suicide risk. Oxford, UK: Oxford University Press; Sep 2017.
4. Rogers ML, Chiurliza B, Hagan CR, Tzoneva M, Hames JL, Michaels MS, et al. Acute suicidal affective disturbance: Factorial structure and initial validation across psychiatric outpatient and inpatient samples. J Affect Disord 2017 Mar 15;211:1-11. [doi: 10.1016/j.jad.2016.12.057] [Medline: 28073092]
5. Glenn CR, Kleiman EM, Cha CB, Deming CA, Franklin JC, Nock MK. Understanding suicide risk within the Research Domain Criteria (RDoC) framework: A meta-analytic review. Depress Anxiety 2018 Jan;35(1):65-88. [doi: 10.1002/da.22686] [Medline: 29064611]
6. Zalsman G, Hawton K, Wasserman D, van Heeringen K, Arensman E, Sarchiapone M, et al. Suicide prevention strategies revisited: 10-year systematic review. Lancet Psychiatry 2016 Jul;3(7):646-659. [doi: 10.1016/S2215-0366(16)30030-X] [Medline: 27289303]
7. O'Connor RC, Nock MK. The psychology of suicidal behaviour. Lancet Psychiatry 2014 Jun;1(1):73-85. [doi: 10.1016/S2215-0366(14)70222-6] [Medline: 26360404]
8. Hagan C, Podlogar M, Joiner T. Testing the interpersonal theory of suicide: the moderating role of hopelessness. International Journal of Cognitive Therapy 2015 Jun;8(2):99-113. [doi: 10.1521/ijct.2015.8.2.99]
9. Tucker RP, Wingate LR, Burkley M, Wells TT. Implicit association with suicide as measured by the Suicide Affect Misattribution Procedure (S-AMP) predicts suicide ideation. Suicide Life Threat Behav 2018 Dec;48(6):720-731. [doi: 10.1111/sltb.12392] [Medline: 28862775]
10. Muehlenkamp JJ, Brausch AM. Protective factors do not moderate risk for past-year suicide attempts conferred by recent NSSI. J Affect Disord 2019 Feb 15;245:321-324. [doi: 10.1016/j.jad.2018.11.013] [Medline: 30419532]
11. Joiner T. Why people die by suicide. Cambridge, MA: Harvard University Press; 2005.
12. Drapeau CW, Nadorff MR. Suicidality in sleep disorders: prevalence, impact, and management strategies. Nat Sci Sleep 2017;9:213-226 [FREE Full text] [doi: 10.2147/NSS.S125597] [Medline: 29075143]

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13. Li SX, Lam SP, Zhang J, Yu MWM, Chan JWY, Chan CSY, et al. Sleep disturbances and suicide risk in an 8-year longitudinal study of schizophrenia-spectrum disorders. Sleep 2016 Jun 01;39(6):1275-1282. [doi: 10.5665/sleep.5852] [Medline: 27091530]
14. Fischer NL, Lamis DA, Petersen-Coleman MN, Moore CS, Zhang H, Kaslow NJ. Mediating effects of existential and religious well-being among abused, suicidal African American women. J Fam Viol 2015 Aug 2;31(3):315-323. [doi: 10.1007/s10896-015-9771-1]
15. Hooley JM, Franklin JC. Why do people hurt themselves? A new conceptual model of nonsuicidal self-injury. Clinical Psychological Science 2017 Dec 28;6(3):428-451. [doi: 10.1177/2167702617745641]
16. Rowe CE. The "undifferentiated selfobject"--a contribution to understanding symptomatic behavior and fixation: the suicidal patient. Psychoanal Rev 2010 Feb;97(1):45-71. [doi: 10.1521/prev.2010.97.1.45] [Medline: 20170268]
17. Branley-Bell D, O'Connor DB, Green JA, Ferguson E, O'Carroll RE, O'Connor RC. Distinguishing suicide ideation from suicide attempts: Further test of the Integrated Motivational-Volitional Model of Suicidal Behaviour. J Psychiatr Res 2019 Oct;117:100-107. [doi: 10.1016/j.jpsychires.2019.07.007] [Medline: 31376620]
18. Mars B, Heron J, Klonsky ED, Moran P, O'Connor RC, Tilling K, et al. What distinguishes adolescents with suicidal thoughts from those who have attempted suicide? A population-based birth cohort study. J Child Psychol Psychiatry 2019 Jan;60(1):91-99. [doi: 10.1111/jcpp.12878] [Medline: 29492978]
19. Al-Dajani N, Czyz EK. Suicidal desire in adolescents: An examination of the interpersonal psychological theory using daily diaries. J Clin Child Adolesc Psychol 2022 Apr 27:1-15. [doi: 10.1080/15374416.2022.2051525] [Medline: 35476615]
20. Hallensleben N, Glaesmer H, Forkmann T, Rath D, Strauss M, Kersting A, et al. Predicting suicidal ideation by interpersonal variables, hopelessness and depression in real-time. An ecological momentary assessment study in psychiatric inpatients with depression. Eur Psychiatry 2019 Feb 05;56(1):43-50. [doi: 10.1016/j.eurpsy.2018.11.003] [Medline: 30530103]
21. Sani G, Tondo L, Koukopoulos A, Reginaldi D, Kotzalidis GD, Koukopoulos AE, et al. Suicide in a large population of former psychiatric inpatients. Psychiatry Clin Neurosci 2011 Apr;65(3):286-295 [FREE Full text] [doi: 10.1111/j.1440-1819.2011.02205.x] [Medline: 21507136]
22. Park W, Yang KI, Kim H. Insufficient sleep and suicidal ideation: a survey of 12,046 female adolescents. Sleep Med 2019 Jan;53:65-69. [doi: 10.1016/j.sleep.2018.08.025] [Medline: 30447401]
23. Rogers ML, Ringer FB, Joiner TE. A meta-analytic review of the association between agitation and suicide attempts. Clin Psychol Rev 2016 Aug;48:1-6. [doi: 10.1016/j.cpr.2016.06.002] [Medline: 27348187]
24. Bernert RA, Kim JS, Iwata NG, Perlis ML. Sleep disturbances as an evidence-based suicide risk factor. Curr Psychiatry Rep 2015 Mar;17(3):554. [doi: 10.1007/s11920-015-0554-4] [Medline: 25698339]
25. Tucker RP, Michaels MS, Rogers ML, Wingate LR, Joiner TE. Construct validity of a proposed new diagnostic entity: Acute Suicidal Affective Disturbance (ASAD). J Affect Disord 2016 Jan 01;189:365-378. [doi: 10.1016/j.jad.2015.07.049] [Medline: 26476421]
26. Kleiman EM, Turner BJ, Fedor S, Beale EE, Huffman JC, Nock MK. Examination of real-time fluctuations in suicidal ideation and its risk factors: Results from two ecological momentary assessment studies. J Abnorm Psychol 2017 Aug;126(6):726-738. [doi: 10.1037/abn0000273] [Medline: 28481571]
27. Davidson CL, Anestis MD, Gutierrez PM. Ecological momentary assessment is a neglected methodology in suicidology. Arch Suicide Res 2017 Jan 02;21(1):1-11. [doi: 10.1080/13811118.2015.1004482] [Medline: 26821811]
28. Klonsky ED, May AM, Saffer BY. Suicide, suicide attempts, and suicidal ideation. Annu Rev Clin Psychol 2016;12:307-330. [doi: 10.1146/annurev-clinpsy-021815-093204] [Medline: 26772209]
29. Kleiman EM, Nock MK. Real-time assessment of suicidal thoughts and behaviors. Curr Opin Psychol 2018 Aug;22:33-37. [doi: 10.1016/j.copsyc.2017.07.026] [Medline: 30122275]
30. Czyz EK, King CA, Nahum-Shani I. Ecological assessment of daily suicidal thoughts and attempts among suicidal teens after psychiatric hospitalization: Lessons about feasibility and acceptability. Psychiatry Res 2018 Sep;267:566-574. [doi: 10.1016/j.psychres.2018.06.031] [Medline: 30031317]
31. Glenn CR, Kleiman EM, Kearns JC, Santee AC, Esposito EC, Conwell Y, et al. Feasibility and acceptability of ecological momentary assessment with high-risk suicidal adolescents following acute psychiatric care. J Clin Child Adolesc Psychol 2022;51(1):32-48. [doi: 10.1080/15374416.2020.1741377] [Medline: 32239986]
32. Vine V, Boyd RL, Pennebaker JW. Natural emotion vocabularies as windows on distress and well-being. Nat Commun 2020 Sep 10;11(1):4525 [FREE Full text] [doi: 10.1038/s41467-020-18349-0] [Medline: 32913209]
33. Claassen CA, Pearson JL, Khodyakov D, Satow PM, Gebbia R, Berman AL, et al. Reducing the burden of suicide in the U.S.: the aspirational research goals of the National Action Alliance for Suicide Prevention Research Prioritization Task Force. Am J Prev Med 2014 Sep;47(3):309-314. [doi: 10.1016/j.amepre.2014.01.004] [Medline: 24750971]
34. Rath D, de Beurs D, Hallensleben N, Spangenberg L, Glaesmer H, Forkmann T. Modelling suicide ideation from beep to beep: Application of network analysis to ecological momentary assessment data. Internet Interv 2019 Dec;18:100292 [FREE Full text] [doi: 10.1016/j.invent.2019.100292] [Medline: 31828015]
35. Littlewood DL, Kyle SD, Carter LA, Peters S, Pratt D, Gooding P. Short sleep duration and poor sleep quality predict next-day suicidal ideation: an ecological momentary assessment study. Psychol Med 2019 Feb;49(3):403-411 [FREE Full text] [doi: 10.1017/S0033291718001009] [Medline: 29697037]

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36. Brüdern J, Hallensleben N, Höller I, Spangenberg L, Forkmann T, Rath D, et al. Sleep disturbances predict active suicidal ideation the next day: an ecological momentary assessment study. BMC Psychiatry 2022 Jan 27;22(1):65 [FREE Full text] [doi: 10.1186/s12888-022-03716-6] [Medline: 35086519]
37. Lynch FL, Peterson EL, Lu CY, Hu Y, Rossom RC, Waitzfelder BE, et al. Substance use disorders and risk of suicide in a general US population: a case control study. Addict Sci Clin Pract 2020 Feb 21;15(1):14 [FREE Full text] [doi: 10.1186/s13722-020-0181-1] [Medline: 32085800]
38. Chu C, Hom MA, Hirsch JK, Joiner TE. Thwarted belongingness and perceived burdensomeness explain the relationship between sleep problems and suicide risk among adults identifying as sexual and/or gender minorities. Psychology of Sexual Orientation and Gender Diversity 2019 Mar;6(1):22-33. [doi: 10.1037/sgd0000301]
39. Bush NE, Smolenski DJ, Denneson LM, Williams HB, Thomas EK, Dobscha SK. A virtual hope box: Randomized controlled trial of a smartphone app for emotional regulation and coping with distress. Psychiatr Serv 2017 Apr 01;68(4):330-336. [doi: 10.1176/appi.ps.201600283] [Medline: 27842473]
40. Luxton S, Reid M, Mavondo F. Integrated marketing communication capability and brand performance. Journal of Advertising 2014 Nov 06;44(1):37-46. [doi: 10.1080/00913367.2014.934938]
41. Ebner-Priemer UW, Trull TJ. Ecological momentary assessment of mood disorders and mood dysregulation. Psychol Assess 2009 Dec;21(4):463-475. [doi: 10.1037/a0017075] [Medline: 19947781]
42. Preacher KJ, Zyphur MJ, Zhang Z. A general multilevel SEM framework for assessing multilevel mediation. Psychol Methods 2010 Sep;15(3):209-233. [doi: 10.1037/a0020141] [Medline: 20822249]
43. Kleiman E. EMAtools: Data management tools for real-time monitoring/ecological momentary assessment data internet. CRAN. 2021 Oct 31. URL: https://CRAN.R-project.org/package=EMAtools [accessed 2022-06-13]
44. Guidance: Research Protocols and Risk of Suicide. UCLA. 2012. URL: https://ora.research.ucla.edu/OHRPP/Documents/Policy/8/Risk_of_Suicide.pdf [accessed 2022-06-16]
45. Nock MK, Kleiman EM, Abraham M, Bentley KH, Brent DA, Buonopane RJ, et al. Consensus statement on ethical & safety practices for conducting digital monitoring studies with people at risk of suicide and related behaviors. Psychiatr Res Clin Pract 2021 Dec 21;3(2):57-66. [doi: 10.1176/appi.prcp.20200029] [Medline: 34414359]

Abbreviations

C-SSRS: Columbia-Suicide Severity Rating Scale
EMA: ecological momentary assessment
IMV: Integrative-Motivational-Volitional
MLM: multivariate linear model
NIH: National Institutes of Health
NSSI: nonsuicidal self-injury
RMSSD: root mean square of successive difference
UCLA: University of California at Los Angeles

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Protocol

Development of Best Practice Guidance on Online Peer Support for People With Young Onset Dementia: Protocol for a Mixed Methods Study

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Abstract

Background: Many people with young onset dementia (YOD) may feel isolated. Peer support has the potential to improve social health, but the inconsistent availability of age-appropriate, in-person (peer) support services for people with YOD suggests that many people with YOD miss out on the potential benefits. Online peer support could be useful, as it overcomes geographical barriers, offers a variety of options, and adjusts to various needs and preferences.

Objective: Our study aims to develop evidence-based best practice guidance on online peer support for people with YOD and group facilitators to improve online peer support for people with YOD.

Methods: Our mixed methods study consists of 4 phases and follows the guidelines of the Medical Research Council on complex interventions. Each phase consists of multiple substudies. The study focuses on the development stage of the Medical Research Council framework and additionally develops a plan for the feasibility/piloting, evaluation, and implementation stages. The participants are people living with YOD and peer support facilitators. The qualitative research methods include interviews, focus groups, and open questions in a web-based survey. The quantitative methods include a web-based survey consisting of existing outcome measures.

Results: The study is funded by the European Union's Horizon 2020 research and innovation program under the Marie Skłodowska-Curie Actions – Innovative Training Networks (H2020-MSCA-ITN-2018; grant agreement number: 813196), and it received ethical approval from the London Bromley Research Ethics Committee (reference number: 21/LO/0248) in April 2021. Recruitment started in May 2021. Data collection and analysis are expected to be finished by September 2022.

Conclusions: The best practice guidance can provide people with YOD with tailored and evidence-based information about online peer support, and it will be disseminated locally (in the United Kingdom) and internationally through dementia organizations, research networks, and academic institutions.

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KEYWORDS

young onset dementia; peer support; eHealth; social health; mixed methods

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Introduction

Young Onset Dementia

In 2018, around 1 million people were living with dementia in the United Kingdom, of whom almost 53,000 were younger than 65 years [1]. When someone is diagnosed before the age of 65 years, this can be defined as *young onset dementia* (YOD) [2]. People with YOD often face different challenges compared to those faced by older adults with dementia [3,4]. People with YOD are more likely to be in employment at the time of their diagnosis [5,6]. Difficulties at work and a YOD diagnosis can lead to (forced) early retirement, which has financial [7,8] and social [5,9] consequences, as this results in a loss of income as well as a loss of contact with colleagues. The loss of work can be perceived as a personal loss, as work is associated with involvement in meaningful activities and one's identity [9,10]. Furthermore, people with YOD are more likely to fulfill an active parenting role toward dependent children. Changes in family structures can be experienced as losing one's identity as a parent and being a burden to the family [7,11]. Additionally, people with YOD often experience a decrease in their social contacts and report losing touch with friends [7], which can be the result of a lack of understanding of YOD in the wider society. Stigmatization can result in the avoidance of social situations, which increases the risk of social isolation and loneliness [5,9,12]. These findings illustrate the unique challenges that people with YOD face when compared to those of older adults with dementia.

The Social Health Framework

The social health framework looks at health within the social domain and includes the following three dimensions: (1) the ability to fulfill potential and obligations, (2) the ability to manage life with some level of independence, and (3) the ability to participate in social activities and work [13]. Dröes et al [14] suggest that when focusing on coping strategies and finding a balance between limitations and the abilities that one still has, people can adapt to living with dementia and still live meaningful and satisfying lives.

Peer support could improve all 3 dimensions of social health; hence, the social health framework will be used as the theoretical foundation for our study. Peers are people who have similar life experiences or health conditions [15,16]. First, peer support can be a way for people with YOD to stay socially connected and reduce the risk of isolation [17]. Besides offering a space for social connection, peer support creates opportunities to be involved in a variety of activities, such as creative and music-related activities, or with advocacy, research, and policy making, thereby allowing people to choose something that is meaningful to them. This relates to the dimension "the ability to participate in social activities and work" [13]. Second, through peer support, people can receive and provide support and share the unique knowledge that they have because of their own personal experiences of living with YOD. This knowledge is also called *experiential knowledge* and can include tips and tricks on how to manage dementia in daily life as well as information about support services [18,19]. This relates to the dimension "the ability to manage life with some level of independence" [13]. Third, the reciprocal nature of peer support and the opportunity to support others can increase feelings of empowerment [15,19,20]. This relates to the dimension "the ability to fulfill potential and obligations" [13]. Moreover, the work of Rabanal et al [21] and Stamou et al [22] shows that peer support can make the postdiagnostic experience more positive and can help people with YOD identify age-appropriate support services.

Online Peer Support

People with YOD often experience difficulties in accessing local, age-appropriate support services, including opportunities for peer support [23,24]. Mayrhofer et al [23] show that support services for people with YOD vary widely across the United Kingdom. Additionally, services are often short-term because of project-based funding or because of services being offered as part of pilot studies [23], making it difficult for people with YOD to locate long-term, local, and age-appropriate (peer) support services [21]. As a result, a large group of people with YOD may miss out on the benefits of peer support, which could negatively impact their postdiagnostic experiences and social health.

A potential solution could be online peer support, such as support from social media, discussion forums, blogs, or video meetings, as it overcomes geographical barriers [25]. This benefit could make online peer support particularly useful for people who do not have access to local, age-appropriate peer support services or are unable to travel. Additionally, not everyone with YOD may feel ready to share their diagnoses and experiences with others. Online peer support allows people to engage in peer support from the comfort of their own homes, potentially lowering the barrier to join a peer support group. Finally, some people may experience challenges with speech due to their dementia symptoms. Online peer support can offer a variety of text-based (eg, social media and discussion forums) options, but it can also offer verbal (eg, video meetings) options for people who prefer those. Thus, online peer support could potentially make peer support accessible to a wide range of people and meet different needs and preferences.

Although previous studies showed how people with dementia use web-based platforms to connect with peers and exchange support, it remains unknown how users perceive this type of support, how such support impacts their daily lives, and what elements make online peer support meaningful [26-29]. Additionally, while previous research has been conducted into the experiences of facilitators of a variety of online peer support communities (eg, research by Coulson and Shaw [30] and Saha et al [31]), to our knowledge, this type of research has not been conducted in the field of dementia.

Aims

Our study aims to develop (1) a best practice guidance on online peer support for people with YOD, so that people have access to evidence-based and tailored information about online peer support, and (2) best practice guidelines for facilitators of online peer support, so that they have access to tailored and evidence-based information that can be used to improve online peer support for people with YOD.

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The study aims to answer the following research questions:

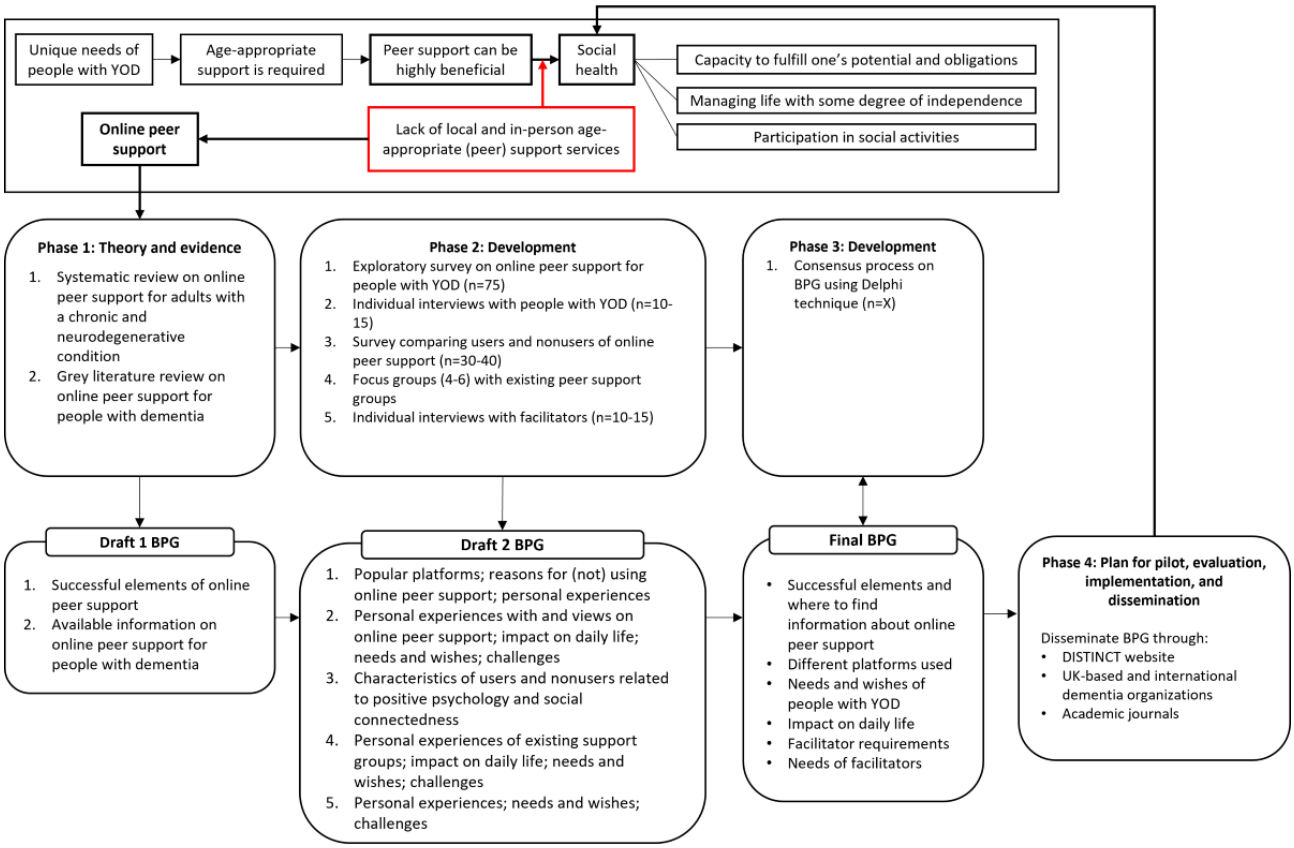
1. How do people with YOD use and experience online peer support?
2. What makes online peer support meaningful for people with YOD?
3. How can online peer support for people with YOD be improved?

Methods

Study Overview

Our mixed methods study consists of 4 phases and follows the guidelines of the Medical Research Council on complex interventions [32]. The study focuses on the development stage of the Medical Research Council framework and develops a plan for the feasibility/piloting, evaluation, and implementation stages. Each phase consists of multiple substudies. Phases 1, 2, and 3 contribute to the development of the best practice guidance, including the guidelines for facilitators. Phase 4 consists of disseminating the best practice guidance and guidelines and developing a plan for a potential future pilot study, evaluation, and further implementation and dissemination. An overview of all 4 phases can be found in Figure 1.

Figure 1. The development of best practice guidance on online peer support for people with YOD within the Medical Research Council framework. BPG: best practice guidance; DISTINCT: Dementia Intersectorial Strategy for Training and Innovation Network for Current Technology; YOD: Young Onset Dementia.



Ethics Approval

The study received ethical approval from the London Bromley Research Ethics Committee (reference number: 21/LO/0248).

Informed Consent

All participants will provide informed consent before participating in any part of the study. Participants of a web-based survey will be asked to confirm that they have read and understand the study information and that they are happy to proceed before they can continue to the questions. Participants who fill in a paper copy or go through it verbally will be asked to do the same. The completion and submission of the survey will be taken as consent. For participants taking part in an individual interview or a focus group, consent will be taken remotely. This is due to the potentially wide range of geographic locations of participants and COVID-19 restrictions. There are 3 ways through which participants can provide consent, as follows: (1) signing a paper consent form and sending it back to the researcher, (2) signing a digital consent form and sending it back to the researcher, or (3) going through a verbal consent process with the researcher over a phone or video call. The members of the research team who are responsible for conducting the consent procedures have all undergone training on the Mental Capacity Act [33].

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Data Collection and Storage

The individual interviews and focus groups will be conducted remotely through Microsoft Teams, the group's usual meeting platform, or a phone call. The interviews and focus groups will be audio recorded with a University of Nottingham–approved recording device, and focus groups will be screen recorded via the videoconferencing platform. The recordings will be transcribed verbatim by a professional transcribing company that has an agreement with the University of Nottingham. Once the transcripts are completed, the recordings will be permanently deleted. The transcripts will leave out any information that could be used to identify a person. The recordings and transcripts will be stored on a password-secured, web-based storage space of the University of Nottingham.

Patient and Public Involvement

During the design process of the study, people with YOD, carers, and health and social care professionals working with people with YOD were consulted. Senior members of the research team have extensive clinical experience in working with people with YOD and experience with patient and public involvement, cocreating research projects, and collaborating with people with dementia and their carers. Throughout the study, regular patient and public involvement consultations with people with YOD and health and social care professionals working with people with YOD will be conducted to discuss the progress of the study and study documents. All participants can receive the initial findings of the parts of the study in which they participated and provide further input on the analysis and findings before they get published.

Phase 1: Theory and Evidence

The aim of this phase is to review the existing academic and grey literature on online peer support. The findings will set the foundation for the next phases and inform the first draft of the best practice guidance. This phase consists of the following two substudies: (1) a narrative synthesis systematic review on online peer support for adults with chronic neurodegenerative conditions and (2) a grey literature review on online peer support for people with dementia. Through the systematic literature review, successful elements of online peer support will be identified. Through Google searches and searches of websites of dementia organizations, the grey literature review will provide insights into the information that is available regarding online peer support for people living with dementia and how much of this information is tailored toward YOD.

Phase 2: Development

Overview of Substudies

The aim of this phase is to identify the needs and wishes of people with YOD regarding online peer support and the kinds of information they need in the best practice guidance. This will be done by gathering experiences from people with YOD who use online peer support and those who do not. As such, this phase consists of the following five substudies: (1) an exploratory survey for people with YOD, (2) individual interviews with people with YOD, (3) a survey for comparing users and nonusers of online peer support, (4) focus groups with existing peer support groups for people with YOD, and (5) individual interviews with peer support facilitators. The findings of phase 2 will inform the second draft of the best practice guidance. An overview of each substudy in this phase is presented below.

Substudy 1

Exploratory Survey

A web-based survey will explore the different types of online peer support that people with YOD use, the benefits and challenges of different web-based platforms, and the positive and potential negative experiences and challenges that people may have undergone. Furthermore, the survey will explore why people do not engage in online peer support and identify potential barriers. This survey will be informed by the findings of phase 1 and set the foundation for the other substudies in this phase. The survey will be developed through Online Surveys (Jisc) [34] and will include multiple choice questions with the option to provide free-text responses. At the beginning of the survey, participants will answer questions on baseline characteristics (eg, age, gender, and time since diagnosis) and experiences with online peer support. At the end of the survey, participants will be asked if they would like to be involved in future parts of the study. Those who answer “yes” can provide their contact details. In this way, this substudy will be used as a pool for recruitment for the next two substudies (more details are provided in the *Substudy 2* and *Substudy 3* sections). Those who answer “no” can complete the survey anonymously.

Participants

People are eligible for the study if (1) they are living with a dementia diagnosis, (2) they received their diagnosis before the age of 65 years, and (3) they understand English. People do not have to be younger than 65 years at the time they take part in the survey. People living in a care facility will be excluded from the study because this population has daily contact with other people with dementia and is thus already involved in a form of in-person peer support, which can reduce the need and desire for remote, online peer support. Additionally, people living in a care facility are more likely to be in the more advanced stages of dementia, which is when the nature of symptoms can make it more difficult for people to use technology and engage in online peer support.

Recruitment

Participants will be recruited via convenience sampling through (1) National Health Service services, (2) dementia charities (eg, Dementia UK and Dementia Engagement and Empowerment Project [DEEP]), (3) dementia research networks (eg, Join Dementia Research and Rare Dementia Support), and (4) academic institutions (eg, the University of Nottingham). Furthermore, the survey will be advertised through social media and the professional network of the research team. The aim for the sample size is 75 participants, which is based on expertise within the research team.

Data Collection and Analysis

Participants can take part in the survey independently by following the link to the survey. Alternatively, they can receive a paper copy or go through the survey verbally with the

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researcher. This substudy will collect qualitative and quantitative data. The qualitative data will be analyzed by using thematic analysis, following the procedures outlined by Braun and Clarke [35], which consists of the following six phases: (1) familiarizing with the data; (2) coding the data; (3) developing initial themes; (4) developing and reviewing themes; (5) refining, defining, and naming the themes; and (6) writing up the findings. The analysis will be performed in NVivo (QSR International). The quantitative data will be analyzed in SPSS (IBM Corporation) by using descriptive statistics.

Substudy 2

Individual Interviews

The individual interviews with people with YOD will be used to build on the findings of substudy 1 and gather further insights into (1) reasons for engaging or not engaging in online peer support, (2) the impact of online peer support on daily life, (3) needs regarding online peer support, and (4) barriers to online peer support and how to overcome these barriers.

Participants and Recruitment

By using purposive sampling, a sample of the participants from substudy 1 who answered "yes" to the question about whether they would like to be involved in future parts of the study will be invited for an individual interview. The sample will be diverse in terms of baseline characteristics, the time since diagnosis, and experiences with online peer support.

Data Collection and Analysis

The individual interviews will be conducted in person or over a phone or video call, depending on the COVID-19 regulations, geographical locations of participants in relation to the researchers' locations, and the participants' preferences. The interviews will be audio recorded by using an external University of Nottingham–approved recording device and will be transcribed verbatim. The transcripts will be analyzed thematically via an inductive approach, following the procedures outlined by Braun and Clarke [35], and the analysis will be performed in NVivo.

Substudy 3

Survey Comparing Characteristics of Users and Nonusers

This survey compares users of online peer support with nonusers, aiming to identify characteristics of users and nonusers of online peer support. The aim is to further explore how online peer support impacts the daily lives of people with YOD and what it could provide to those who do not engage in (online) peer support. Participants will go through existing outcome measures related to social health and positive psychology, which will be informed by substudies 1 and 2. The survey will be developed through Online Surveys. Participants can go through the survey independently by following the link, receive a paper copy, or go through the survey verbally with the researcher.

Participants, Recruitment, Data Collection, and Analysis

Through purposive sampling, the pool of participants from study 1 will be used to select a sample from the participants who said "yes" to the opportunity to be involved in future parts of the project. The aim is to recruit 30 to 40 participants with an equal number of users and nonusers. To obtain 2 comparable groups, participants will be selected based on baseline characteristics. This substudy will collect quantitative data by using existing scales in the selected outcome measures.

Substudy 4

Focus Groups With Existing Peer Support Groups

This substudy consists of focus group interviews with existing peer support groups that have their meetings on the internet. During the COVID-19 pandemic, many support services for people with dementia have been disrupted and have had to move to the internet [36]. Videoconferencing platforms, such as Zoom (Zoom Video Communications Inc) and Microsoft Teams, have become more popular. The focus groups will be held on Microsoft Teams or the groups' usual meeting platforms and will aim to provide insights into how people with YOD experience peer support through video meetings, how this experience impacts their daily life, and what the impact was of moving the meetings to the internet. This substudy will also explore the pros and cons of providing and receiving peer support through video meetings, the differences between in-person and online peer support, the potential challenges of online peer support, and how to overcome these challenges.

Participants

Participants will be subject to the same eligibility criteria as those in substudy 1, with the addition that they have to be part of an existing peer support group that meets on the internet or has experience with meeting on the internet. Groups do not have to be online-only groups; they are also eligible if they used to meet in person but moved their meetings to the internet during the COVID-19 pandemic.

Recruitment

Existing peer support groups will be recruited by using convenience and purposive sampling. With regard to convenience sampling, the study will be advertised through dementia charities (eg, Dementia UK and DEEP), dementia research networks (eg, Join Dementia Research and Rare Dementia Support), and academic institutions (eg, the University of Nottingham). Group facilitators and members can contact the research team if they are interested. With regard to purposeful sampling, the professional network of the research team will be consulted. The aim is to conduct 4 to 6 peer support groups, as data saturation tends to occur after 4 to 6 focus groups have been conducted [37]. The number of people in each focus group will depend on how many members of each peer support group want to take part.

Data Collection and Analysis

The focus groups will be screen and audio recorded by using the recording function of the videoconferencing platform and an external University of Nottingham–approved recording device, and the recordings will be transcribed verbatim. Additionally, the facilitator will take field notes. The transcripts will be analyzed thematically via an inductive approach, using the procedures outlined by Braun and Clarke [35], and the analysis will be performed in NVivo.

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Substudy 5

Individual Interviews With Facilitators

The aim is to explore how facilitators of online peer support experience their role and what they believe is important. This will provide insights into (1) the role and tasks of a facilitator, (2) personal experiences of facilitating online peer support for people with YOD, and (3) challenges and how to overcome these challenges. The findings can contribute to a better understanding of how to facilitate online peer support for people with YOD.

Participants

People are eligible if they (1) are an online peer support facilitator, (2) are above the age of 18 years, and (3) speak and understand English. Someone will be considered a facilitator if they are responsible for setting up web-based meetings and facilitating such meetings or if they are facilitating or monitoring discussions on a text-based online peer support platform (eg, a Facebook group or a discussion forum).

Recruitment, Data Collection, and Analysis

With regard to the purposive sampling approach, peer support facilitators will be identified through substudies 1 and 4 and the professional network of the research team. With regard to snowball sampling, the researcher will ask participants if they know someone else who meets the eligibility criteria and would like to participate in the study. The aim is to conduct 10 to 15 interviews. This substudy will use the same data collection and analysis procedures as those in substudy 2.

Phases 3 and 4: Development and Dissemination

Delphi Study

A draft of the best practice guidance and guidelines will be added to a web-based survey, which will consist of questions about content, format, readability, and dissemination. Those invited to take part in this study will be (1) everyone who took part in the study and said that they were interested in being involved in future parts of the study, (2) dementia charities (eg, Dementia UK and DEEP), and (3) professionals working with people with YOD. By using purposive sampling, participants from the previous substudies will be invited, and the survey will be shared through dementia charities, National Health Service services, and the professional network of the research team.

Consensus Meeting

A consensus meeting will be held to build on the findings of the Delphi study and gather input from study participants, supporters of people with YOD, and (health care) professionals working with people with YOD on the content and dissemination of the best practice guidance. A draft of the guidance will be shared with participants beforehand. Based on the outcomes of the meeting, the final guidance and guidelines will be developed.

The findings of the Delphi study and the consensus meeting will inform phase 4, during which a dissemination plan will be developed. The aim is to disseminate the best practice guidance and guidelines locally (in the United Kingdom) and internationally through dementia organizations and services, research networks, and academic institutions. Furthermore, a plan for a potential future pilot study that will test the best practice guidance and guidelines and for further implementation and dissemination will be developed.

Results

Our study is funded by the European Union's Horizon 2020 research and innovation program under the Marie Skłodowska-Curie Actions – Innovative Training Networks (H2020-MSCA-ITN-2018; grant agreement number: 813196). Phase 1 (theory and evidence) started in October 2019, and it is being updated throughout the study. In April 2021, the study received ethical approval from the London Bromley Research Ethics Committee (reference number: 21/LO/0248). Recruitment and data collection for phase 2 (development) started in May 2021. Data collection and analysis are expected to be completed by September 2022. Phase 3 (development) and phase 4 (dissemination) are expected to start in June 2022 and be completed by September 2022.

Discussion

Emerging Findings

Peer support can be a valuable source of support and make a positive impact on the postdiagnostic experiences of people with YOD [21,22]. This suggests that everyone living with YOD should have access to such support. Yet, research shows that many people with YOD experience difficulties with accessing age-appropriate (peer) support services [23,24]. Online peer support could be a solution. Although the nature of dementia symptoms can pose challenges to the use of technology, with the right guidance and support, many people can overcome such challenges and successfully use technology as a support tool in their daily lives. During the COVID-19 pandemic, many health and social care services have been disrupted and have moved to the internet, highlighting how important it is for people with dementia to be able to use technology [36]. However, for people with dementia to have better access to online peer support, the necessary guidance and support tools should be in place and be easy to access.

A best practice guidance on online peer support could raise awareness on the availability of this form of support, how to access it, and what it could provide to people. It could also help people to decide whether online peer support is something that could be helpful and, if so, which form of online peer support would be most suitable for them. Furthermore, best practice guidelines for facilitators will be developed to support them in improving online peer support and ensuring that such support meets the needs and wishes of people with YOD.

Strengths and Limitations

The main strength of our study is that it addresses the inconsistent availability of health and social care services for people with YOD in the United Kingdom. Furthermore, the study includes people with YOD and health and social care professionals working with people with YOD throughout all phases. However, while online peer support overcomes geographical barriers and offers opportunities for international

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communication, the advertisement of and recruitment for the study will be conducted within the United Kingdom. Therefore, the findings will be specific to the UK context, and one should be cautious when generalizing the findings to other countries. Furthermore, some people may be unable to access online peer support for a variety of reasons, such as experiencing dementia symptoms that limit one's ability to use technology or not having the (financial) resources for such support.

Conclusions

People with YOD often experience different challenges compared to those of older adults with dementia and therefore need age-appropriate support. Peer support can contribute to a more positive postdiagnostic experience and every dimension of the social health framework. However, many people with YOD experience a lack of age-appropriate (peer) support services in their local area, indicating that online peer support could be a solution. Although research into online support for people with dementia is increasing, it remains unknown how users perceive this type of support, how such support impacts their daily lives, and what elements make it meaningful. Our study aims to explore how people with YOD use and experience online peer support and how online peer support can be improved. The findings will lead toward the development of a best practice guidance on online peer support that provides people with YOD with tailored and evidence-based information about online peer support. The guidance will also include guidelines for peer support facilitators who are aiming to improve existing online peer support opportunities and develop new online peer support opportunities.

Acknowledgments

The study is funded by the European Union's Horizon 2020 research and innovation program under the Marie Skłodowska-Curie Actions – Innovative Training Networks (H2020-MSCA-ITN-2018; grant agreement number: 813196).

Data Availability

Data sharing not applicable to this article as no data sets were generated or analyzed during the current study.

Authors' Contributions

EVG is an early career researcher under the supervision of OM and MO, of whom both are senior researchers. EVG, OM, and MO are responsible for designing the study. EVG took the lead in developing the study materials. EVG is responsible for promoting the study, recruiting participants, conducting the informed consent procedures, and collecting data. EVG will take the lead in the analysis and dissemination of the study findings. OM and MO will provide guidance and support throughout all stages of the study.

Conflicts of Interest

None declared.

References

1. Dementia in Europe Yearbook 2019: Estimating the prevalence of dementia in Europe. Alzheimer Europe. 2019. URL: https://www.alzheimer-europe.org/sites/default/files/alzheimer_europe_dementia_in_europe_yearbook_2019.pdf [accessed 2022-06-14]
2. van de Veen D. Young onset dementia - challenges in nomenclature and clinical definition. In: de Vugt M, Carter J, editors. Understanding Young Onset Dementia: Evaluation, Needs and Care. New York: Routledge; 2022:8-9.
3. Millenaar J, Hvidsten L, de Vugt ME, Engedal K, Selbæk G, Wyller TB, et al. Determinants of quality of life in young onset dementia - results from a European multicenter assessment. Aging Ment Health 2017 Jan;21(1):24-30. [doi: 10.1080/13607863.2016.1232369] [Medline: 27676211]
4. Oliver K, O'Malley M, Parkes J, Stamou V, La Fontaine J, Oyebode J, et al. Living with young onset dementia and actively shaping dementia research - The Angela Project. Dementia (London) 2020 Jan;19(1):41-48. [doi: 10.1177/1471301219876414] [Medline: 31875707]
5. Johannessen A, Möller A. Experiences of persons with early-onset dementia in everyday life: a qualitative study. Dementia (London) 2013 Jul;12(4):410-424. [doi: 10.1177/1471301211430647] [Medline: 24336952]
6. Griffin J, Oyebode JR, Allen J. Living with a diagnosis of behavioural-variant frontotemporal dementia: The person's experience. Dementia (London) 2016 Nov;15(6):1622-1642. [doi: 10.1177/1471301214568164] [Medline: 25645139]
7. Harris PB, Keady J. Living with early onset dementia: Exploring the experience and developing evidence-based guidelines for practice. Alzheimers care today 2004;5(2):111-122 [FREE Full text]
8. Galvin JE, Howard DH, Denny SS, Dickinson S, Tatton N. The social and economic burden of frontotemporal degeneration. Neurology 2017 Nov 14;89(20):2049-2056. [doi: 10.1212/WNL.0000000000004614] [Medline: 28978658]
9. Greenwood N, Smith R. The experiences of people with young-onset dementia: A meta-ethnographic review of the qualitative literature. Maturitas 2016 Oct;92:102-109 [FREE Full text] [doi: 10.1016/j.maturitas.2016.07.019] [Medline: 27621246]

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10. Roach P, Drummond N. 'It's nice to have something to do': early-onset dementia and maintaining purposeful activity. J Psychiatr Ment Health Nurs 2014 Dec;21(10):889-895. [doi: 10.1111/jpm.12154] [Medline: 24841949]
11. van Vliet D, de Vugt ME, Bakker C, Koopmans RTCM, Verhey FRJ. Impact of early onset dementia on caregivers: a review. Int J Geriatr Psychiatry 2010 Nov;25(11):1091-1100. [doi: 10.1002/gps.2439] [Medline: 20957692]
12. Spreadbury JH, Kipps C. Measuring younger onset dementia: What the qualitative literature reveals about the 'lived experience' for patients and caregivers. Dementia (London) 2019 Feb;18(2):579-598. [doi: 10.1177/1471301216684401] [Medline: 28114802]
13. Huber M, Knottnerus JA, Green L, van der Horst H, Jadad AR, Kromhout D, et al. How should we define health? BMJ 2011 Jul 26;343:d4163. [doi: 10.1136/bmj.d4163] [Medline: 21791490]
14. Dröes RM, Chattat R, Diaz A, Gove D, Graff M, Murphy K, INTERDEM sOcial Health Taskforce. Social health and dementia: a European consensus on the operationalization of the concept and directions for research and practice. Aging Ment Health 2017 Jan;21(1):4-17. [doi: 10.1080/13607863.2016.1254596] [Medline: 27869503]
15. Keyes SE, Clarke CL, Wilkinson H, Alexjuk EJ, Wilcockson J, Robinson L, et al. "We're all thrown in the same boat … ": A qualitative analysis of peer support in dementia care. Dementia (London) 2016 Jul;15(4):560-577. [doi: 10.1177/1471301214529575] [Medline: 24742876]
16. Solomon P. Peer support/peer provided services underlying processes, benefits, and critical ingredients. Psychiatr Rehabil J 2004;27(4):392-401. [doi: 10.2975/27.2004.392.401] [Medline: 15222150]
17. Pierse T, Keogh F, Challis D, O'Shea E. Resource allocation in dementia care: comparing the views of people with dementia, carers and health and social care professionals under constrained and unconstrained budget scenarios. Aging Ment Health 2022 Apr;26(4):679-687. [doi: 10.1080/13607863.2021.1889969] [Medline: 33663288]
18. Dennis CL. Peer support within a health care context: a concept analysis. Int J Nurs Stud 2003 Mar;40(3):321-332. [doi: 10.1016/s0020-7489(02)00092-5] [Medline: 12605954]
19. Kingod N, Cleal B, Wahlberg A, Husted GR. Online peer-to-peer communities in the daily lives of people with chronic illness: A qualitative systematic review. Qual Health Res 2017;27(1):89-99. [doi: 10.1177/1049732316680203] [Medline: 27956659]
20. Barak A, Boniel-Nissim M, Suler J. Fostering empowerment in online support groups. Comput Human Behav 2008 Sep;24(5):1867-1883. [doi: 10.1016/j.chb.2008.02.004]
21. Rabanal LI, Chatwin J, Walker A, O'Sullivan M, Williamson T. Understanding the needs and experiences of people with young onset dementia: a qualitative study. BMJ Open 2018 Oct 21;8(10):e021166 [FREE Full text] [doi: 10.1136/bmjopen-2017-021166] [Medline: 30344167]
22. Stamou V, La Fontaine J, O'Malley M, Jones B, Gage H, Parkes J, et al. The nature of positive post-diagnostic support as experienced by people with young onset dementia. Aging Ment Health 2021 Jun;25(6):1125-1133. [doi: 10.1080/13607863.2020.1727854] [Medline: 32067481]
23. Mayrhofer A, Mathie E, McKeown J, Bunn F, Goodman C. Age-appropriate services for people diagnosed with young onset dementia (YOD): a systematic review. Aging Ment Health 2018 Aug;22(8):927-935. [doi: 10.1080/13607863.2017.1334038] [Medline: 28621549]
24. Stamou V, La Fontaine J, Gage H, Jones B, Williams P, O'Malley M, et al. Services for people with young onset dementia: The 'Angela' project national UK survey of service use and satisfaction. Int J Geriatr Psychiatry 2021 Mar;36(3):411-422. [doi: 10.1002/gps.5437] [Medline: 32979287]
25. Moorhead SA, Hazlett DE, Harrison L, Carroll JK, Irwin A, Hoving C. A new dimension of health care: systematic review of the uses, benefits, and limitations of social media for health communication. J Med Internet Res 2013 Apr 23;15(4):e85 [FREE Full text] [doi: 10.2196/jmir.1933] [Medline: 23615206]
26. Craig D, Strivens E. Facing the times: A young onset dementia support group: Facebook™ style. Australas J Ageing 2016 Mar;35(1):48-53. [doi: 10.1111/ajag.12264] [Medline: 27010874]
27. Clare L, Rowlands JM, Quin R. Collective strength: The impact of developing a shared social identity in early-stage dementia. Dementia 2008 Feb 01;7(1):9-30. [doi: 10.1177/1471301207085365]
28. Rodriquez J. Narrating dementia: self and community in an online forum. Qual Health Res 2013 Sep;23(9):1215-1227. [doi: 10.1177/1049732313501725] [Medline: 23907588]
29. Talbot CV, O'Dwyer ST, Clare L, Heaton J, Anderson J. How people with dementia use twitter: A qualitative analysis. Comput Human Behav 2020 Jan;102:112-119 [FREE Full text] [doi: 10.1016/j.chb.2019.08.005]
30. Coulson NS, Shaw RL. Nurturing health-related online support groups: Exploring the experiences of patient moderators. Comput Human Behav 2013 Jul;29(4):1695-1701. [doi: 10.1016/j.chb.2013.02.003]
31. Saha K, Ernala SK, Dutta S, Sharma E, De Choudhury M. Understanding moderation in online mental health communities. In: Social Computing and Social Media. Participation, User Experience, Consumer Experience, and Applications of Social Computing. 2020 Jul Presented at: 22nd HCI International Conference, HCII 2020; July 19-24, 2020; Copenhagen, Denmark. [doi: 10.1007/978-3-030-49576-3_7]
32. Skivington K, Matthews L, Simpson SA, Craig P, Baird J, Blazeby JM, et al. A new framework for developing and evaluating complex interventions: update of Medical Research Council guidance. BMJ 2021 Sep 30;374:n2061 [FREE Full text] [doi: 10.1136/bmj.n2061] [Medline: 34593508]

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33. Mental Capacity Act 2005: Code of practice. Department for Constitutional Affairs. 2007. URL: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/921428/Mental-capacity-act-code-of-practice.pdf [accessed 2022-06-14]
34. Online surveys. Online Surveys. URL: https://www.onlinesurveys.ac.uk/ [accessed 2022-06-14]
35. Braun V, Clarke V. Thematic Analysis: A Practical Guide. Los Angeles, CA: SAGE Publications; 2021:35-36.
36. Giebel C, Cannon J, Hanna K, Butchard S, Eley R, Gaughan A, et al. Impact of COVID-19 related social support service closures on people with dementia and unpaid carers: a qualitative study. Aging Ment Health 2021 Jul;25(7):1281-1288. [doi: 10.1080/13607863.2020.1822292] [Medline: 32954794]
37. Hennink MM, Kaiser BN, Weber MB. What influences saturation? Estimating sample sizes in focus group research. Qual Health Res 2019 Aug;29(10):1483-1496. [doi: 10.1177/1049732318821692] [Medline: 30628545]

Abbreviations

DEEP: Dementia Engagement and Empowerment Project
YOD: young onset dementia

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Protocol

Endovascular Abdominal Aortic Aneurysm Repair With Ovation Alto Stent Graft: Protocol for the ALTAIR (ALTo endograft Italian Registry) Study

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Abstract

Background: Since 2010, the Ovation Abdominal Stent Graft System has offered an innovative sealing option for abdominal aortic aneurysm (AAA) by including a sealing ring filled with polymer 13 mm from the renal arteries. In August 2020, the redesigned Ovation Alto, with a sealing ring 6 mm closer to the top of the fabric, received CE Mark approval.

Objective: This registry study aims to evaluate intraoperative, perioperative, and postoperative results in patients treated by the Alto stent graft (Endologix Inc.) for elective AAA repair in a multicentric consecutive experience.

Methods: All consecutive eligible patients submitted to endovascular aneurysm repair (EVAR) by Alto Endovascular AAA implantation will be included in this analysis. Patients will be submitted to EVAR procedures based on their own preferences, anatomical features, and operators experience. An estimated number of 300 patients submitted to EVAR with Alto stent graft should be enrolled. It is estimated that the inclusion period will be 24 months. The follow-up period is set to be 5 years. Full data sets and cross-sectional images of contrast-enhanced computed tomography scan performed before EVAR, at the first postoperative month, at 24 or 36 months, and at 5-year follow-up interval will be reported in the central database for a centralized core laboratory review of morphological changes. The primary endpoint of the study is to evaluate the technical and clinical success of EVAR with the Alto stent graft in short- (90-day), mid- (1-year), and long-term (5-year) follow-up periods. The following secondary endpoints will be also addressed: operative time; intraoperative radiation exposure; contrast medium usage; AAA sac shrinkage at 12-month and 5-year follow-up; any potential role of patients' baseline characteristics, valuated on preoperative computed tomography angiographic study, and of device configuration (number of component) in the primary endpoint.

Results: The study is currently in the recruitment phase and the final patient is expected to be treated by the end of 2023 and then followed up for 5 years. A total of 300 patients will be recruited. Analyses will focus on primary and secondary endpoints. Updated results will be shared at 1- and 3-5-year follow-ups.

Conclusions: The results from this registry study could validate the safety and effectiveness of the new design of the Ovation Alto Stent Graft. The technical modifications to the endograft could allow for accommodation of a more comprehensive range of anatomies on-label.

Trial Registration: ClinicalTrials.gov NCT05234892; https://clinicaltrials.gov/ct2/show/NCT05234892

International Registered Report Identifier (IRRID): PRR1-10.2196/36995

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(JMIR Res Protoc 2022;11(7):e36995) doi:10.2196/36995

KEYWORDS

abdominal aortic aneurysm; endovascular aneurysm repair; endograft; low-profile endograft

Introduction

Background

An abdominal aortic aneurysm (AAA) is a dilatation in the lower part of the major vessel (aorta) that supplies blood to the body. The most accepted definition of AAA is based on a diameter of 3.0 cm or more, which is usually higher than 2 SDs above the mean diameter for men [1,2]. Over the last decades, the treatment options have changed. The traditional approach is represented by the open surgical repair [3,4]. As an alternative, the less invasive endovascular treatment has been proposed (endovascular aneurysm repair [EVAR]), which has become the first treatment of choice in patients with suitable anatomy [5,6]. EVAR represents a minimally invasive technique that has overcome some critical issues of open surgical repair such as higher intraoperative and perioperative risk; the necessity of general anesthesia; intensive care unit stay; and higher cardiac, pulmonary, and renal complications [7]. These advantages led to a constant increase in the AAA treatment feasibility, especially in elderly patients with a substantial number of comorbidities that could be treated with reasonable perioperative risks [8] and good early and mid-term outcomes [9] even in emergency settings [10].

Thirty years ago, Juan Parodi [11] developed the first prototype of endograft for EVAR, a handmade device made of a tube-shaped aorto-aortic graft sutured at each end to a balloon-expandable stent based on the design of radiologist Julio Palmaz. This device was implanted in a human body for the first time on September 7, 1990, in Buenos Aires, Argentina [12]. By 1994, the first commercially available device had been launched into the market [13]. Stent-graft material and design changed in various ways to improve conformability, reduce fracture, and minimize device migration rates [14]. Over the years EVAR has become an effective treatment for AAA in patients with challenging anatomy such as hostile neck and small access [15]. Tremendous success has been achieved owing to the continuous technological development that was able to overcome the previous limitations in EVAR applicability. Since 2010, the Ovation Abdominal Stent Graft System (Endologix Inc.) has offered a new concept of sealing, achieved by a network of O-rings filled by a polymer that can treat a great variety of difficult anatomies through a low-profile platform [16]. In the latest version of the stent graft, called Ovation Alto, the conformable O-rings with CustomSeal polymer have been repositioned near the top of the endograft, providing a seal just below the renal arteries. Very few papers highlighting the early and late outcomes of this new device, however, have been published. In this regard, this is intended to be the first multicenter prospective registry study on the implantation of the Alto stent graft in a large cohort of patients, who were also followed up for 5 years with a centralized core laboratory analysis of morphological changes. The aim of this study is to evaluate intraoperative, perioperative, and postoperative results in patients treated by the Alto stent graft (Endologix Inc.) for elective AAA repair in a multicentric consecutive experience.

Device Under Investigation

The device under investigation represents the evolution of the low-profile Ovation Prime and iX endograft (Figure 1) [17]. The inflatable channels and the sealing rings, which are the most peculiar features of the predecessor endograft, remained unchanged. This ring network is still filled by a low-viscosity radiopaque polymer intraoperatively, which creates a customized sealing of the infrarenal neck.

Iliac limbs have also not changed and are deployed through a 12-15-Fr delivery system (outer diameter) with various lengths and diameters ranging from 80 to 160 mm and 10 to 28 mm, respectively. The new feature of Ovation Alto is the relocation of the proximal sealing ring at 7 mm from the main body fabric's proximal edge. In the previous versions, this distance was 13 mm. The low-permeability graft material and the suprarenal 35-mm free-flow stent remained unchanged. It is still delivered via a flexible, hydrophilic-coated, low-profile delivery system (15-Fr outer diameter for all main body measures).

Another design improvement is the integration of a compliant balloon within the delivery system. The balloon is highlighted by a proximal radiopaque marker that coincides with the first sealing ring location, helping in the precise placement of the endograft.

The deployment of the device is performed in a 2-time maneuver (Figure 2). Initially, the lower part of the uncovered stent and the endograft module are deployed and expanded using the integrated, compliant balloon. The upper part of the bare stent remains temporarily undeployed. This system allows the repositioning of the endograft before the final deployment. After full stent-graft positioning and polymer injection, the balloon is advanced by 5-7 mm and re-inflated. This enables a more precise customization of the first sealing ring.

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Figure 1. Comparison between Ovation Alto endograft (left) and Ovation iX (right) endograft.

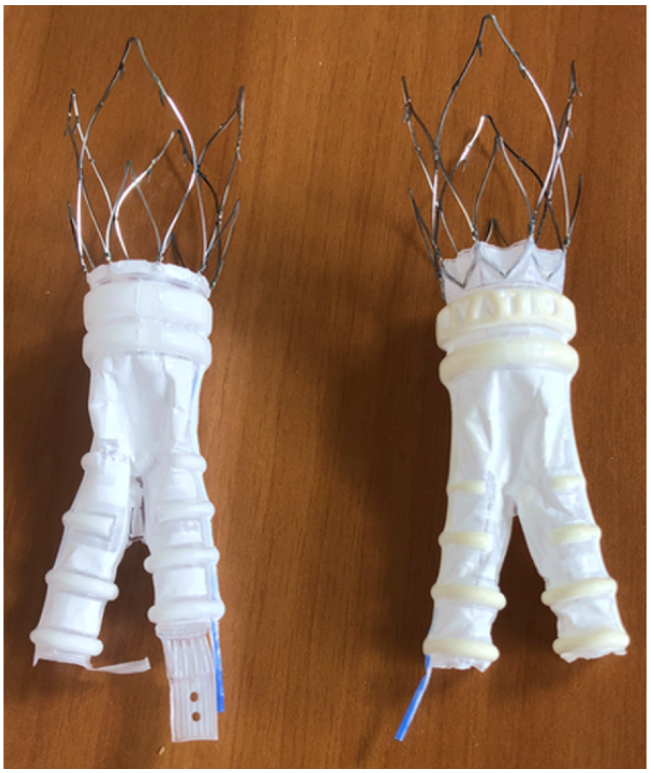
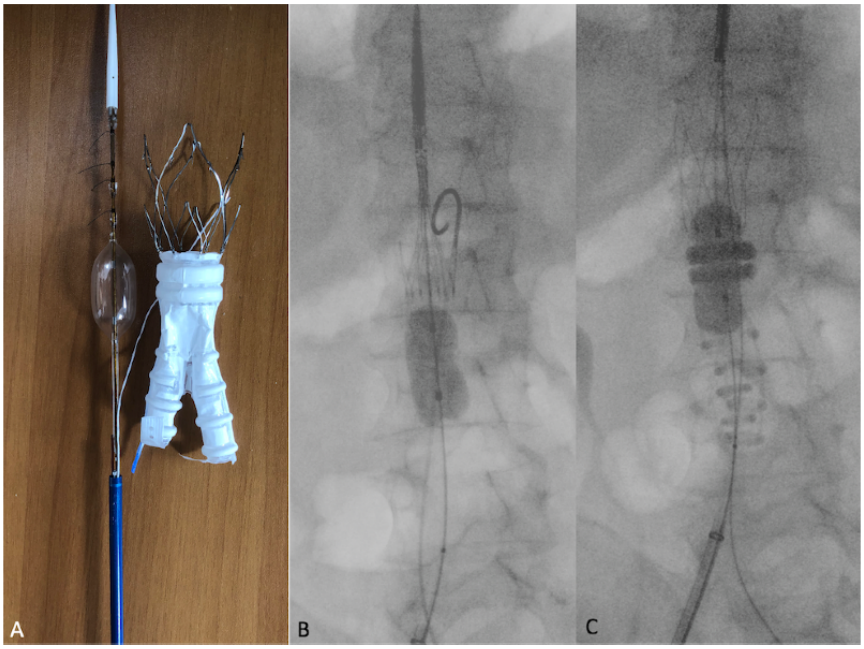


Figure 2. A) Ovation Alto endograft model with the incorporated compliant balloon inflated. B) Intraoperative fluoroscopy with Ovation Alto semi-deployed with the incorporated balloon partially inflated. C) Intraoperative fluoroscopy with Ovation Alto endograft main body deployed, with O-rings polymer filled. The incorporated balloon is advanced of 5-7 mm and fully inflated.



Other minor modifications of the Ovation Alto design are as follows: (1) the inner diameter of the docking limb has been increased to 11 mm for all main body sizing; (2) a more definite web enriched the device bifurcation to avoid a prolapse of the contralateral limb during guide-wire access; (3) the aortic body limbs were offset by 5 mm to improve their identification during the procedure.

According to the current instruction for use, the following anatomical criteria are required [18]:

- adequate iliac/femoral access compatible with vascular access techniques (femoral cutdown or percutaneous), devices, or accessories;
- a proximal aortic landing zone for the sealing ring 7 mm below the inferior renal artery;
- an aortic sealing zone consisting of healthy aorta defined as
  - a lack of significant thrombus greater than 8 mm in thickness at any point along the aortic circumference at the level of 7 mm below the inferior renal artery;

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  - a lack of significant calcification at the level of 7 mm below the inferior renal artery;
  - conicity <10% as measured from the inferior renal artery to the aorta 7 mm below the inferior renal artery;
  - an inner wall diameter of no less than 16 mm and no greater than 30 mm at 7 mm below the inferior renal artery; and
  - an aortic angle of ≤60°.
- a distal iliac landing zone:
  - with a length of at least 10 mm and
  - with an inner wall diameter no less than 8 mm and no greater than 25 mm.

The contraindications for Alto stent-graft implantation according to the instruction for use are:

- patients who have a condition that threatens to infect the graft and
- patients with known sensitivities or allergies to the device materials (including polytetrafluoroethylene, polyethylene glycol–based polymers, contrast agents, fluorinated ethylene propylene, titanium, nickel, platinum, or iridium).

Methods

Study Patients

All consecutive eligible patients submitted to EVAR by Alto Endovascular AAA implantation will be included in analysis. Patients will be submitted to EVAR procedures based on their own preferences, anatomical features, and operators experience.

Recruitment

An estimated number of 300 patients submitted to EVAR with Alto stent graft will be enrolled. It is estimated that the inclusion period will be 24 months. The follow-up period is set to be 5 years. Prior to enrollment into the clinical investigation, patients will be evaluated by their physician for inclusion criteria. Each patient's medical condition should be stable, with no underlying medical condition that would prevent them from performing the required testing or from completing the study. Patients should be geographically stable, willing and able to cooperate in this clinical study, and remain available for midterm follow-up. Patients who do not wish to participate in this study can obtain the best available EVAR therapy as indicated; refusal to participate in this study will in no way affect their care at the institution. Inclusion and exclusion criteria are detailed in Textbox 1.

This study respects all the principles reported in the current version of Helsinki declaration (2013). AAA morphology will be assessed by OsiriX MD (OsiriX software; PIXMEO) on a computer (with Mac operating system) in a preoperative, contrast-enhanced, computed tomography angiographic (CTA) study. CTA must be performed with a biphasic acquisition protocol (unenhanced and contrast-enhanced scanning with a bolus tracking system) and reconstructions to 1-mm slices. All measurements (diameter, length, and angles) will be evaluated on a workstation with dedicated reconstruction software and center lumen line analysis and multiplanar reconstruction.

Textbox 1. Inclusion and exclusion criteria.

Inclusion Criteria

- Patients with abdominal aortic aneurysm who are scheduled for elective repair according to Endologix Alto endograft device's instruction for use.
- Patient is willing to comply with specified follow-up evaluations at the specified times for the duration of the study.
- Patient is aged over 18 years.
- Patient, or his/her legal representative, understands the nature of the procedure and provides written informed consent prior to enrollment in the study.

Exclusion Criteria

- Abdominal endovascular aneurysm repair performed in an urgent/emergent setting.
- Patients treated outside Endologix Alto endograft device's instruction for use.
- Patients refusing treatment.
- Patients for whom antiplatelet therapy, anticoagulants, or antihypertensive drug are contraindicated.
- Patients with a history of prior life-threatening contrast medium reaction.
- Life expectancy less than the follow-up period.

A patient is considered enrolled in the study if he/she has full compliance with the study inclusion and exclusion criteria and after successful EVAR procedure at completion angiography.

Clinical data will be collected at patients' enrollment, EVAR procedure, discharge, planned follow-ups (1-3 and 12 months after the procedure, yearly thereafter), unplanned or interim follow-ups, and patient death. CTA within 90 days, 24 or 36 months, and 5 years after the index procedure is mandatory. Duplex ultrasound scan will be performed at the same follow-up interval, and also at 12, 24, 36, and 48 months. A new CTA will be performed in case of unexpected events during follow-up. The follow-up protocol is based on the most recent European guidelines for the management of the AAAs [1].

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Endpoint

The primary endpoint of the study is to evaluate the technical and clinical success of EVAR with Alto stent graft in short- (90-day), mid- (1-year), and long-term (5-year) follow-up periods. Technical success is defined as the correct graft deployment without any unintentional occlusion of the aortic visceral branches or both hypogastric arteries, with aneurysm exclusion confirmed by the intraoperative angiography, without signs of type I/III endoleak or conversion to open surgery or mortality. Clinical success includes successful deployment of the endovascular device at the intended location without death as a result of aneurysm-related treatment, type I or III endoleak, or graft infection or thrombosis, aneurysm expansion (>5 mm), aneurysm rupture, or conversion to open repair. Moreover, the presence of graft dilatation of 20% or more by diameter, graft migration, or a failure of device integrity will be evaluated.

The clinical and technical successes are defined "assisted" in case of unplanned endovascular procedures, or "secondary" if unplanned surgery is necessary [19].

The following secondary endpoints will be also addressed: (1) operative time; (2) intraoperative radiation exposure; (3) contrast medium usage; (4) AAA sac shrinkage at 12-month and 5-year follow-up; (5) any potential role of patients' baseline characteristics, valuated on preoperative CTA, and of device configuration (number of component) in primary endpoint.

Data Collection and Analysis

Patient data will be captured electronically using a computer-based platform accessible to all investigators. Descriptive data summaries will be used to present and summarize the collected data. For categorical variables (eg, gender), frequency distributions and cross tabulations will be given. For numeric variables (eg, patient age), range, mean, median, and SD will be calculated. For all variables, a 95% CI for the relevant parameters of the underlying distribution will be calculated. For all time-dependent events, life tables will be calculated using the Kaplan-Meier estimate method for a period starting on the date of the procedure up to and including all follow-up visits. Stratification to risk factors will be performed and the log-rank test will be used to compare between the different outcomes; associated *P* values <.05 will be defined as significant.

All preoperative and follow-up CTAs were assessed and independently evaluated by 2 experienced vascular surgeons at core laboratory center. Disagreements will be discussed and resolved by consensus.

Patients' Confidentiality

All information and data concerning patients or their participation in this clinical investigation will be considered confidential. Only authorized personnel will have access to these confidential files. Authorized personnel of health authorities will have the right to inspect and copy all records pertinent to this clinical investigation. All data used in the analysis and reporting of this clinical investigation will be anonymized.

Ethical Consideration

This study adheres to the guidelines of European Good Clinical Practice (ICH: 6 R2) and adopted by the Italian Agenzia Italiana del Farmaco (AIFA), in accordance to Legislative Decree 196/2003 and 21/2007 of the Italian Ministry of Health. The local institutional review boards of the participating centers were informed of the descriptive, nonexperimental nature of this registry study. The device under investigation is already available for standard clinical practice.

Data Availability

The data sets generated during or analyzed during this study will be available from the corresponding author on reasonable request.

Results

Patient enrollment started in January 2022. It is anticipated that 300 patients will be recruited to the study. All variables will be evaluated in a dedicated central database. All morphological changes will be examined in a centralized core laboratory. After data analysis, results will be shared with each investigator. Updates to results will be published at 1-year follow-up and at 3-5-year follow-up.

Discussion

The purpose of this registry study is to demonstrate that the adaptive sealing technology of the Alto stent graft is safe and effective in the treatment of infrarenal AAA in different anatomical scenarios.

Since its appearance in the market in 2010, the Ovation endograft has offered an innovative sealing concept involving a nonexpansive circumferential apposition of inflatable rings filled by a low-viscosity polymer [20]. The polymer-filled system adapts to the patients' aortic neck, thus ensuring a continuous, customized concentric seal. This feature allows a broadening of patient's eligibility that is higher than other stent graft [21].

The Ovation Alto abdominal stent-graft system received Food and Drug Administration (FDA) approval on March 16, 2020. The commercial launch of the device in the United States was announced on July 30, 2020. On August 5, 2020, Endologix proclaimed CE Mark approval in the European Union for EVAR. In Italy, the commercial launch started in November 2020, in centers having a vast experience with Ovation Prime and iX. The new Alto sealing zone is closer to the renal arteries and may offer sealing in aneurysms with irregular or less than 1-cm long neck. We have already described the possibility to treat juxtarenal aortic aneurysms unfit for open surgery and for fenestrated/branched EVAR. The solution was to perform a physician-modified implantation of Ovation iX, in a procedure termed the "vent" technique. It involves an off-label, aggressive deployment of the sealing ring between 1 and 3 mm below the lowermost renal artery rather than 13 mm. The proximal edge of the collar zone's fabric was moved down by bare-metal stents contemporarily deployed to assure renal arteries' patency [22]. The vent technique offered a preliminary evaluation of how the

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polymer ring may behave close to the renal ostium in very challenging necks, which is now possible with the new design of the Ovation Alto.

An inaccurate deployment of the sealing ring with the previous Ovation version has been described as the cause for an early technical failure [23]. The compliant balloon in the new version of the Alto stent graft may help operators to identify the first ring's landing, thereby making the deployment more precise. Moreover, the sealing ring's early ballooning may guarantee a more accurate customization of polymer to aortic wall shape.

The low-profile delivery system (15 F) establishes small iliac access (>6 mm) with the possibility to perform percutaneous procedures, achieving a reduction in blood loss, groin complications, and earlier discharge.

Holden and Lyden [24] reported promising results in the first-in-human experience with the Ovation Alto. At the moment, only early outcomes in a series of 7 patients have been published, while the 5-year results from the Expanding Patient Applicability with Polymer Sealing Ovation Alto Stent Graft (ELEVATE) clinical trial are expected to be published in 2023.

Recently, another initial experience [25] confirmed the early technical and clinical success of the new Ovation Alto stent graft.

Good 5-year EVAR results with the Ovation platform have been reported, demonstrating excellent long-term durability of this endograft, despite 41% of patients having an anatomy unfit for other stent grafts [26]. Results from our registry study may further confirm durability results with the novel version. Moreover, the technical modifications to the endograft may allow for accommodation of a more comprehensive range of anatomies on-label.

Authors' Contributions

We acknowledge the support by the entire group of ALTAIR collaborators: Andrea Gaggiano, Michelangelo Ferri (Torino), Massimo Maione, Edoardo Frola (Cuneo), Matteo Tozzi, Gabriele Piffaretti, Nicola Rivolta (Varese), Piero Trabattoni, Stefano Zoli (Milano), Franco Grego, Michele Antonello, Michele Piazza (Padova), Paolo Frigatti, Maria Pia Borrelli (Udine), Nicola Tusini, Giovanni Giannace (Reggio Emilia), Roberto Silingardi, Francesco Andreoli (Modena), Leonardo Ercolini, Giorgio Ventoruzzo, Giulia Mazzitelli (Arezzo), Federico Filippi, Claudia Panzano (Grosseto), Giovanni Credi, Jacopo Nottoli (Massa Carrara), Stefano Michelagnoli, Emiliano Chisci (Firenze), Stefano Camparini, Selina Russo, Roberta Arzedi, Arianna Serra (Cagliari), Luca di Marzo, Wassim Mansour (Roma), Roberto Gattuso, Simone Cuozzo (Roma), Arnaldo Ippoliti, Stefano Fazzini, Fabio Massimo Oddi (Roma), Nicola Mangialardi, Matteo Orrico (Roma), Stefano Bartoli, Andrea Siani (Roma), Sonia Ronckey, Matteo Barbante (Roma), Emanuela Setteducati, Paola Orlando (Roma); Pietro Volpe, Mafalda Massara (Reggio Calabria), Carlo Dionisi, Gianluca Palasciano (Tricase), Gennaro Vigliotti, Fabio Spinetti (Napoli), Costantino Di Angelo (Nuoro), Piero Modugno, Veronica Picone (Campobasso); Arduino Farina, Angelo Sanfiorenzo (Palermo); Alessandro Cappelli, Giuseppe Galzerano, Claudio Baldi, Domenico Benevento, Giuseppe Alba, Giulia Ferrante, Giulia Casilli, Bruno Gargiulo, Elisa Lazzeri, Greta Ferraro, Cecilia Molino, Leonardo Pasquetti (Siena).

Conflicts of Interest

GDD is a consultant for Endologix. The authors have no other conflicts to declare.

References

1. Wanhainen A, Verzini F, Van Herzeele I, Allaire E, Bown M, Cohnert T, Esvs Guidelines Committee, Document Reviewers, et al. Editor's Choice - European Society for Vascular Surgery (ESVS) 2019 Clinical Practice Guidelines on the Management of Abdominal Aorto-iliac Artery Aneurysms. Eur J Vasc Endovasc Surg 2019 Jan;57(1):8-93 [FREE Full text] [doi: 10.1016/j.ejvs.2018.09.020] [Medline: 30528142]
2. Thompson SG, Bown MJ, Glover MJ, Jones E, Masconi KL, Michaels JA, et al. Screening women aged 65 years or over for abdominal aortic aneurysm: a modelling study and health economic evaluation. Health Technol Assess 2018 Aug;22(43):1-142 [FREE Full text] [doi: 10.3310/hta22430] [Medline: 30132754]
3. Davidovic LB, Maksic M, Koncar I, Ilic N, Dragas M, Fatic N, et al. Open Repair of AAA in a High Volume Center. World J Surg 2017 Mar;41(3):884-891. [doi: 10.1007/s00268-016-3788-3] [Medline: 27803955]
4. Williams CR, Brooke BS. Effectiveness of open versus endovascular abdominal aortic aneurysm repair in population settings: A systematic review of statewide databases. Surgery 2017 Oct;162(4):707-720. [doi: 10.1016/j.surg.2017.01.014] [Medline: 28242088]
5. Suckow BD, Goodney PP, Columbo JA, Kang R, Stone DH, Sedrakyan A, et al. National trends in open surgical, endovascular, and branched-fenestrated endovascular aortic aneurysm repair in Medicare patients. J Vasc Surg 2018 Jun;67(6):1690-1697.e1 [FREE Full text] [doi: 10.1016/j.jvs.2017.09.046] [Medline: 29290495]
6. Bacharach JM, Wood EA, Slovut DP. Management of Aortic Aneurysms: Is Surgery of Historic Interest Only? Curr Cardiol Rep 2015 Sep 22;17(11):105. [doi: 10.1007/s11886-015-0654-0]
7. Antoniou GA, Antoniou SA, Torella F. Editor's Choice - Endovascular vs. Open Repair for Abdominal Aortic Aneurysm: Systematic Review and Meta-analysis of Updated Peri-operative and Long Term Data of Randomised Controlled Trials. Eur J Vasc Endovasc Surg 2020 Mar;59(3):385-397 [FREE Full text] [doi: 10.1016/j.ejvs.2019.11.030] [Medline: 31899100]

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8. Han Y, Zhang S, Zhang J, Ji C, Eckstein H. Outcomes of Endovascular Abdominal Aortic Aneurysm Repair in Octogenarians: Meta-analysis and Systematic Review. Eur J Vasc Endovasc Surg 2017 Oct;54(4):454-463 [FREE Full text] [doi: 10.1016/j.ejvs.2017.06.027] [Medline: 28822680]
9. Pasqui E, de Donato G, Giannace G, Panzano C, Setacci C, Palasciano G. Management of abdominal aortic aneurysm in nonagenarians: A single-centre experience. Vascular 2021 Feb;29(1):27-34. [doi: 10.1177/1708538120936831] [Medline: 32611281]
10. Tan T, Eslami M, Rybin D, Doros G, Zhang WW, Farber A. Outcomes of endovascular and open surgical repair of ruptured abdominal aortic aneurysms in elderly patients. J Vasc Surg 2017 Jul;66(1):64-70 [FREE Full text] [doi: 10.1016/j.jvs.2016.10.119] [Medline: 28216354]
11. Parodi JC. The challenges of medical innovation. J Vasc Surg 2020 Jan;71(1):212-215 [FREE Full text] [doi: 10.1016/j.jvs.2019.07.104] [Medline: 31864644]
12. Veith FJ, Marin ML, Cynamon J, Schonholz C, Parodi J. 1992: Parodi, Montefiore, and the first abdominal aortic aneurysm stent graft in the United States. Ann Vasc Surg 2005 Sep;19(5):749-751. [doi: 10.1007/s10016-005-6858-9] [Medline: 16052384]
13. Ivancev K, Vogelzang R. A 35 Year History of Stent Grafting, and How EVAR Conquered the World. Eur J Vasc Endovasc Surg 2020 May;59(5):685-694 [FREE Full text] [doi: 10.1016/j.ejvs.2020.03.017] [Medline: 32307304]
14. Kontopodis N, Papadopoulos G, Galanakis N, Tsetis D, Ioannou CV. Improvement of patient eligibility with the use of new generation endografts for the treatment of abdominal aortic aneurysms. A comparison study among currently used endografts and literature review. Expert Rev Med Devices 2017 Mar;14(3):245-250. [doi: 10.1080/17434440.2017.1281738] [Medline: 28076989]
15. de Donato G, Pasqui E, Nano G, Lenti M, Mangialardi N, Speziale F, LoLopro Registry Collaborators. Long-term results of low-profile stent grafts for treatment of infrarenal aortic aneurysms: Results from a retrospective multicenter registry. J Vasc Surg 2022 Apr 09:1242-1252. [doi: 10.1016/j.jvs.2021.09.036] [Medline: 34634415]
16. de Donato G, Setacci F, Sirignano P, Galzerano G, Borrelli MP, di Marzo L, et al. Ultra-low profile Ovation device: is it the definitive solution for EVAR? J Cardiovasc Surg (Torino) 2014 Feb;55(1):33-40. [Medline: 24356044]
17. de Donato G, Pasqui E, Panzano C, Brancaccio B, Grottola G, Galzerano G, et al. The Polymer-Based Technology in the Endovascular Treatment of Abdominal Aortic Aneurysms. Polymers (Basel) 2021 Apr 07;13(8):1196 [FREE Full text] [doi: 10.3390/polym13081196] [Medline: 33917214]
18. Trivascular. URL: https://www.trivascular.com/IFU [accessed 2022-05-01]
19. Chaikof EL, Blankensteijn JD, Harris PL, White GH, Zarins CK, Bernhard VM, Ad Hoc Committee for Standardized Reporting Practices in Vascular Surgery of The Society for Vascular Surgery/American Association for Vascular Surgery. Reporting standards for endovascular aortic aneurysm repair. J Vasc Surg 2002 May;35(5):1048-1060 [FREE Full text] [doi: 10.1067/mva.2002.123763] [Medline: 12021727]
20. Sirignano P, Mansour W, Capoccia L, Cuozzo S, Camparini S, de Donato G, et al. Endovascular aortic repair in patients with challenging anatomies: the EXTREME study. EuroIntervention 2021 Apr;16(18):e1544-e1550. [doi: 10.4244/eij-d-19-00547]
21. Kontopodis N, Galanakis N, Tzartzalou I, Tavlas E, Georgakarakos E, Dimopoulos I, et al. An update on the improvement of patient eligibility with the use of new generation endografts for the treatment of abdominal aortic aneurysms. Expert Rev Med Devices 2020 Nov;17(11):1231-1238. [doi: 10.1080/17434440.2020.1841629] [Medline: 33089719]
22. de Donato G, Pasqui E, Mele M, Panzano C, Giannace G, Setacci F, et al. The use of a low-profile stent graft with a polymer ring sealing technology combined with bare renal stent (vent technique) in patients with juxtarenal aneurysm not eligible for open surgery and fenestrated endograft. J Vasc Surg 2020 Jun;71(6):1843-1850. [doi: 10.1016/j.jvs.2019.06.220] [Medline: 31676183]
23. Kontopodis N, Tavlas E, Galanakis N, Chronis C, Kafetzakis A, Tsetis D, et al. Spontaneous Type Ia Endoleak Sealing in Patients Undergoing Endovascular Aneurysm Repair With the Ovation Stent Graft. Ann Vasc Surg 2019 Jan;54:240-247. [doi: 10.1016/j.avsg.2018.04.041] [Medline: 30092430]
24. Holden A, Lyden S. Initial experience with polymer endovascular aneurysm repair using the Alto stent graft. J Vasc Surg Cases Innov Tech 2020 Mar;6(1):6-11 [FREE Full text] [doi: 10.1016/j.jvscit.2019.04.007] [Medline: 32025596]
25. de Donato G, Pasqui E, Panzano C, Galzerano G, Cappelli A, Palasciano G. Early Experience with the New Ovation Alto Stent Graft in Endovascular Abdominal Aortic Aneurysm Repair. EJVES Vasc Forum 2022;54:7-12 [FREE Full text] [doi: 10.1016/j.ejvsvf.2021.11.003] [Medline: 34950916]
26. Barleben A, Mathlouthi A, Mehta M, Nolte T, Valdes F, Malas MB, Ovation trial investigators. Long-term outcomes of the Ovation Stent Graft System investigational device exemption trial for endovascular abdominal aortic aneurysm repair. J Vasc Surg 2020 Nov;72(5):1667-1673.e1. [doi: 10.1016/j.jvs.2020.01.066] [Medline: 32249041]

Abbreviations

AAA: abdominal aortic aneurysm
CTA: computed tomography angiography

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ELEVATE: Expanding Patient Applicability with Polymer Sealing Ovation Alto Stent Graft
EVAR: endovascular aneurysm repair
FDA: Food and Drug Administration

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Protocol

Multimodal Assessment of Schizophrenia and Depression Utilizing Video, Acoustic, Locomotor, Electroencephalographic, and Heart Rate Technology: Protocol for an Observational Study

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Abstract

Background: Current standards of psychiatric assessment and diagnostic evaluation rely primarily on the clinical subjective interpretation of a patient's outward manifestations of their internal state. While psychometric tools can help to evaluate these behaviors more systematically, the tools still rely on the clinician's interpretation of what are frequently nuanced speech and behavior patterns. With advances in computing power, increased availability of clinical data, and improving resolution of recording and sensor hardware (including acoustic, video, accelerometer, infrared, and other modalities), researchers have begun to demonstrate the feasibility of cutting-edge technologies in aiding the assessment of psychiatric disorders.

Objective: We present a research protocol that utilizes facial expression, eye gaze, voice and speech, locomotor, heart rate, and electroencephalography monitoring to assess schizophrenia symptoms and to distinguish patients with schizophrenia from those with other psychiatric disorders and control subjects.

Methods: We plan to recruit three outpatient groups: (1) 50 patients with schizophrenia, (2) 50 patients with unipolar major depressive disorder, and (3) 50 individuals with no psychiatric history. Using an internally developed semistructured interview, psychometrically validated clinical outcome measures, and a multimodal sensing system utilizing video, acoustic, actigraphic, heart rate, and electroencephalographic sensors, we aim to evaluate the system's capacity in classifying subjects (schizophrenia, depression, or control), to evaluate the system's sensitivity to within-group symptom severity, and to determine if such a system can further classify variations in disorder subtypes.

Results: Data collection began in July 2020 and is expected to continue through December 2022.

Conclusions: If successful, this study will help advance current progress in developing state-of-the-art technology to aid clinical psychiatric assessment and treatment. If our findings suggest that these technologies are capable of resolving diagnoses and symptoms to the level of current psychometric testing and clinician judgment, we would be among the first to develop a system that can eventually be used by clinicians to more objectively diagnose and assess schizophrenia and depression with the possibility of less risk of bias. Such a tool has the potential to improve accessibility to care; to aid clinicians in objectively evaluating diagnoses, severity of symptoms, and treatment efficacy through time; and to reduce treatment-related morbidity.

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KEYWORDS

digital biomarker; machine learning; computer vision; schizophrenia; depression; multimodal; technology; acoustic; heart rate; biomarker

Introduction

Background

Mental disorders represent the second most common cause of years of life lived with disability worldwide [1]. Among mental illnesses, depression and schizophrenia represent the first and third highest contributors to years of life lived with disability, respectively, with over 200 million people suffering from either condition across the globe [2]. Schizophrenia is one of the most severe psychiatric disorders and affects self-image, physical health, employment, and social life [3]. While the cost of both conditions is tremendous, schizophrenia is particularly dramatic, with reports estimating an average of 14.5 to 28.5 years of life lost in those who suffer with the disorder [4,5]. The profound impact on the individual notwithstanding, these disorders are also of tremendous public concern. The World Health Organization estimates that the cost of schizophrenia reaches 2.6% of health care spending in high-income nations [6]. In the US, studies have found that the costs of depression and schizophrenia reach an annual US $210 billion and US $155 billion, respectively [7,8]. To put that in perspective, the Center for Medicare and Medicaid Services reported that in 2016, annual health care expenditure was US $3.3 trillion [9], meaning that depression and schizophrenia accounted for 11.1% of annual American health care costs. The largest contributors to these costs include unemployment, caregiving, and inpatient care [7,8]. Limiting the individual- and population-level impact of these disorders has been the subject of much research and has been a focus of the health care system.

Current evidence suggests that early identification and optimized treatment of depression and schizophrenia improves outcomes and reduces illness progression [10-14], which may consequently reduce societal costs. Unfortunately, the duration of untreated disease can be long. For example, in the Recovery After an Initial Schizophrenia Episode Early Treatment Program study, the median duration of untreated psychosis was 74 weeks [15]. Multiple factors contribute to delays in the diagnosis of these conditions, including limited access to psychiatric care [16,17]. Even in high-income nations, such as the US, access to specialty care is limited, with reports finding that up to 20.1% of adults seeking care do not receive treatment meeting their needs [18].

At present, depression and schizophrenia are diagnosed through the subjective clinical evaluation of signs and symptoms established by the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) [19] or the International Classification of Diseases, 10th revision [20]. Structured interviews can be used to improve diagnostic accuracy, but are infrequently used in clinical practice [21]. While at their extremes these conditions are far from nuanced, symptoms can be subtle in the early phases [22]. In such instances, disorder identification requires extended interviews, gathering of collateral information, and a high degree of expertise from the interviewer. Unfortunately, the current and likely future state of the behavioral health system significantly restricts patient access to the necessary extended interviews by the appropriate experts. In fact, a 2017 report estimated that the supply of psychiatrists in the United States would decrease by 20% over the next decade, despite increasing demand over the same period [23]. As a consequence, behavioral health care is increasingly being managed by primary care providers who have neither the time nor the expertise to evaluate subtle variations in certain behavioral health conditions [24]. This represents an opportunity for the integration of technological support tools to improve patient access to quality care.

Current Digital Biomarker Research

The development of easy-to-use, objective clinical tools to aid clinicians in the diagnosis and evaluation of mental illness has the potential to limit the impact of these illnesses on patients and on society. The cost of powerful computing hardware has fallen, and improvements in the field of computer science and health care suggest that various types of computer sensors and recording hardware could be used to aid in the assessment and diagnostic prediction of mental illness [25-30]. Research groups have demonstrated the efficacy in numerous mental health populations of these technologies, which include computer vision for distinguishing phases of depression [25,26], schizophrenia [27], and cognitive impairment [31], actigraphy for the differentiation of patients with schizophrenia from controls [28,29], and heart rate monitoring for distinguishing patients with schizophrenia or posttraumatic stress disorder from controls [28-30]. This research has demonstrated that with heart rate variability and actigraphic assessments alone, patients with schizophrenia may be differentiated from controls with up to 95.3% accuracy [28,29]. Other groups have similarly demonstrated the efficacy of each of these technologies in schizophrenia.

Few studies, however, have been conducted to assess variations in patients with depression or schizophrenia and control subjects with video technology, although some studies have observed statistically significant differences between schizophrenia and control groups in certain combinations of facial action clustering [32-34]. Furthermore, the extent of facial action expressivity has been demonstrated to be well correlated with clinical assessments of symptoms of schizophrenia [32,34,35]. Similar to facial expressions, video recording assessments have also allowed for differentiation of eye gaze behavior between subtypes of schizophrenia [36]. Similarly, actigraphic data has been demonstrated to be of value, with one group demonstrating a correlation between actigraphy recordings and changes in patient clinical conditions and drug regimens [37,38]. In a separate study of 25 patients with psychosis, the same research group assessed variations in motor richness, typicality, and consistency in patient subtypes with “high-positive,”

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"high-negative," and "low-level" symptoms, finding differences in richness and typicality, but not in consistency, between the subgroups [39]. Other groups have similarly found computerized voice and speech assessment to be clinically useful, with findings suggesting that voice pause and, to some extent, pitch can be discriminative of schizophrenia [40]. Furthermore, it has been demonstrated that speech coherence assessments have discriminative capacity in differentiating patients with schizophrenia from controls [41] and in predicting progression from prodrome to psychosis [42].

Past research groups have also found that electroencephalographic (EEG) recordings can accurately classify schizophrenia. For instance, one group found that EEG recordings could classify schizophrenia with 91.5% to 93.9% accuracy [43]. Multiple research groups have also studied automated EEG-based diagnosis of depression. In a review of several computer-aided diagnostic methods based on EEG data [44], one group showed that nonlinear dynamical analysis of EEG data is a promising approach for the differentiation of normal and depressed subjects [45]. Moreover, depression detection has been demonstrated using 3-electrode EEG-based analysis using wavelet transformation, feature selection, and multiple classification algorithms [46]. More recently, there has been a considerable number of deep neural network approaches [47,48]. However, generally, these approaches use small study populations and overfit without proper sampling and stratification.

Combining biomarkers may be a promising approach to improving diagnostic precision and treatment options [49,50] and may be applicable to the study of digital biomarkers. Approaches using multiple digital inputs have been used to differentiate individuals with depression from those without depression [51] and also to predict mood states (eg, depression, mania, and hypomania) in patients with mood disorders [52]. While research groups have assessed the role of these technologies in differentiating limited subtypes of schizophrenia, in addition to differentiating patients with schizophrenia from control groups, few have assessed the combination of these technologies in the assessment of schizophrenia, including the potential of combined technologies to improve predictive efficacy in differentiating patients with schizophrenia from controls, discriminate schizophrenia from other mental illnesses, predict illness severity, assess symptom change over time, and assess illness-related movement disorders with video technology.

Research Aims and Hypotheses

We present a research protocol to assess the efficacy of a multimodal sensor system combining video, audio, actigraphy, noninvasive EEG, and heart rate monitoring to assess differences in individuals with schizophrenia and unipolar major depressive disorder and controls (patients with no history of mental illness in the preceding year). The data collected from the subjects will be utilized to develop a machine learning model to evaluate the presence, severity, and possible subtypes of schizophrenia and depression. We seek to assess the performance of the developed model and its ability to differentiate schizophrenia from depression and control groups based on high-value input features from different modalities. We hypothesize that the predictive model will discriminate between schizophrenia, depression, and control groups. For the depression group only, we will evaluate within-group preprocessed outputs of the sensor data to discriminate depression severity scores using the Patient Health Questionnaire-9 (PHQ-9) [53] and the Clinical Global Impression (CGI) [54], commonly utilized rating scales to measure illness severity. For the schizophrenia group, we will evaluate within-group preprocessed outputs of the sensor data to discriminate severity scores using the Positive and Negative Syndrome Scale (PANSS) [55], Clinician-Rated Dimensions of Psychosis Symptom Severity in Patients with Schizophrenia (CRDPSS) [19,56] and the CGI. Finally, we will evaluate sensor sensitivity to within-subject outcome changes over time for both groups.

Methods

Participants

The research assessments will be conducted at the Grady Outpatient Behavioral Health Clinic, which is part of the broader Grady Health System, a metropolitan safety-net hospital in Atlanta, Georgia. The study seeks to recruit 50 individuals with schizophrenia, 50 individuals with unipolar major depressive disorder, and 50 controls without a prior history of mental illness.

Inclusion and Exclusion Criteria

The 3 groups of participants (aged 18 years or older) will include outpatients with a DSM-5 diagnosis of schizophrenia or a DSM-5 diagnosis of major depressive disorder and individuals with no mental health diagnosis (as controls). All diagnoses will be confirmed by the Mini International Neuropsychiatric Interview (MINI) [57]. All subjects must have the ability to consent to participation. Individuals that have a legal guardian may participate in the study with the guardian's signed consent. Participants recruited digitally must have access to a webcam (either on a desktop, tablet, or cell phone) and have internet connectivity with at least 2 to 4 megabytes per second upload speed. Subjects who do not have the capacity to consent to participation, who meet the criteria for nonschizophrenia psychotic illness (eg, schizoaffective disorder, mood disorder with psychotic features, or substance-induced psychotic disorder), whose differential diagnosis includes an active substance-induced mental illness, who present as unreliable with the equipment, who cannot participate in full assessments, or whose differential diagnosis includes a personality disorder will be excluded from the study. Those who are not native English speakers will be excluded from the study. The study team will make it clear that mental health treatment is not provided in this research study. If individuals (who are either included or excluded from the study) express an interest in connecting to local mental health resources, the team will make reasonable attempts to help them do so. If subjects present with signs or symptoms suggestive of a mental health emergency, a clinician (study author ROC) will be contacted for subject evaluation to determine whether emergency care is necessary.

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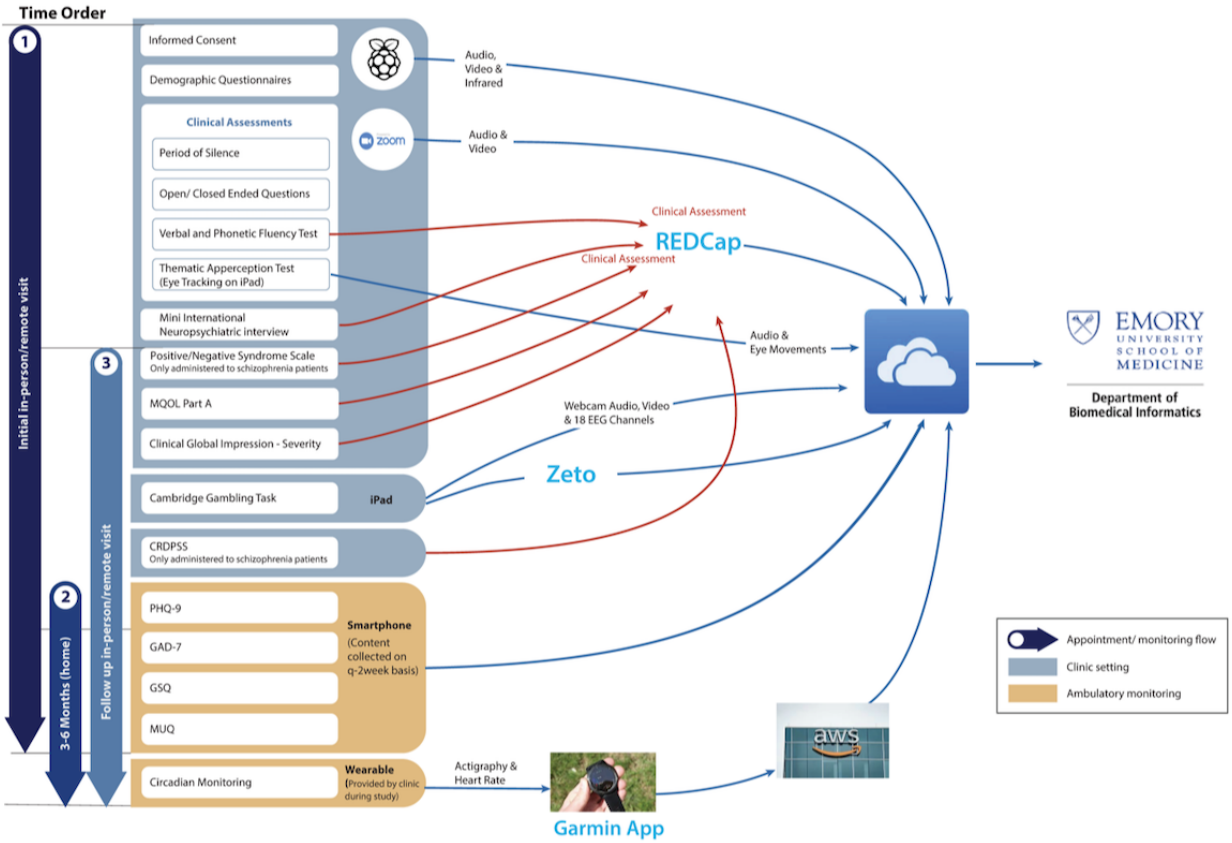
Procedure

All participant groups will be recruited (1) from a database of interested research participants from prior research studies, from clinician referrals, and from respondents to a general research interest form provided in the outpatient waiting rooms of the Grady Outpatient Behavioral Health Clinic; (2) through a regional digital recruitment strategy, part of ResearchMatch (of which Emory University is an institutional participant), that will target the metro Atlanta area for in-person interviews and the entire United States for remote or telehealth interviews; and (3) through a digital recruitment strategy based on Amazon Mechanical Turk (Amazon Inc) in which individuals that respond to a short questionnaire will be able to reach out to the study team via email if they are interested in participating in the study.

The schizophrenia and control groups that participate in person will be interviewed at 2 time points (the initial encounter and a second encounter, 3 to 6 months after the initial encounter) for all measures, as indicated below. Figure 1 shows a schematic of the initial interview data collection process. The depression, schizophrenia, and control groups that participate remotely will only be interviewed at baseline and will not have a follow-up assessment for any of the measures indicated below. Given the established need for continuous assessment of heart rate variability and locomotor activity to adequately discriminate patients with schizophrenia from controls [28], all in-person (schizophrenia and control) outpatient populations will be assessed for heart rate variability and locomotor activity for the 3 months leading up to second appointment. This study involves the collection of video, voice and speech, actigraphic, pulse oximetry, heart rate, EEG, questionnaire, interview, and available clinical data only.

Figure 1. Initial interview data collection process. MQOL Part A: McGill Quality of Life Questionnaire-Revised Part A; CRDPSS: Clinician-Rated Dimensions of Psychosis Symptom Severity in Patients with Schizophrenia; PHQ-9: Patient Health Questionnaire-9; GAD-7: General Anxiety Disorder-7; GSQ: General Symptom Questionnaire; MUQ: Medication Utilization Questionnaire; EEG: electroencephalogram.



All assessments will take place over Zoom (Zoom Inc), a secure, encrypted, telehealth platform that is compliant with the Health Insurance Portability and Accountability Act of 1996 (HIPAA). In-person assessments will consist of an interviewer conducting an interview via Zoom on a computer, with the participant on a different computer located in an adjacent room in the research suite. For remote assessments, the interviewer will be physically located at the research suite and the participant will be on their own computer at the location of their choice (usually their home). Due to the COVID-19 pandemic, assessments will be conducted in person when local case counts are low and the research team is safely able to complete interviews with social distancing measures in place and appropriate personal protective equipment (PPE).

In-person participants will be interviewed twice, 3 to 6 months apart, and offered a US $30 honorarium at the completion of study visit 1 and a US $30 honorarium at the completion of study visit 2. Between visits the participants may complete a battery of assessments offered every 2 weeks on their devices, for which they will be compensated US $5 for each battery. Remote participants will be interviewed once and offered a US

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$30 honorarium at the completion of the study visit. Individuals who participate in the study but are unable to complete it will be offered a US $10 honorarium. Those subjects screened and determined to not meet the eligibility criteria will not be offered compensation.

Ethics Approval

The study was approved by the Emory University Institutional Review Board in November 2018 (IRB00105142) and the Grady Research Oversight Committee in January 2019 (00-105142).

Measures

The schedule of assessments is found in Table 1 for the in-person assessments and Table 2 for the remote assessments. For subjects with schizophrenia in ambulatory treatment, monitoring will occur in one of two ways: the subjects will be evaluated at the initial encounter and 3 months after the initial encounter in person, or they will be evaluated remotely once via Zoom.

Table 1. Schedule of assessments for in-person visits.

Assessments	Visit 1	Biweekly[a]	Visit 2 (3-6 months)[a]
Informed consent	✓		
Semistructured interview	✓		✓
Demographic assessment	✓		
Sociodemographic assessment	✓		
Mini International Neuropsychiatric Interview	✓		
Positive and Negative Syndrome Scale[b]	✓		✓
McGill Quality of Life Questionnaire-Revised Part A	✓		✓
Clinician-Rated Dimensions of Psychosis Symptom Severity in Patients with Schizophrenia[b]	✓		✓
Clinical Global Impression-Severity	✓		✓
Clinical Global Impression-Improvement			✓
Cambridge Gambling Task[a,c]	✓		✓
Patient Health Questionnaire-9[d]	✓	✓	✓
Generalized Anxiety Disorder-7[d]	✓	✓	✓
General Symptom Questionnaire[a,d]	✓	✓	✓
Medication Utilization Questionnaire[a,d]	✓	✓	✓
Facial expressivity and eye gaze	✓		✓
Voice and speech data collection	✓		✓
Electroencephalography[a,c]	✓		✓
Actigraphy and heart rate (continuous)[a,c]	✓	✓	✓

[a]Depression group excluded.

[b]Only administered for schizophrenia group.

[c]Only for in-person visits (ie, excluding subjects who were recruited digitally).

[d]Completed on participant devices for the schizophrenia and control groups only.

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Table 2. Schedule of assessments for remote visits.

Assessments	Visit 1
Informed consent	✓
Semistructured interview	✓
Demographic assessment	✓
Sociodemographic assessment	✓
Mini International Neuropsychiatric Interview	✓
Positive and Negative Syndrome Scale[a]	✓
McGill Quality of Life Questionnaire-Revised Part A	✓
Clinician-Rated Dimensions of Psychosis Symptom Severity in Patients with Schizophrenia[a]	✓
Clinical Global Impression-Severity	✓
Patient Health Questionnaire-9	✓
General Anxiety Disorder-7	✓
Facial expressivity and eye gaze	✓
Voice and speech data collection	✓

[a]Only administered for schizophrenia group.

The initial assessment will include demographic and clinical information that will be collected via self-reporting. Clinical information will include information about self-reported psychiatric and medical comorbidities and current medications. The evaluations will include a clinical record review; a battery of psychometric tests, including a semistructured group developed interview that will include the Thematic Apperception Test (TAT) [58], the Semantic Fluency Task [59], and the Phonetic Fluency Task [60] (more details are available in Multimedia Appendix 1); and demographic and sociodemographic questionnaires, including the MINI, the McGill Quality of Life Questionnaire-Revised Part A (MQOL Part A) [61], the Clinical Global Impression Severity (CGI-S) and Clinical Global Impression Improvement (CGI-I) scales (in-person only) [54], PHQ-9 [53], the General Anxiety Disorder-7 (GAD-7) [62], and the Cambridge Gambling Task (CGT) (in-person only) [63,64]. The evaluations will also include audiovisual recordings, and the in-person evaluations will include pulse oximetry recordings taken during the entirety of the interview and electroencephalographic recordings taken during selected points of the interview, including the CGT. Actigraphy and heart rate recordings will be assessed for the 3-month period between the patient interviews for applicable participants. Only subjects with schizophrenia will receive the PANSS and CRDPSS. Further description of the rating scales used in the study can be found in Multimedia Appendix 1.

Depression subjects will only be evaluated once. The evaluations will include a clinical record review; a battery of psychometric tests, including a semistructured group developed interview; and demographic and sociodemographic questionnaires, including the MINI, MQOL Part A, CGI-S, PHQ-9, GAD-7, and CGT (in-person only). The evaluations will also include audiovisual recordings, and in-person evaluations will include pulse oximetry and electroencephalographic recordings.

For control subjects, monitoring will occur in one of two ways: the subjects will be evaluated at the initial encounter and 3 months after initial encounter in person, or they will be evaluated remotely once via Zoom. Evaluation will include clinical record review; a battery of psychometric tests, including a semistructured group developed interview; and demographic and sociodemographic questionnaires, including the MINI, MQOL Part A, CGI-S, PHQ-9, GAD-7, and CGT (in-person only). Audiovisual, pulse oximetry (in-person only), and electroencephalographic recording (in-person only) will be performed for the entirety of the interview and actigraphy and heart rate recording will be assessed for the 3-month period between interviews for applicable patients. All evaluations will be conducted in person during times when visits can be completed safely with social distancing measures and appropriate PPE use; otherwise, they will be conducted remotely via Zoom.

Statistical Analysis, Model Development, and Data Integration

The data will undergo a descriptive statistical analysis and assessment of classifier and regressor capacity to predict diagnostic and psychometric scores, respectively. Descriptive statistical assessment of the collected data will be conducted. Diagnostic and psychometric score prediction will be conducted utilizing extracted features from the collected data. Sample data descriptions including demographics, clinical diagnosis, and psychometric scores will be analyzed. Cross-group variations in psychometric scores will be reported and analyzed via inferential statistical methods (2-way *t* testing).

Recordings of the interviews will be captured using Zoom at various resolutions, depending on the interviewee's camera and network conditions. The participants will be asked to sit close enough to the camera that the interviewer can clearly see their face, with a minimum of 10% of the participant's face filling the viewable screen. Three different simultaneous audio files

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will be generated, corresponding to the bidirectional conversation, the interviewee only, and the interviewer only. This separation will enable the research team to isolate the individual speaker, and also to evaluate how the system might work in a single-microphone environment.

Video analysis of the full face involves both the dynamics of facial action units [65,66], and full-face emotion interpretation using a deep convolutional neural network. We will follow our earlier work [67] and use an extensive pretrained network to identify the amount of time spent in 1 of 7 basic emotions (including neutrality, happiness, surprise, anger, sadness, fear, and disgust), and then use transfer learning to retrain the network on the new subjects using severity of depression or schizophrenia as a new target.

The audio will be analyzed in several ways. First, we will compare the outputs of two HIPAA-compliant commercial services for transcription of the audio recordings: the Otter.ai (Otter.ai Inc) service through Zoom's transcription service and Amazon Transcribe (Amazon Inc). At the time of writing, no information on the performance of Otter.ai is available publicly. Amazon Transcribe has been shown to have word error rates of 10% to 20%, with small biases for gender and medical condition [68]. We will match the separate and combined transcripts for each service and compare a subsample to expert overreads to identify error rates. Natural language tools, such as the Linguistic Inquiry and Word Count dictionary [69], Word2Vec [70], and other related natural language processing tools [71-73] will be used to associate word- and sentence-level features with severity of depression or schizophrenia. These tools will be utilized throughout the interview and specifically for certain elements of the semistructured group developed interviews, including the TAT, the Semantic Fluency Task, and the Phonetic Fluency Task. Natural language processing measures analyzed from the TAT have been used to discriminate between patients with a first episode of psychosis and controls [74]; generally, semantic verbal fluency is more affected than phonemic fluency in schizophrenia [75,76]. We will also test the performance as a function of the transcription error rate. The nonsemantic content of the speech will be determined from the pitch, relative temporal ordering, duration information, and the dynamics of the audio recordings [25]. Here, statistical analysis, standard machine learning (eg, random forests), and deep neural networks will be utilized.

EEG recordings will be made using noninvasive scalp leads attached during the CGT [64,77] and baseline measurements. After the EEG device is in place and immediately prior to the CGT, the participant will undergo a 1-minute evaluation in a restful, eyes-open state. Following this, the participant will undergo an additional 1-minute evaluation in a restful, eyes-closed state. EEG recordings will be conducted only during in-person visits. The EEG analysis will involve standard approaches, such as EEG band–related signal (delta, theta, alpha, and beta) analysis [78] and state-of-the-art deep neural network analysis [79,80]. Different statistical descriptors, Hjorth parameters [81], and synchrony [82] will be analyzed for the EEG band–related signals. The recurrent neural networks [83,84] will be utilized for capturing the dynamical properties of the EEG signal. The heart rate and the actigraphy data recorded from the wearable devices will be analyzed with the multiscale network analysis developed in Reinertsen et al [85].

As described above and shown in Figure 1, data from all modalities will be captured, stored, and processed in HIPAA-compliant environments. More specifically, all the data will be stored in Emory University's OneDrive server (Microsoft Corp) and will be processed in the high-performance computing cluster located in the Department of Biomedical Informatics at Emory University. Access to the identifiable personal data will be limited to the personnel approved by the institutional review board at Emory University.

In addition to the feature extraction and analyses within each modality, we aim to investigate the interaction between features from different modalities and fuse them together to build a multimodal machine learning model to estimate the presence and the severity of depression and schizophrenia. For interaction, we will check the Pearson correlations between features and between the predictions made with features from each single modality. Additionally, we will use dynamic time warping and general dynamic time warping [86] to check the similarity and alignment between time series of features from different modalities. For integration, we will use both model-agnostic and model-based approaches. For instance, we will test late fusion of the predicted results using features from each modality and early direct fusion of the features extracted from all modalities. We will also use temporal models, such as multi-view long short-term memory networks [87] and multimodal transformers [88].

Results

Data collection began in July 2020 and is expected to continue through December 2022. We present some preliminary data here, highlighting a comparison of the fluctuation of emotions using computer vision. Figure 2 visualizes the level of neutrality, happiness, surprise, anger, sadness, fear, and disgust of a patient with schizophrenia (on the left) versus a control (on the right) during the interview. Distinct differences could be found between these 2 participants, including the average strength and average length of different emotions and how fast they switched between emotions. In the case of these 2 participants, the patient with schizophrenia was found to have a longer duration of neutrality, shorter duration of happiness, and a faster change between emotions. Statistical tests need to be performed on the final, larger groups to provide concrete evidence on whether there indeed exist group-level differences.

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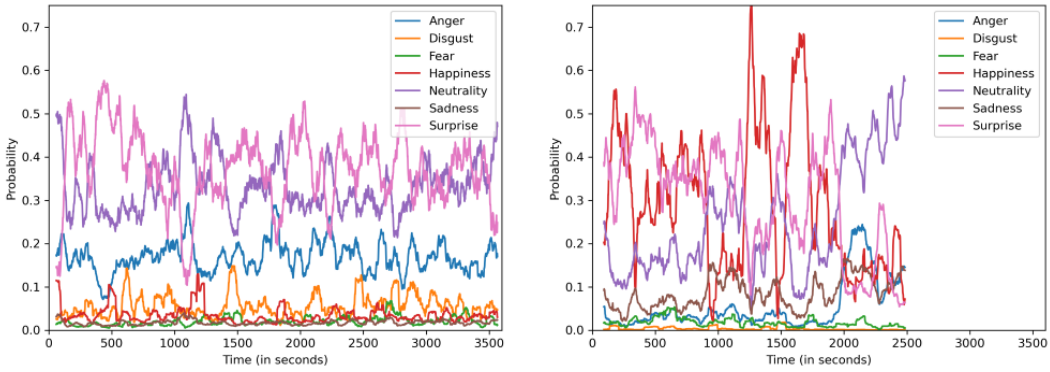
Figure 2. Measures of facial expression when comparing a patient with schizophrenia (left) to a control subject (right).



Discussion

This study aims to advance current progress in the use of state-of-the-art technology for assisting clinical psychiatric assessments by using a novel multimodal sensing system.

Strengths

The in-person recruitment site, Grady Health System, allows access to a racially and ethnically diverse group of potential participants. Furthermore, the study methods will allow for data collection to continue irrespective of local case fluctuations in COVID-19 infection rates. The study team will be able to recruit and evaluate participants in person or pivot to virtual recruitment and data collection using a national recruitment database.

Limitations

This study has a number of limitations. Larger data sets will be needed and the model will need to be prospectively validated. Additionally, remote participation is only available to those who have access to the internet, a video camera, and a microphone. The quality of these recordings is subject to variation based upon the devices accessible to the participants and the areas where they are located, which may impact the quality of the recordings and limit recruitment efforts. The protocol has provided an option for subjects to participate in person, which will allow the study team to better standardize the technology used. However, there may be differences between subjects who participate in their homes and those who travel to the research site to complete the interviews. The research site will provide a private room to complete the Zoom interview and will mimic, as much as possible, the environment of those participating remotely from their homes. Furthermore, the interviewers may be at risk of bias in their ratings, and their physical presence or absence may affect patient responses. All assessments will be recorded, which will allow for the verification of all ratings by the interviewers and the study psychiatrist. The interviewers will also follow a script to maintain as much between-subject consistency in the interviews as possible.

Conclusions

If our findings suggest that these technologies are capable of resolving diagnoses and revealing symptoms at the same level as current psychometric testing and clinician judgment, we will be among the first in the world to have developed a clinical decision support system that can be used by expert and nonexpert clinicians for objectively diagnosing and tracking schizophrenia and depression over time. Such a tool would improve accessibility to care; aid clinicians in objectively evaluating diagnoses, severity of symptoms, and treatment efficacy; reduce treatment-related morbidity; and potentially empower patients to gain a deeper insight into their day-to-day symptoms and stressors to guide self-management.

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Data Availability

The data sets generated during or analyzed during the current study will not be publicly available because they contain protected health information, but deidentified subsets of the data will be made available from the corresponding author on reasonable request, if the resources to perform and validate the deidentification process are available.

Conflicts of Interest

ROC received institutional research funding from Alkermes, Roche, and Otsuka and is a consultant to Saladax Biomedical and the American Psychiatric Association. The remaining authors declare no conflicts of interest.

Multimedia Appendix 1
Supplemental Materials.

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References

1. GBD 2019 Diseases and Injuries Collaborators. Global burden of 369 diseases and injuries in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet 2020 Oct 17;396(10258):1204-1222 [FREE Full text] [doi: 10.1016/S0140-6736(20)30925-9] [Medline: 33069326]
2. GBD 2019 Mental Disorders Collaborators. Global, regional, and national burden of 12 mental disorders in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet Psychiatry 2022 Feb;9(2):137-150 [FREE Full text] [doi: 10.1016/S2215-0366(21)00395-3] [Medline: 35026139]
3. Solanki R, Singh P, Midha A, Chugh K. Schizophrenia: Impact on quality of life. Indian J Psychiatry 2008 Jul;50(3):181-186 [FREE Full text] [doi: 10.4103/0019-5545.43632] [Medline: 19742235]
4. Hjorthøj C, Stürup AE, McGrath JJ, Nordentoft M. Years of potential life lost and life expectancy in schizophrenia: a systematic review and meta-analysis. Lancet Psychiatry 2017 Apr;4(4):295-301. [doi: 10.1016/S2215-0366(17)30078-0] [Medline: 28237639]
5. Olfson M, Gerhard T, Huang C, Crystal S, Stroup TS. Premature Mortality Among Adults With Schizophrenia in the United States. JAMA Psychiatry 2015 Dec 01;72(12):1172-1181. [doi: 10.1001/jamapsychiatry.2015.1737] [Medline: 26509694]
6. Barbato A. Schizophrenia and public health. World Health Organization. 1997. URL: https://apps.who.int/iris/bitstream/handle/10665/63837/WHO_MSA_NAM_97.6.pdf [accessed 2022-06-07]
7. Cloutier M, Aigbogun MS, Guerin A, Nitulescu R, Ramanakumar AV, Kamat SA, et al. The Economic Burden of Schizophrenia in the United States in 2013. J Clin Psychiatry 2016 Jun;77(6):764-771. [doi: 10.4088/JCP.15m10278] [Medline: 27135986]
8. Greenberg PE, Fournier A, Sisitsky T, Pike CT, Kessler RC. The economic burden of adults with major depressive disorder in the United States (2005 and 2010). J Clin Psychiatry 2015 Feb;76(2):155-162 [FREE Full text] [doi: 10.4088/JCP.14m09298] [Medline: 25742202]
9. National Health Expenditure Data: Historical 2017. Center For Medicare and Medicaid Services. URL: https://tinyurl.com/ye2yj77v [accessed 2022-06-07]
10. Kraus C, Kadriu B, Lanzenberger R, Zarate CA, Kasper S. Prognosis and improved outcomes in major depression: a review. Transl Psychiatry 2019 Apr 03;9(1):127 [FREE Full text] [doi: 10.1038/s41398-019-0460-3] [Medline: 30944309]
11. Wyatt RJ, Henter ID. The effects of early and sustained intervention on the long-term morbidity of schizophrenia. J Psychiatr Res 1998;32(3-4):169-177 [FREE Full text] [doi: 10.1016/s0022-3956(97)00014-9] [Medline: 9793870]
12. Albert N, Melau M, Jensen H, Hastrup LH, Hjorthøj C, Nordentoft M. The effect of duration of untreated psychosis and treatment delay on the outcomes of prolonged early intervention in psychotic disorders. NPJ Schizophr 2017 Sep 26;3(1):34 [FREE Full text] [doi: 10.1038/s41537-017-0034-4] [Medline: 28951544]
13. Kane JM, Robinson DG, Schooler NR, Mueser KT, Penn DL, Rosenheck RA, et al. Comprehensive Versus Usual Community Care for First-Episode Psychosis: 2-Year Outcomes From the NIMH RAISE Early Treatment Program. Am J Psychiatry 2016 Apr 01;173(4):362-372 [FREE Full text] [doi: 10.1176/appi.ajp.2015.15050632] [Medline: 26481174]
14. Howes OD, Whitehurst T, Shatalina E, Townsend L, Onwordi EC, Mak TLA, et al. The clinical significance of duration of untreated psychosis: an umbrella review and random-effects meta-analysis. World Psychiatry 2021 Feb 12;20(1):75-95 [FREE Full text] [doi: 10.1002/wps.20822] [Medline: 33432766]
15. Addington J, Heinssen RK, Robinson DG, Schooler NR, Marcy P, Brunette MF, et al. Duration of Untreated Psychosis in Community Treatment Settings in the United States. Psychiatr Serv 2015 Jul;66(7):753-756. [doi: 10.1176/appi.ps.201400124] [Medline: 25588418]
16. Psychosis and schizophrenia in adults: prevention and management. National Institute for Health and Care Excellence. URL: https://www.nice.org.uk/guidance/cg178
17. Birchwood M, Connor C, Lester H, Patterson P, Freemantle N, Marshall M, et al. Reducing duration of untreated psychosis: care pathways to early intervention in psychosis services. Br J Psychiatry 2013 Jul 02;203(1):58-64. [doi: 10.1192/bjp.bp.112.125500] [Medline: 23703317]
18. Mental Health In America - Access to Care Data 2018. Mental Health America. URL: https://www.mhanational.org/issues/mental-health-america-access-care-data-2018 [accessed 2022-06-09]
19. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, 5th ed. Washington, DC: American Psychiatric Association; 2013.
20. World Health Organization. ICD-10: International statistical classification of diseases and related health problems, tenth revision. Geneva, Switzerland: World Health Organization; 2004.
21. Ramirez Basco M, Bostic JQ, Davies D, Rush AJ, Witte B, Hendrickse W, et al. Methods to improve diagnostic accuracy in a community mental health setting. Am J Psychiatry 2000 Oct;157(10):1599-1605. [doi: 10.1176/appi.ajp.157.10.1599] [Medline: 11007713]
22. Lieberman JA, Fenton WS. Delayed detection of psychosis: causes, consequences, and effect on public health. Am J Psychiatry 2000 Nov;157(11):1727-1730. [doi: 10.1176/appi.ajp.157.11.1727] [Medline: 11058464]

XSL•FO
RenderX

23. Behavioral Health Workforce Projections, 2017-2030. Health Resources and Services Administration. URL: https://bhw.hrsa.gov/sites/default/files/bureau-health-workforce/data-research/bh-workforce-projections-fact-sheet.pdf [accessed 2022-06-07]
24. Wittchen H, Mühlig S, Beesdo K. Mental disorders in primary care. Dialogues Clin Neurosci 2003 Jun;5(2):115-128 [FREE Full text] [doi: 10.31887/DCNS.2003.5.2/huwittchen] [Medline: 22034245]
25. Harati S, Crowell A, Mayberg H, Jun Kong, Nemati S. Discriminating clinical phases of recovery from major depressive disorder using the dynamics of facial expression. Annu Int Conf IEEE Eng Med Biol Soc 2016 Aug;2016:2254-2257. [doi: 10.1109/EMBC.2016.7591178] [Medline: 28268777]
26. Crowell A, Harati S, Nemati S, Mayberg H. Quantification of Subjective Intraoperative Response to Deep Brain Stimulation of the Subcallosal Cingulate Using Facial Dynamics. Biol Psychiatry 2017 May;81(10):S334. [doi: 10.1016/j.biopsych.2017.02.890]
27. Jiang Z, Luskus M, Seyedi S, Griner EL, Rad AB, Clifford GD, et al. Utilizing computer vision for facial behavior analysis in schizophrenia studies: A systematic review. PLoS One 2022 Apr 8;17(4):e0266828 [FREE Full text] [doi: 10.1371/journal.pone.0266828] [Medline: 35395049]
28. Reinertsen E, Osipov M, Liu C, Kane JM, Petrides G, Clifford GD. Continuous assessment of schizophrenia using heart rate and accelerometer data. Physiol Meas 2017 Jun 27;38(7):1456-1471 [FREE Full text] [doi: 10.1088/1361-6579/aa724d] [Medline: 28653659]
29. Osipov M, Behzadi Y, Kane JM, Petrides G, Clifford GD. Objective identification and analysis of physiological and behavioral signs of schizophrenia. J Ment Health 2015 Jul 20;24(5):276-282 [FREE Full text] [doi: 10.3109/09638237.2015.1019048] [Medline: 26193048]
30. Reinertsen E, Nemati S, Vest AN, Vaccarino V, Lampert R, Shah AJ, et al. Heart rate-based window segmentation improves accuracy of classifying posttraumatic stress disorder using heart rate variability measures. Physiol Meas 2017 Jun 10;38(6):1061-1076 [FREE Full text] [doi: 10.1088/1361-6579/aa6e9c] [Medline: 28489609]
31. Jiang Z, Seyedi S, Haque RU, Pongos AL, Vickers KL, Manzanares CM, et al. Automated analysis of facial emotions in subjects with cognitive impairment. PLoS One 2022 Jan 21;17(1):e0262527 [FREE Full text] [doi: 10.1371/journal.pone.0262527] [Medline: 35061824]
32. Tron T, Peled A, Grinsphoon A, Weinshall D. Facial expressions and flat affect in schizophrenia, automatic analysis from depth camera data. 2016 Presented at: IEEE-EMBS International Conference on Biomedical and Health Informatics; Feb 24-27, 2016; Las Vegas, NV p. 24-27. [doi: 10.1109/bhi.2016.7455874]
33. Bishay M, Palasek P, Priebe S, Patras I. SchiNet: Automatic Estimation of Symptoms of Schizophrenia from Facial Behaviour Analysis. IEEE Trans Affective Comput 2021 Oct 1;12(4):949-961. [doi: 10.1109/taffc.2019.2907628]
34. Tron T, Peled A, Grinsphoon A, Weinshall D. Automated Facial Expressions Analysis. In: Schizophrenia: A Continuous Dynamic Approach. Cham, Switzerland: Springer; 2016.
35. Vijay S, Baltrusaitis T, Pennant L, Ongur D, Baker J, Morency L. Computational study of psychosis symptoms and facial expressions. Carnegie Mellon University. URL: http://multicomp.cs.cmu.edu/wp-content/uploads/2017/09/2016_CMHW_vijay_computational.pdf [accessed 2022-06-09]
36. Vail A, Baltrusaitis T, Pennant L, Liebson E, Baker J, Morency L. Visual attention in schizophrenia: Eye contact and gaze aversion during clinical interactions. 2017 Presented at: 2017 Seventh International Conference on Affective Computing and Intelligent Interaction (ACII); Oct 23-26, 2017; San Antonio, TX URL: https://ieeexplore.ieee.org/document/8273644 [doi: 10.1109/acii.2017.8273644]
37. Tron T, Resheff Y, Bazhmin M, Peled A, Weinshall D. Real-time schizophrenia monitoring using wearable motion sensitive devices. 2017 Presented at: 7th EAI International Conference on Wireless Mobile Communication and Healthcare (MobiHealth); Nov 14-15, 2017; Vienna, Austria URL: https://link.springer.com/chapter/10.1007/978-3-319-98551-0_28 [doi: 10.1007/978-3-319-98551-0_28]
38. Tron T, Resheff Y, Bazhmin M, Weinshall D, Peled A. ARIMA-based motor anomaly detection in schizophrenia inpatients. 2018 Presented at: 2018 IEEE EMBS International Conference on Biomedical & Health Informatics (BHI); March 4-7, 2018; Las Vegas, NV. [doi: 10.1109/bhi.2018.8333460]
39. Tron T, Resheff Y, Bazhmin M, Peled A, Grinsphoon A, Weinshall D. Topic models for automated motor analysis in schizophrenia patients. 2018 Presented at: 2018 IEEE 15th International Conference on Wearable and Implantable Body Sensor Networks; March 4-7, 2018; Las Vegas, NV. [doi: 10.1109/bsn.2018.8329678]
40. Parola A, Simonsen A, Bliksted V, Fusaroli R. Acoustic patterns in schizophrenia: a systematic review and meta-analysis. Schizophr Bull 2018 Apr 01;44:S169 [FREE Full text] [doi: 10.1093/schbul/sby016.414]
41. Iter D, Yoon J, Jurafsky D. Automatic Detection of Incoherent Speech for Diagnosing Schizophrenia. In: Proceedings of the Fifth Workshop on Computational Linguistics and Clinical Psychology: From Keyboard to Clinic.: Association for Computational Linguistics; 2018 Presented at: Fifth Workshop on Computational Linguistics and Clinical Psychology: From Keyboard to Clinic; Jun 5, 2018; New Orleans, LA p. 136-146. [doi: 10.18653/v1/w18-0615]
42. Bedi G, Carrillo F, Cecchi GA, Slezak DF, Sigman M, Mota NB, et al. Automated analysis of free speech predicts psychosis onset in high-risk youths. NPJ Schizophr 2015;1:15030 [FREE Full text] [doi: 10.1038/npjschz.2015.30] [Medline: 27336038]

XSL•FO
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43. Dvey-Aharon Z, Fogelson N, Peled A, Intrator N. Schizophrenia detection and classification by advanced analysis of EEG recordings using a single electrode approach. PLoS One 2015;10(4):e0123033 [FREE Full text] [doi: 10.1371/journal.pone.0123033] [Medline: 25837521]
44. Acharya UR, Sudarshan VK, Adeli H, Santhosh J, Koh JE, Adeli A. Computer-Aided Diagnosis of Depression Using EEG Signals. Eur Neurol 2015;73(5-6):329-336 [FREE Full text] [doi: 10.1159/000381950] [Medline: 25997732]
45. Acharya UR, Sudarshan VK, Adeli H, Santhosh J, Koh JE, Puthankatti SD, et al. A Novel Depression Diagnosis Index Using Nonlinear Features in EEG Signals. Eur Neurol 2015;74(1-2):79-83. [doi: 10.1159/000438457] [Medline: 26303033]
46. Cai H, Han J, Chen Y, Sha X, Wang Z, Hu B, et al. A Pervasive Approach to EEG-Based Depression Detection. Complexity 2018;2018:1-13 [FREE Full text] [doi: 10.1155/2018/5238028]
47. Seal A, Bajpai R, Agnihotri J, Yazidi A, Herrera-Viedma E, Krejcar O. DeprNet: A Deep Convolution Neural Network Framework for Detecting Depression Using EEG. IEEE Trans Instrum Meas 2021;70:1-13. [doi: 10.1109/tim.2021.3053999]
48. Acharya UR, Oh SL, Hagiwara Y, Tan JH, Adeli H, Subha DP. Automated EEG-based screening of depression using deep convolutional neural network. Comput Methods Programs Biomed 2018 Jul;161:103-113. [doi: 10.1016/j.cmpb.2018.04.012] [Medline: 29852953]
49. Goldsmith DR, Crooks CL, Walker EF, Cotes RO. An Update on Promising Biomarkers in Schizophrenia. Focus (Am Psychiatr Publ) 2018 Apr;16(2):153-163 [FREE Full text] [doi: 10.1176/appi.focus.20170046] [Medline: 31975910]
50. Olmert T, Cooper JD, Han SYS, Barton-Owen G, Farrag L, Bell E, et al. A Combined Digital and Biomarker Diagnostic Aid for Mood Disorders (the Delta Trial): Protocol for an Observational Study. JMIR Res Protoc 2020 Aug 10;9(8):e18453 [FREE Full text] [doi: 10.2196/18453] [Medline: 32773373]
51. Rykov Y, Thach T, Bojic I, Christopoulos G, Car J. Digital Biomarkers for Depression Screening With Wearable Devices: Cross-sectional Study With Machine Learning Modeling. JMIR Mhealth Uhealth 2021 Oct 25;9(10):e24872 [FREE Full text] [doi: 10.2196/24872] [Medline: 34694233]
52. Cho C, Lee T, Kim M, In HP, Kim L, Lee H. Mood Prediction of Patients With Mood Disorders by Machine Learning Using Passive Digital Phenotypes Based on the Circadian Rhythm: Prospective Observational Cohort Study. J Med Internet Res 2019 Apr 17;21(4):e11029 [FREE Full text] [doi: 10.2196/11029] [Medline: 30994461]
53. Kroenke K, Spitzer RL, Williams JBW. The PHQ-9: validity of a brief depression severity measure. J Gen Intern Med 2001 Sep;16(9):606-613 [FREE Full text] [doi: 10.1046/j.1525-1497.2001.016009606.x] [Medline: 11556941]
54. Guy W. ECDEU assessment manual for psychopharmacology. Rockville, MD: US Department of Health, Education, and Welfare; 1976.
55. Kay SR, Fiszbein A, Opler LA. The positive and negative syndrome scale (PANSS) for schizophrenia. Schizophr Bull 1987;13(2):261-276. [doi: 10.1093/schbul/13.2.261] [Medline: 3616518]
56. Park S, Lee KU, Choi J. Factor Structure of the Clinician-Rated Dimensions of Psychosis Symptom Severity in Patients with Schizophrenia. Psychiatry Investig 2016 Mar;13(2):253-254 [FREE Full text] [doi: 10.4306/pi.2016.13.2.253] [Medline: 27081390]
57. Sheehan D, Lecrubier Y, Sheehan K, Amorim P, Janavs J, Weiller E, et al. The Mini-International Neuropsychiatric Interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. J Clin Psychiatry 1998;59 Suppl 20:22-33;quiz 34. [Medline: 9881538]
58. Moretti R, Rossini E. The Thematic Apperception Test (TAT). In: Hilsenroth MJ, Segal DL, Hersen M, editors. Comprehensive handbook of psychological assessment, Vol 2: Personality assessment. Hoboken, NJ: John Wiley & Sons; 2004:356-371.
59. Goodglass H, Kaplan E. The assessment of aphasia and related disorders. Philadelphia, PA: Lea & Febiger; 1972.
60. Benton A, Hamsher K, Sivan A. Multilingual aphasia examination. Iowa City, IA: AJA Associates; 1994.
61. Cohen SR, Sawatzky R, Russell LB, Shahidi J, Heyland DK, Gadermann AM. Measuring the quality of life of people at the end of life: The McGill Quality of Life Questionnaire-Revised. Palliat Med 2017 Feb;31(2):120-129. [doi: 10.1177/0269216316659603] [Medline: 27412257]
62. Spitzer RL, Kroenke K, Williams JBW, Löwe B. A brief measure for assessing generalized anxiety disorder: the GAD-7. Arch Intern Med 2006 May 22;166(10):1092-1097. [doi: 10.1001/archinte.166.10.1092] [Medline: 16717171]
63. Rogers RD, Owen AM, Middleton HC, Williams EJ, Pickard JD, Sahakian BJ, et al. Choosing between small, likely rewards and large, unlikely rewards activates inferior and orbital prefrontal cortex. J Neurosci 1999 Oct 15;19(20):9029-9038 [FREE Full text] [Medline: 10516320]
64. Rogers R, Everitt B, Baldacchino A, Blackshaw A, Swainson R, Wynne K, et al. Dissociable deficits in the decision-making cognition of chronic amphetamine abusers, opiate abusers, patients with focal damage to prefrontal cortex, and tryptophan-depleted normal volunteers: evidence for monoaminergic mechanisms. Neuropsychopharmacology 1999 Apr;20(4):322-339. [doi: 10.1016/S0893-133X(98)00091-8] [Medline: 10088133]
65. Ekman P, Friesen WV. Measuring facial movement. Environ psychol nonverbal behav 1976;1(1):56-75. [doi: 10.1007/bf01115465]
66. Ekman P, Friesen WV. Facial action coding system. American Psychological Association. 1978. URL: https://psycnet.apa.org/doiLanding?doi=10.1037%2Ft27734-000 [accessed 2022-06-10]

XSL•FO
RenderX

67. Jiang Z, Harati S, Crowell A, Mayberg HS, Nemati S, Clifford GD. Classifying Major Depressive Disorder and Response to Deep Brain Stimulation Over Time by Analyzing Facial Expressions. IEEE Trans Biomed Eng 2021 Feb;68(2):664-672. [doi: 10.1109/tbme.2020.3010472]
68. Schultz BG, Tarigoppula VSA, Noffs G, Rojas S, van der Walt A, Grayden DB, et al. Automatic speech recognition in neurodegenerative disease. Int J Speech Technol 2021 May 04;24(3):771-779 [FREE Full text] [doi: 10.1007/s10772-021-09836-w]
69. Pennebaker JW, Booth RJ, Boyd RL, Francis ME. Linguistic Inquiry Word Count: LIWC2015. 2015. URL: https://s3-us-west-2.amazonaws.com/downloads.liwc.net/LIWC2015_OperatorManual.pdf [accessed 2022-06-07]
70. Mikolov T, Chen K, Corrado G, Dean J. Efficient estimation of word representations in vector space. ArXiv. Preprint posted online on Jan 16, 2013 2022:1-12.
71. Straw I, Callison-Burch C. Artificial Intelligence in mental health and the biases of language based models. PLoS One 2020;15(12):e0240376 [FREE Full text] [doi: 10.1371/journal.pone.0240376] [Medline: 33332380]
72. De Choudhury M, De S. Mental Health Discourse on Reddit: Self-Disclosure, Social Support, and Anonymity. In: Proceedings of the International AAAI Conference on Web and Social Media. 2014 Presented at: International AAAI Conference on Web and Social Media; Jun 1-4, 2014; Ann Arbor, MI p. 71-80 URL: https://ojs.aaai.org/index.php/ICWSM/article/view/14526
73. De Choudhury M, Gamon M, Counts S, Horvitz E. Predicting Depression via Social Media. In: Proceedings of the International AAAI Conference on Web and Social Media. 2013 Presented at: International AAAI Conference on Web and Social Media; Jul 8-11, 2013; Cambridge, MA p. 128-137 URL: https://ojs.aaai.org/index.php/ICWSM/article/view/14432
74. Morgan SE, Diederen K, Vértes PE, Ip SHY, Wang B, Thompson B, et al. Natural Language Processing markers in first episode psychosis and people at clinical high-risk. Transl Psychiatry 2021 Dec 13;11(1):630 [FREE Full text] [doi: 10.1038/s41398-021-01722-y] [Medline: 34903724]
75. Szöke A, Trandafir A, Dupont M, Méary A, Schürhoff F, Leboyer M. Longitudinal studies of cognition in schizophrenia: meta-analysis. Br J Psychiatry 2008 Apr 02;192(4):248-257. [doi: 10.1192/bjp.bp.106.029009] [Medline: 18378982]
76. Henry J, Crawford J. A meta-analytic review of verbal fluency deficits in schizophrenia relative to other neurocognitive deficits. Cogn Neuropsychiatry 2005 Jan;10(1):1-33. [doi: 10.1080/13546800344000309] [Medline: 16571449]
77. Deakin J, Aitken M, Robbins T, Sahakian B. Risk taking during decision-making in normal volunteers changes with age. J Int Neuropsychol Soc 2004 Jul;10(4):590-598. [doi: 10.1017/S1355617704104104] [Medline: 15327737]
78. Newson JJ, Thiagarajan TC. EEG Frequency Bands in Psychiatric Disorders: A Review of Resting State Studies. Front Hum Neurosci 2018;12:521 [FREE Full text] [doi: 10.3389/fnhum.2018.00521] [Medline: 30687041]
79. de Bardeci M, Ip CT, Olbrich S. Deep learning applied to electroencephalogram data in mental disorders: A systematic review. Biol Psychol 2021 May;162:108117 [FREE Full text] [doi: 10.1016/j.biopsycho.2021.108117] [Medline: 33991592]
80. Sun J, Cao R, Zhou M, Hussain W, Wang B, Xue J, et al. A hybrid deep neural network for classification of schizophrenia using EEG Data. Sci Rep 2021 Feb 25;11(1):4706 [FREE Full text] [doi: 10.1038/s41598-021-83350-6] [Medline: 33633134]
81. Hjorth B. EEG analysis based on time domain properties. Electroencephalogr Clin Neurophysiol 1970 Sep;29(3):306-310. [doi: 10.1016/0013-4694(70)90143-4] [Medline: 4195653]
82. Spencer KM, Nestor PG, Niznikiewicz MA, Salisbury DF, Shenton ME, McCarley RW. Abnormal neural synchrony in schizophrenia. J Neurosci 2003 Aug 13;23(19):7407-7411 [FREE Full text] [Medline: 12917376]
83. Koppe G, Toutounji H, Kirsch P, Lis S, Durstewitz D. Identifying nonlinear dynamical systems via generative recurrent neural networks with applications to fMRI. PLoS Comput Biol 2019 Aug;15(8):e1007263 [FREE Full text] [doi: 10.1371/journal.pcbi.1007263] [Medline: 31433810]
84. Guler N, Ubeyli E, Guler I. Recurrent neural networks employing Lyapunov exponents for EEG signals classification. Expert Syst Appl 2005 Oct;29(3):506-514. [doi: 10.1016/j.eswa.2005.04.011]
85. Reinertsen E, Shashikumar SP, Shah AJ, Nemati S, Clifford GD. Multiscale network dynamics between heart rate and locomotor activity are altered in schizophrenia. Physiol Meas 2018 Oct 30;39(11):115001 [FREE Full text] [doi: 10.1088/1361-6579/aae1ed] [Medline: 30222594]
86. Zhou F, De la Torre F. Generalized time warping for multi-modal alignment of human motion. 2012 Presented at: IEEE Conference on Computer Vision and Pattern Recognition; Jun 16-21, 2012; Providence, RI p. 1282-1289 URL: https://ieeexplore.ieee.org/document/6247812 [doi: 10.1109/cvpr.2012.6247812]
87. Rajagopalan S, Morency L, Baltrusaitis T, Goecke R. Extending Long Short-Term Memory for Multi-View Structured Learning. In: Leibe B, Matas J, Sebe N, Welling M, editors. Computer Vision – ECCV 2016. Cham, Switzerland: Springer; 2016:338-353.
88. Tsai Y, Bai S, Pu LP, Kolter J, Morency LP, Salakhutdinov R. Multimodal Transformer for Unaligned Multimodal Language Sequences. In: Proceedings of the 57th Annual Meeting of the Association for Computational Linguistics. 2019 Presented at: 57th Annual Meeting of the Association for Computational Linguistics; Jul 28-Aug 2, 2019; Florence, Italy p. 6558-6569. [doi: 10.18653/v1/p19-1656]

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Abbreviations

CGI-I: Clinical Global Impression-Improvement
CGI-S: Clinical Global Impression-Severity
CGT: Cambridge Gambling Task
CRDPSS: Clinician-Rated Dimensions of Psychosis Symptom Severity in Patients with Schizophrenia
DSM-5: Diagnostic and Statistical Manual of Mental Disorders
EEG: electroencephalogram
GAD-7: General Anxiety Disorder-7
GSQ: General Symptom Questionnaire
HIPAA: Health Insurance Portability and Accountability Act of 1996
MINI: Mini International Neuropsychiatric Interview
MQOL Part A: McGill Quality of Life Questionnaire-Revised Part A
MUQ: Medication Utilization Questionnaire
PANSS: Positive and Negative Syndrome Scale
PHQ-9: Patient Health Questionnaire-9
PPE: Personal Protective Equipment
TAT: Thematic Apperception Test

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Protocol

Adapting a Motivational Interviewing Intervention to Improve HIV Prevention Among Young, Black, Sexual Minority Men in Alabama: Protocol for the Development of the Kings Digital Health Intervention

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Abstract

Background: African American or Black young men who have sex with men (BYMSM) are at a disproportionate risk for contracting HIV and have high rates of undiagnosed, and therefore untreated, HIV infection. In the southern United States, BYMSM face region-specific hurdles to HIV prevention, such as limited access to care and high levels of racism and intersectional stigma, necessitating HIV testing and pre-exposure prophylaxis interventions that address sociocultural and structural barriers while motivating BYMSM to engage in prevention. Brothers Saving Brothers (BSB) is a motivational interviewing behavioral intervention that successfully and simultaneously increased community-based HIV testing and prevention counseling and education among BYMSM in the midwestern United States.

Objective: The aim of this protocol is to detail the process for the adaption of the BSB intervention for midwestern BYMSM to the Kings intervention for southern BYMSM. During the adaptation process, the intervention will be modernized to include rapid HIV testing, as opposed to HIV testing that requires BYMSM to return for test results, pre-exposure prophylaxis, and the provision of structural supports, and for relevance in the southern United States.

Methods: Aim 1 is to gather qualitative data through focus groups and in-depth interviews with BYMSM aged 18 to 29 years in Alabama and in-depth interviews with prevention and outreach workers who routinely work with BYMSM in Alabama. NVivo qualitative software (QSR International) will be used for the coding and analysis of the transcripts via a thematic analysis approach. For aim 2, intervention mapping will guide the adaptation process, intervention content, components, and design. Both aims 1 and 2 will leverage the Exploration, Preparation, Implementation, Sustainment implementation science framework, with emphasis on the exploration and preparation phases of this model. By applying these frameworks, the original midwestern BSB intervention will be scientifically adapted to the southern BYMSM Kings intervention.

Results: This study is ongoing as of 2022 and is expected to conclude in 2024, with aims 1 and 2 being completed in 2023. Qualitative data will offer insight into the current real-world experiences and preferences of BYMSM in Alabama. Feedback will

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be collected through the adaptation process to inform intervention refinement. Institutional review board approvals have been received.

Conclusions: The findings will inform next steps, that is, testing the Kings intervention for feasibility, acceptability, and preliminary effectiveness in a pilot hybrid type 1 effective-implementation randomized controlled trial. The study results will provide insights about important considerations for HIV prevention among BYMSM in the southern United States.

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International Registered Report Identifier (IRRID): PRR1-10.2196/36655

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KEYWORDS

HIV; men who have sex with men; pre-exposure prophylaxis; youth; implementation science; intervention; Alabama; African American; sociocultural; structural barriers

Introduction

Background

Over the past decade, African American or Black young men who have sex with men (BYMSM) have seen a doubling of new HIV infections [1-3]. The Centers for Disease Control and Prevention and state public health departments concur that 70% to 75% of new youth infections are linked to condomless anal sex, and these infections are concentrated among BYMSM (54.4%) [1-5]. The Centers for Disease Control and Prevention also report that BYMSM have the highest rate of undiagnosed, and therefore untreated, HIV infection [3,4,6]. Young men who have sex with men (MSM) are less likely to know their HIV status compared to older MSM [7]. The proportion of MSM who are unaware of their HIV status is highest among African American and Black populations (59%) and lowest among those who identify as White (26%) [7,8]. Nationally, over half of MSM have not been tested in the past year; these rates are lower in the southern United States [1,3,5,9], making studies that address barriers to testing and prevention among BYMSM critical and urgently needed to address the epidemic, particularly in the southern United States.

BYMSM in the Deep South—a subgroup of southern states—face significant barriers to HIV testing and prevention. The seven Deep South states—Texas, Georgia, Alabama, South Carolina, Mississippi, Florida, and Louisiana—have populations that hold more conservative values; are more rural, with less access to health care; and tend to embrace strong religiosity that stigmatizes sexually active youth and MSM [10]. The Deep South holds some of the highest rates of HIV and poverty in the country, and these rates are pronounced among southern racial minorities [1,3,5,7-14]. Southern BYMSM are at greater HIV risk than peers living elsewhere in the United States due to sociocultural factors, including stigma related to HIV and same-sex behaviors, structural racism, and limited health care infrastructure [7-21]. Stigma and structural racism are consistently associated with HIV risk behaviors as well as negative health outcomes [7-11,22,23]. Interventions that combat sociocultural and structural barriers to HIV prevention have the potential to motivate BYMSM to routinely test and consider pre-exposure prophylaxis (PrEP).

Considering the urgent need to address the HIV epidemic among BYMSM in the southern United States, in this protocol, we detail the adaptation of the Brothers Saving Brothers (BSB) HIV prevention intervention for midwestern BYMSM to the Kings intervention for southern BYMSM.

The BSB Intervention

BSB is a 2-part, face-to-face counseling intervention that was developed and tested in Detroit, Michigan, that aims to improve rates of community-based HIV testing, the return for HIV test results, and prevention education among BYMSM. BSB was developed by using Information-Motivation-Behavioral Skills (IMB) theory, and it delivers messaging with developmentally tailored motivational interviewing (MI). In the first part of BSB, using MI, BYMSM are offered an orientation to HIV ("HIV 101"), are encouraged to accept HIV testing in the community, and return for test results. The second part of BSB is conducted after the participant has tested, if the participant returns for test results, and if the test result was nonreactive. In the second BSB module, the outreach worker shares the test results and offers extended HIV prevention education with MI. Each part is 20 to 30 minutes long (total: 40-60 minutes). In the Michigan BSB trial (trial number: H97HA0378; N=188), participants in the intervention group were more likely to engage in community-based HIV testing (49% vs 20%) and return for HIV test results (98%) compared to the control (72%; χ^2_1=10.22; N=65; *P*=.001) [24,25].

Kings Intervention

In the adaptation of BSB to Kings, the following changes will be made. First, while the 2-part format will be retained and the first module will continue to be focused on promoting HIV testing, in Kings, the second module will promote PrEP uptake instead of being focused on prevention education, which was the focus in the original BSB intervention. Second, BSB was delivered in person within community settings. Kings will be delivered digitally in community settings. Third, BSB was tailored to leverage the language of the urban Midwest; Kings will employ language that is commonly used in the southern United States. Both BSB and Kings use IMB theory and tailored MI. More information on the adaptation process is provided in the *Methods* section.

Summary of Scientific Premise

To our knowledge, BSB is one of the few behavioral interventions that successfully and simultaneously targets community-based HIV testing and prevention education among

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BYMSM, warranting adaptation for BYMSM in the southern United States. If BSB is successfully adapted to Kings, the Kings intervention could improve rates of testing and prevention services, thereby preventing HIV acquisition in the southern United States. Thus, the purpose of this protocol is to detail the steps within the following two research aims: (1) elucidate experiences, beliefs, and perspectives related to the delivery and utilization of HIV testing and prevention services for BYMSM and (2) adapt the BSB intervention to include two HIV prevention tools (rapid testing and PrEP).

Methods

Ethics Approval

This protocol, including all associated data collection tools and informed consent forms, was reviewed and approved by the University of Alabama at Birmingham Institutional Review Board (approval number: IRB-300002136).

Theories and Tools for Behavior Change

Behavior Change Theory

This study is guided by the IMB model [26-31]. BSB, when adapted to Kings, will aim to improve knowledge of HIV prevention and PrEP (information) and self-efficacy (motivation), resulting in HIV testing and PrEP initiation when appropriate (behavioral skills to enact behavior change). Enhanced knowledge will provide BYMSM with the information they need to make evidence-informed decisions about their own health. Enhanced motivation is protective against stigma, which is routinely experienced by BYMSM, and enhanced behavior skills will enable BYMSM to access HIV testing, PrEP, and health care that is imperative to their well-being. IMB will inform the development of the standardized in-depth interview and focus group guides for aim 1, and the intervention components will map to IMB domains for aim 2.

Implementation Science Framework

The Exploration, Preparation, Implementation, Sustainment (EPIS) implementation science framework [32-34] will be used to inform this protocol. EPIS [32-34] can be used to move behavioral interventions from development or adaptation to full-scale and ongoing practice by building understanding of relevance and applicability to new contexts and through identifying factors that affect dissemination, adoption, integration, sustained use, and the impact on target populations. During the early phases of EPIS, which are relevant to this study, the model stresses intervention users'—BYMSM and HIV prevention and outreach staff—beliefs and impressions of the intervention and the inner and outer contexts affecting routine practice (aim 1). Therefore, during the dissemination of the intervention (aim 2), we can take these factors into consideration to increase the likelihood of acceptability, feasibility, and effectiveness, which result in longer-term sustainability [7,8,32-36].

Overview of MI

MI is a highly specified behavior change communication approach to improving relationships between clients and providers [37-40]. Miller and Rollnick [41] state the following:

> *MI is a collaborative, goal-oriented style of communication with particular attention to the language of change. It is designed to strengthen personal motivation for and commitment to a specific goal by eliciting and exploring the person's own reasons for change within an atmosphere of acceptance and compassion.*

MI promotes behavior change and treatment engagement across a range of behaviors [42-44]. MI's emphasis on autonomy support and its ability to address apathy toward behavior change makes it an optimal evidence-based approach to embed within behavioral interventions for youth [45]. MI is already included in clinical guidelines for HIV care and HIV risk reduction in the United States [46]. Given the benefits of MI in BSB, MI will be retained in the Kings adaptation.

Protocol Inclusion Criteria and Recruitment

The study participants will be BYMSM aged 18 to 29 years and HIV prevention and outreach workers aged ≥18 years who are of any race, gender, sex, and orientation. All participants must reside in the state of Alabama.

We are collaborating with two community-based organizations. Birmingham AIDS Outreach provides services to people in the Birmingham metropolitan area and is affiliated with the Magic City Wellness Center [47]. Selma AIDS Information and Referral provides services to populations in rural Alabama and refers clients to the Medical Advocacy and Outreach clinics in Selma, Montgomery, Dothan, and Atmore, Alabama [48]. These agencies will recruit eligible participants from their catchment areas through health fairs, clinic-based recruitment, and flyers.

Needs Assessment

The needs assessment phase was guided by aim 1—elucidate experiences, beliefs, and predictors related to the delivery and utilization of HIV testing and prevention services for BYMSM by using qualitative research methods to inform the adaptation of BSB (ie, *Exploration* in EPIS).

Qualitative Guides

Informed by the EPIS framework, the IMB model, and prior research on HIV prevention in the southern United States and HIV prevention with young sexual and gender minorities, the team developed standardized guides—a focus group guide for BYMSM, an in-depth interview guide for BYMSM, and an in-depth interview guide for HIV prevention and outreach workers. The guides cover a standardized set of domains, specifically HIV prevention barriers and facilitators, stigma, culture, racism, structural factors, and COVID-19. The guides were developed by using language at an eighth-grade reading level, and prompts focused on elucidating the sociocultural environment that may affect how the intervention is accepted and received [32,34,49-54]. The guides were pilot-tested with key informants for acceptability related to language, content, and length. The prevention and outreach worker interview guide is provided in Multimedia Appendix 1.

Data Collection With BYMSM

Focus groups and interviews were conducted with BYMSM (estimated sample size: n=36-48). BYMSM selected their

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preferred modalities—focus groups or in-depth interviews that were conducted either face-to-face via the web-based, Health Insurance Portability and Accountability Act–compliant Zoom platform (Zoom Video Communications Inc) or by phone call. Face-to-face in-depth interviews and focus groups were conducted at our community-based organization partners' sites in a private room to protect confidentiality. The target sample sizes are provided, but data collection continued until data saturation. An African American or Black research assistant conducted in-depth interviews and focus groups. An example question set was "What do we need to do to get rid of barriers to HIV testing? What would help?"

Data Collection With Prevention and Outreach Staff

Face-to-face in-depth interviews were conducted with HIV prevention and outreach staff (estimated sample size: n=10-12) from both community-based organizations. Topics specific to these interviews included views on how youth-friendly and minority-friendly their services are, approaches to discussing PrEP and prevention with clients, opinions on how to increase the utilization of prevention services by African American or Black youth and BYMSM, and the sociostructural support services that are available or are needed. The principal investigator conducted these interviews on-site at community-based organizations in a private room. Example questions included "How do you explain the importance of HIV testing to clients" and "What kinds of issues do you encounter with promoting HIV testing?"

Analytical Methods

Qualitative in-depth interviews and focus groups were audio-recorded by using digital recorders, and audio files were uploaded to an encrypted server. Audio files were transcribed into Microsoft Word by Landmark Associates. Coding and analysis involved applying a thematic analysis approach [55], in which a priori themes and subthemes from theory and literature are supplemented with emerging themes "grounded" in data [56]. Two experienced coders cocoded transcripts by using NVivo software (QSR International). As a first step, a preliminary coding scheme was developed based on the literature and the topics included in the interview guide, such as HIV prevention barriers and facilitators, stigma, culture, racism, structural factors, and COVID-19. This coding scheme was used and appended during the initial review and coding of the transcripts, resulting in a refined coding scheme. Transcripts were then rereviewed and were made more detailed; second-level fine coding was conducted. As of June 2022, analytic reports have been compiled; analyses are underway.

Intervention Design

The intervention design phase is informed by aim 2—adapt the BSB intervention to include HIV rapid testing and PrEP, address structural barriers, and be acceptable to BYMSM in Alabama (ie, *Preparation* in EPIS).

Intervention Mapping

The 4-step intervention mapping model [57] will be employed to guide the adaptation process. Using intervention mapping will enable us to prioritize key targets while considering barriers to testing and prevention. The steps are needs assessment, change objectives, intervention design, and production (Figure 1), which are described as follows:

1. Needs assessment: This step is part of aim 1—qualitative data collection from both stakeholders and beneficiaries.
2. Create change objectives: Change objectives relate to the behavior change targeted by the intervention. BSB has 2 parts, necessitating 2 objectives. The first is to increase HIV testing, and the second is to increase PrEP uptake.
3. Intervention design: This step includes decision-making about the intervention's structure based on the knowledge generated for aim 1. Since a premise of intervention mapping is that all intervention components must be informed by theory, it should be noted that we will continue to use the IMB framework that informed the creation of the original BSB intervention for this proposed modernization and adaptation.
4. Production: This includes the adaptation of intervention components and intervention pretesting.

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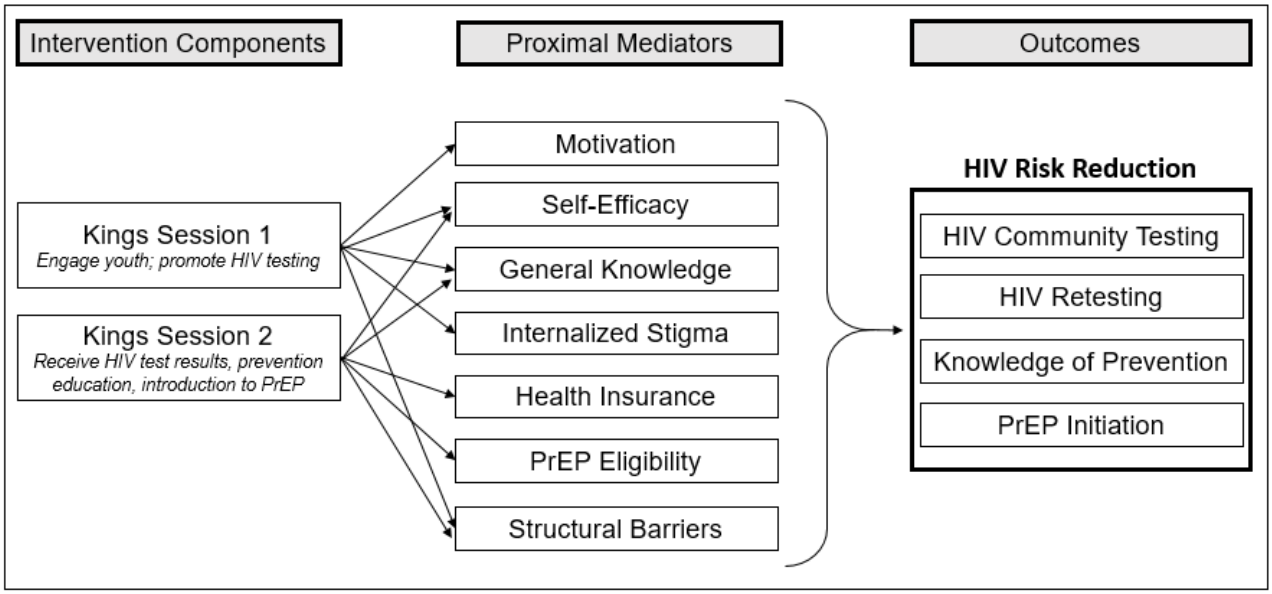
Figure 1. Intervention mapping framework for adapting the Brothers Saving Brothers intervention to the Kings intervention. PrEP: pre-exposure prophylaxis.



Digital Delivery

There is a strong body of evidence that suggests that the digital delivery of HIV-related interventions is preferred by young MSM and sexual and gender minorities [58], especially in high-stigma or remote settings. Additionally, our data for aim 1 indicated that the most acceptable way to deliver Kings is via the internet; thus, Kings will be developed as a 2-session digital health intervention that is built by using web-based MI [59].

Results

The tasks outlined in this protocol will be completed in 2023. Aim 1—qualitative data collection—concluded in 2021. As of June 2022, the aim 2 adaptation process is underway.

Discussion

Study Overview

We anticipate that this study will provide two outcomes. The first is insight (provided via the conduct of aim 1) into how to motivate and support BYMSM in accepting HIV testing and engaging in HIV prevention in the unique environment of the southern United States. The second is the development of a testable HIV prevention digital health intervention.

Limitations

Although our study is poised to make a positive impact on the HIV prevention continuum among BYMSM in the southern United States, African American or Black transgender women are not included in this project. Transgender women are also disproportionately affected by HIV in Alabama and therefore may benefit from an HIV prevention intervention that is tailored to their lived experiences. Of note, this protocol is being conducted in part during the COVID-19 pandemic, which will likely affect outcomes and influence how the BSB intervention is adapted for current contexts and sociopolitical circumstances. Although our team selected intervention mapping to guide the adaptation process, there are other frameworks that could have been applied; these frameworks could have potentially resulted in different intervention modifications.

Future Directions

The immediate future directions are to complete the analysis of the aim 1 qualitative data, finalize the adaptation of the digital health intervention, and evaluate the adapted Kings digital health intervention with BYMSM in Alabama.

Data Availability

The data that will be generated during the study will be available from the corresponding author on request.

Authors' Contributions

HB is the lead author and principal investigator. JMT and SN are senior scholars who guided the development of this protocol. BMK, MOJ, MJM, LBHW, AYO, and RAO contributed to the scientific framing of the original protocol. All authors contributed to the writing of this paper.

Conflicts of Interest

None declared.

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Multimedia Appendix 1
Interview guide for HIV prevention and outreach staff (example).
[DOCX File , 25 KB - resprot_v11i7e36655_app1.docx]

References

1. CDC fact sheet: HIV among gay and bisexual men. Centers for Disease Control and Prevention. URL: https://www.cdc.gov/nchhstp/newsroom/docs/factsheets/cdc-msm-508.pdf [accessed 2019-03-01]
2. Aghaizu A, Nardone A, Copas A, Mercey D, Wayal S, Parsons V, et al. O5 Understanding continuing high hiv incidence: sexual behavioural trends among msm in london, 2000–2013. Sex Transm Infect 2015 May 18;91(Suppl 1):A2. [doi: 10.1136/sextrans-2015-052126.5]
3. Centers for Disease Control and Prevention (CDC). Vital signs: HIV infection, testing, and risk behaviors among youths - United States. MMWR Morb Mortal Wkly Rep 2012 Nov 30;61(47):971-976 [FREE Full text] [Medline: 23190571]
4. Hall HI, An Q, Tang T, Song R, Chen M, Green T, Centers for Disease Control and Prevention (CDC). Prevalence of diagnosed and undiagnosed HIV infection--United States, 2008-2012. MMWR Morb Mortal Wkly Rep 2015 Jun 26;64(24):657-662 [FREE Full text] [Medline: 26110835]
5. State of Alabama HIV surveillance 2014 annual report. Alabama Department of Public Health. 2016. URL: https://www.alabamapublichealth.gov/hiv/assets/2014_hivsurveillance_annualupdate.pdf [accessed 2019-03-01]
6. Johnson AS, Hall HI, Hu X, Lansky A, Holtgrave DR, Mermin J. Trends in diagnoses of HIV infection in the United States, 2002-2011. JAMA 2014 Jul;312(4):432-434 [FREE Full text] [doi: 10.1001/jama.2014.8534] [Medline: 25038362]
7. Han CS, Ayala G, Paul JP, Boylan R, Gregorich SE, Choi KH. Stress and coping with racism and their role in sexual risk for HIV among African American, Asian/Pacific Islander, and Latino men who have sex with men. Arch Sex Behav 2015 Feb;44(2):411-420 [FREE Full text] [doi: 10.1007/s10508-014-0331-1] [Medline: 25060122]
8. Konkle-Parker DJ, Erlen JA, Dubbert PM. Lessons learned from an HIV adherence pilot study in the Deep South. Patient Educ Couns 2010 Jan;78(1):91-96 [FREE Full text] [doi: 10.1016/j.pec.2009.04.010] [Medline: 19560307]
9. Prejean J, Tang T, Hall HI. HIV diagnoses and prevalence in the southern region of the United States, 2007-2010. J Community Health 2013 Jun;38(3):414-426. [doi: 10.1007/s10900-012-9633-1] [Medline: 23179388]
10. LGBT data and demographics. The Williams Institute. URL: https://williamsinstitute.law.ucla.edu/visualization/lgbt-stats/?topic=LGBT&area=1#density [accessed 2019-04-17]
11. Alabama 2012-2016 statewide jurisdictional HIV prevention plan. Alabama Department of Public Health. URL: https://www.alabamapublichealth.gov/hiv/assets/HIVplan2012-2016.pdf [accessed 2019-04-17]
12. Peirce NR. The Deep South States of America: People, Politics, and Power in the Seven Deep South States. New York, NY: W.W. Norton & Company; 1974.
13. Amico KR, Konkle-Parker DJ, Cornman DH, Barta WD, Ferrer R, Norton WE, et al. Reasons for ART non-adherence in the Deep South: adherence needs of a sample of HIV-positive patients in Mississippi. AIDS Care 2007 Nov;19(10):1210-1218 [FREE Full text] [doi: 10.1080/09540120701426516] [Medline: 18071964]
14. Garofalo R, Mustanski B, Johnson A, Emerson E. Exploring factors that underlie racial/ethnic disparities in HIV risk among young men who have sex with men. J Urban Health 2010 Mar;87(2):318-323 [FREE Full text] [doi: 10.1007/s11524-009-9430-z] [Medline: 20155329]
15. Reif S, Mugavero M, Raper J, Thielman N, Leserman J, Whetten K, et al. Highly stressed: stressful and traumatic experiences among individuals with HIV/AIDS in the Deep South. AIDS Care 2011 Feb;23(2):152-162 [FREE Full text] [doi: 10.1080/09540121.2010.498872] [Medline: 21259127]
16. Doshi RK, Malebranche D, Bowleg L, Sangaramoorthy T. Health care and HIV testing experiences among Black men in the South: implications for "Seek, Test, Treat, and Retain" HIV prevention strategies. AIDS Patient Care STDS 2013 Feb;27(2):123-133 [FREE Full text] [doi: 10.1089/apc.2012.0269] [Medline: 23268586]
17. Eaton LA, Driffin DD, Kegler C, Smith H, Conway-Washington C, White D, et al. The role of stigma and medical mistrust in the routine health care engagement of black men who have sex with men. Am J Public Health 2015 Feb;105(2):e75-e82 [FREE Full text] [doi: 10.2105/AJPH.2014.302322] [Medline: 25521875]
18. Irvin R, Wilton L, Scott H, Beauchamp G, Wang L, Betancourt J, et al. A study of perceived racial discrimination in Black men who have sex with men (MSM) and its association with healthcare utilization and HIV testing. AIDS Behav 2014 Jul;18(7):1272-1278 [FREE Full text] [doi: 10.1007/s10461-014-0734-y] [Medline: 24569888]
19. Santos GM, Beck J, Wilson PA, Hebert P, Makofane K, Pyun T, et al. Homophobia as a barrier to HIV prevention service access for young men who have sex with men. J Acquir Immune Defic Syndr 2013 Aug 15;63(5):e167-e170. [doi: 10.1097/QAI.0b013e318294de80] [Medline: 24135782]
20. Skarbinski J, Rosenberg E, Paz-Bailey G, Hall HI, Rose CE, Viall AH, et al. Human immunodeficiency virus transmission at each step of the care continuum in the United States. JAMA Intern Med 2015 Apr;175(4):588-596. [doi: 10.1001/jamainternmed.2014.8180] [Medline: 25706928]
21. Levy ME, Wilton L, Phillips G2, Glick SN, Kuo I, Brewer RA, et al. Understanding structural barriers to accessing HIV testing and prevention services among black men who have sex with men (BMSM) in the United States. AIDS Behav 2014 May;18(5):972-996 [FREE Full text] [doi: 10.1007/s10461-014-0719-x] [Medline: 24531769]

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22. Budhwani H, De P, Sun R. Perceived stigma in health care settings mediates the relationships between depression, diabetes, and hypertension. Popul Health Manag 2022 Apr;25(2):164-171. [doi: 10.1089/pop.2021.0268] [Medline: 35442794]
23. Budhwani H, Yigit I, Ofotokun I, Konkle-Parker DJ, Cohen MH, Wingood GM, et al. Examining the relationships between experienced and anticipated stigma in health care settings, patient-provider race concordance, and trust in providers among women living with HIV. AIDS Patient Care STDS 2021 Nov;35(11):441-448. [doi: 10.1089/apc.2021.0096] [Medline: 34739336]
24. Outlaw AY, Naar-King S, Parsons JT, Green-Jones M, Janisse H, Secord E. Using motivational interviewing in HIV field outreach with young African American men who have sex with men: a randomized clinical trial. Am J Public Health 2010 Apr 01;100 Suppl 1(Suppl 1):S146-S151. [doi: 10.2105/AJPH.2009.166991] [Medline: 20147689]
25. Konkle-Parker DJ, Erlen JA, Dubbert PM. Barriers and facilitators to medication adherence in a southern minority population with HIV disease. J Assoc Nurses AIDS Care 2008;19(2):98-104 [FREE Full text] [doi: 10.1016/j.jana.2007.09.005] [Medline: 18328960]
26. Amico KR. Developing an "HIV Prevention Cascade": Current approach and future directions. In: International Association of Providers of AIDS Care. 2015 Jun 30 Presented at: 10th International Conference on HIV Treatment and Prevention Adherence (IAPAC); June 28-30, 2015; Miami, FL URL: http://iapac.org/AdherenceConference/presentations/ADH10_Plenary4-Amico.pdf
27. Fisher WA, Fisher JD. A general social psychological model for changing AIDS risk behavior. In: Pryor JB, Reeder GD, editors. The Social Psychology of HIV Infection. London, England: Psychology Press; 2017:27-53.
28. Fisher WA, Fisher JD. Understanding and promoting sexual and reproductive health behavior: theory and method. Annu Rev Sex Res 1998;9:39-76. [Medline: 10349025]
29. Fisher WA, Fisher JD, Harman J. The Information–Motivation–Behavioral Skills Model: A general social psychological approach to understanding and promoting health behavior. In: Suls J, Wallston KA, editors. Social Psychological Foundations of Health and Illness. Hoboken, NJ: Blackwell Publishing Ltd; 2003:82-106.
30. Hochbaum GM. Public Participation in Medical Screening Programs: A Sociopsychological Study. Washington, DC: US Government Printing Office; 1958.
31. Bandura A. Perceived self-efficacy in the exercise of control over AIDS infection. Eval Program Plann 1990;13(1):9-17. [doi: 10.1016/0149-7189(90)90004-g]
32. Aarons GA, Hurlburt M, Horwitz SM. Advancing a conceptual model of evidence-based practice implementation in public service sectors. Adm Policy Ment Health 2011 Jan;38(1):4-23 [FREE Full text] [doi: 10.1007/s10488-010-0327-7] [Medline: 21197565]
33. Brownson RC, Colditz GA, Proctor EK. Dissemination and Implementation Research in Health: Translating Science to Practice. New York, NY: Oxford University Press; 2012.
34. Glisson C, Landsverk J, Schoenwald S, Kelleher K, Hoagwood KE, Mayberg S, Research Network on Youth Mental Health. Assessing the organizational social context (OSC) of mental health services: implications for research and practice. Adm Policy Ment Health 2008 Mar;35(1-2):98-113. [doi: 10.1007/s10488-007-0148-5] [Medline: 18085434]
35. Curran GM, Bauer M, Mittman B, Pyne JM, Stetler C. Effectiveness-implementation hybrid designs: combining elements of clinical effectiveness and implementation research to enhance public health impact. Med Care 2012 Mar;50(3):217-226 [FREE Full text] [doi: 10.1097/MLR.0b013e3182408812] [Medline: 22310560]
36. Sullivan P, Goldmann D. The promise of comparative effectiveness research. JAMA 2011 Jan 26;305(4):400-401. [doi: 10.1001/jama.2011.12] [Medline: 21266687]
37. Rollnick S, Miller WR, Butler CC. Motivational Interviewing in Health Care: Helping Patients Change Behavior. New York, NY: Guilford Press; 2008.
38. Miller WR, Rollnick S. Meeting in the middle: motivational interviewing and self-determination theory. Int J Behav Nutr Phys Act 2012 Mar 02;9:25 [FREE Full text] [doi: 10.1186/1479-5868-9-25] [Medline: 22385872]
39. Budhwani H, Robles G, Starks TJ, MacDonell KK, Dinaj V, Naar S. Healthy Choices intervention is associated with reductions in stigma among youth living with HIV in the United States (ATN 129). AIDS Behav 2021 Apr;25(4):1094-1102 [FREE Full text] [doi: 10.1007/s10461-020-03071-1] [Medline: 33098483]
40. Budhwani H, Naar S. Training providers in Motivational Interviewing to promote behavior change. Pediatr Clin North Am (forthcoming) 2022.
41. Miller WR, Rollnick S. Motivational Interviewing: Helping People Change, 3rd Edition. New York, NY: Guilford Press; 2013.
42. Ashman JJ, Conviser R, Pounds MB. Associations between HIV-positive individuals' receipt of ancillary services and medical care receipt and retention. AIDS Care 2002 Aug;14 Suppl 1:S109-S118. [doi: 10.1080/09540120220149993a] [Medline: 12204145]
43. Parsons JT, Lelutiu-Weinberger C, Botsko M, Golub SA. A randomized controlled trial utilizing motivational interviewing to reduce HIV risk and drug use in young gay and bisexual men. J Consult Clin Psychol 2014 Feb;82(1):9-18 [FREE Full text] [doi: 10.1037/a0035311] [Medline: 24364800]
44. Burke BL, Arkowitz H, Menchola M. The efficacy of motivational interviewing: a meta-analysis of controlled clinical trials. J Consult Clin Psychol 2003 Oct;71(5):843-861. [doi: 10.1037/0022-006X.71.5.843] [Medline: 14516234]

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45. Naar S, Suarez M. Motivational Interviewing with Adolescents and Young Adults. New York, NY: Guilford Press; 2021.
46. Fundamentals of motivational interviewing for HIV. Centers for Disease Control and Prevention. URL: https://www.cdc.gov/hiv/effective-interventions/treat/motivational-interviewing/index.html [accessed 2021-12-23]
47. Magic City Wellness Center. Magic City Wellness Center. URL: https://www.magiccitywellnesscenter.org/ [accessed 2022-01-12]
48. Medical advocacy and outreach. Medical Advocacy and Outreach. URL: https://maoi.org/ [accessed 2022-01-12]
49. Arnett JJ. Emerging Adulthood: The Winding Road from the Late Teens through the Twenties. New York, NY: Oxford University Press, Inc; 2004.
50. Arnett JJ. Afterword: Aging out of care--toward realizing the possibilities of emerging adulthood. New Dir Youth Dev 2007(113):151-161. [doi: 10.1002/yd.207] [Medline: 17523528]
51. Fixsen DL, Naoom SF, Blase KA, Friedman RM, Wallace F. Implementation research: A synthesis of the literature. National Implementation Research Network. 2005 Jan. URL: https://nirn.fpg.unc.edu/sites/nirn.fpg.unc.edu/files/resources/NIRN-MonographFull-01-2005.pdf [accessed 2022-06-28]
52. Parsons ML, Cornett PA. Leading change for sustainability. Nurse Lead 2011 Aug 01;9(4):36-40. [doi: 10.1016/j.mnl.2011.05.005]
53. Meyers DC, Durlak JA, Wandersman A. The quality implementation framework: a synthesis of critical steps in the implementation process. Am J Community Psychol 2012 Dec;50(3-4):462-480. [doi: 10.1007/s10464-012-9522-x] [Medline: 22644083]
54. Glisson C. Assessing and changing organizational culture and climate for effective services. Res Soc Work Pract 2007 Nov 01;17(6):736-747. [doi: 10.1177/1049731507301659]
55. Attride-Stirling J. Thematic networks: an analytic tool for qualitative research. Qual Res 2001 Dec 01;1(3):385-405. [doi: 10.1177/146879410100100307]
56. Strauss A, Corbin J. Basics of Qualitative Research: Techniques and Procedures for Developing Grounded Theory, Second Edition. Thousand Oaks, CA: Sage Publications; 1998.
57. Merlin JS, Young SR, Johnson MO, Saag M, Demonte W, Kerns R, et al. Intervention mapping to develop a Social Cognitive Theory-based intervention for chronic pain tailored to individuals with HIV. Contemp Clin Trials Commun 2018 Feb 19;10:9-16. [doi: 10.1016/j.conctc.2018.02.004] [Medline: 29696153]
58. Budhwani H, Kiszla BM, Hightow-Weidman LB. Adapting digital health interventions for the evolving HIV landscape: examples to support prevention and treatment research. Curr Opin HIV AIDS 2022 Mar 01;17(2):112-118. [doi: 10.1097/COH.0000000000000721] [Medline: 35225251]
59. Shingleton RM, Palfai TP. Technology-delivered adaptations of motivational interviewing for health-related behaviors: A systematic review of the current research. Patient Educ Couns 2016 Jan;99(1):17-35 [FREE Full text] [doi: 10.1016/j.pec.2015.08.005] [Medline: 26298219]

Abbreviations

BSB: Brothers Saving Brothers
BYMSM: Black young men who have sex with men
EPIS: Exploration, Preparation, Implementation, Sustainment
IMB: Information-Motivation-Behavioral Skills
MI: motivational interviewing
MSM: men who have sex with men
PrEP: pre-exposure prophylaxis

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Protocol

Investigating Microtemporal Processes Underlying Health Behavior Adoption and Maintenance: Protocol for an Intensive Longitudinal Observational Study

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Abstract

Background: Young adulthood (ages 18-29 years) is marked by substantial weight gain, leading to increased lifetime risks of chronic diseases. Engaging in sufficient levels of physical activity and sleep, and limiting sedentary time are important contributors to the prevention of weight gain. Dual-process models of decision-making and behavior that delineate reflective (ie, deliberative, slow) and reactive (ie, automatic, fast) processes shed light on different mechanisms underlying the adoption versus maintenance of these energy-balance behaviors. However, reflective and reactive processes may unfold at different time scales and vary across people.

Objective: This paper describes the study design, recruitment, and data collection procedures for the Temporal Influences on Movement and Exercise (TIME) study, a 12-month intensive longitudinal data collection study to examine real-time microtemporal influences underlying the adoption and maintenance of physical activity, sedentary behavior, and sleep.

Methods: Intermittent ecological momentary assessment (eg, intentions, self-control) and continuous, sensor-based passive monitoring (eg, location, phone/app use, activity levels) occur using smartwatches and smartphones. Data analyses will combine idiographic (person-specific, data-driven) and nomothetic (generalizable, theory-driven) approaches to build models that may predict within-subject variation in the likelihood of behavior "episodes" (eg, ≥10 minutes of physical activity, ≥120 minutes of sedentary time, ≥7 hours sleep) and "lapses" (ie, not attaining recommended levels for ≥7 days) as a function of reflective and reactive factors.

Results: The study recruited young adults across the United States (N=246). Rolling recruitment began in March 2020 and ended August 2021. Data collection will continue until August 2022.

Conclusions: Results from the TIME study will be used to build more predictive health behavior theories, and inform personalized behavior interventions to reduce obesity and improve public health.

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KEYWORDS

emerging adulthood; behavior change; longitudinal data collection; ecological momentary assessment; sensing; theory; young adult; weight gain; EMA; chronic disease; physical activity

Introduction

Engaging in sufficient levels of physical activity [1] and sleep [2], and limiting sedentary time [3] are important contributors to the prevention of weight gain and decreased lifetime risks of cancer, diabetes, cardiovascular disease, and mortality [4-7]. However, engagement in these healthy behaviors steeply declines during young adulthood (ages 18-29 years) [8-10]. Existing interventions designed to promote physical activity, reduce sedentary time, and support sufficient sleep among young adults typically focus on the *adoption* of these behaviors. Yet, often, when these interventions are successful, new patterns of behavior are not *maintained* and regress back to baseline levels [11]. Temporary disengagements are frequent among individuals attempting to maintain healthy behaviors, but little is known about how to help individuals avoid or manage these disruptions [12].

The first generation of health behavior theories provide limited guidance regarding factors underlying the transition from initiating to maintaining a pattern of behavior [13-16]. More recently, dual-process models of decision-making and behavior have offered explanations for different mechanisms underlying adoption versus maintenance [17-19]. Reflective processes, which are slow and deliberative (eg, deliberating, evaluating one's efficacy, exerting self-control) [20-23], may be engaged to a greater extent when adopting a behavior, whereas reactive processes, which are fast and automatic (eg, contextual cues, habits) [24,25], may be more involved in behavior maintenance. Thus, understanding the independent and interactive effects of reflective and reactive factors may afford more precise predictions of behavior adoption and maintenance [26,27].

The dynamic and idiographic properties that characterize reflective and reactive processes, which may change dynamically, within a day, and differently across individuals [28,29], are not well captured using static, cross-sectional, laboratory-based, or retrospective research methods [30]. The application of methods and tools for collecting and analyzing intensive longitudinal data (ILD) may enable better research on factors influencing reflective and reactive processes, and thus support new theory and intervention development. ILD are collected from real-world settings in temporally dense micro time scales (eg, seconds, minutes, hours). Improved miniaturization, capability, affordability, and pervasiveness of mobile and wearable devices in recent years have enabled the capture of ILD.

In the Temporal Influences of Movement and Exercise (TIME) study, we are using real-time mobile technologies (consumer-grade smartphones and smartwatches) to collect ILD to examine differences in the microtemporal processes underlying the adoption and maintenance of physical activity, low sedentary time, and sufficient sleep duration among young adults. We aim to predict within-subject variation in the likelihood of behavior "episodes" (eg, ≥10 minutes of physical activity, ≥120 minutes sedentary time, ≥7 hours sleep) and "lapses" (ie, not attaining recommended levels for ≥7 days) as a function of reflective and reactive factors. Overall, this study seeks to yield new insights into the behaviors, states, and contexts that influence health behavior and decision-making, and to build better predictive models that can be used to drive personalized interventions targeting a wide variety of health behaviors that can be implemented in real time. In this paper, we describe the TIME study protocol.

Methods

Design Overview

The TIME study uses a prospective within-subject case-crossover observational design that collects ILD using smartphone and smartwatch technology worn continuously across a 12-month period in a sample of socioeconomically and racially/ethnically diverse young adults. In case-crossover designs, a subject serves as their own control to assess the within-subject effects of time-varying predictors and moderators on a repeatedly measured dependent variable. With this longitudinal design, the phase of behavior change (adoption vs maintenance) will vary between people and within people (who change over time). We are deploying a combination of continuous passive (sensor-based) and intermittent active (self-reported ecological momentary assessment [EMA]) monitoring methods (see Figure 1).

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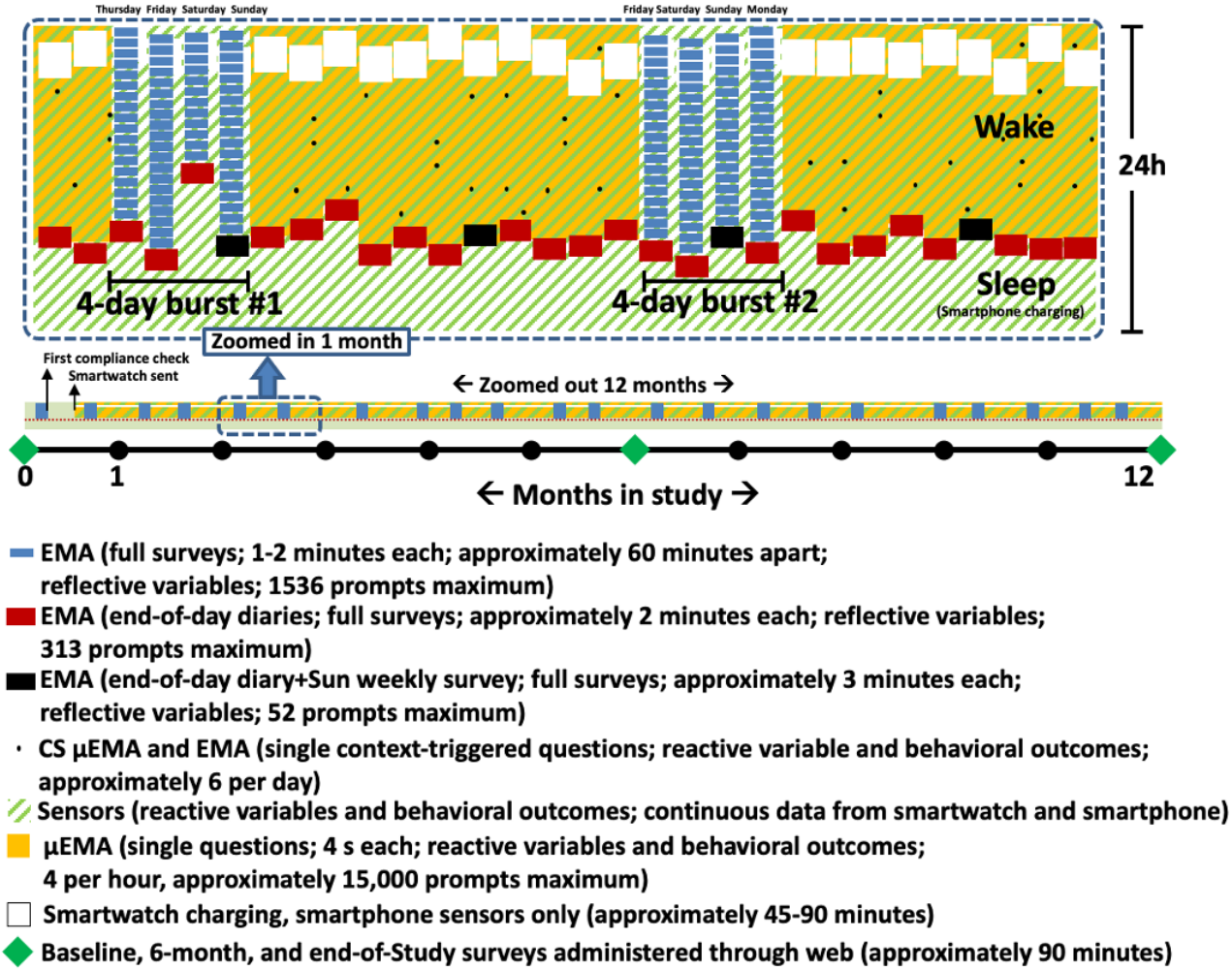
Figure 1. Temporal Influences of Movement and Exercise (TIME) study protocol with nested ecological momentary assessment (EMA) bursts and micro-EMA (µEMA) on nonburst days. ea: each; CS: context-sensitive.



Across the 12-month study period, physical activity, sedentary behavior, and sleep outcomes are captured continuously using a smartwatch activity sensor. Time-varying reactive predictor variables (eg, location, phone/app use, time of day/week) are captured continuously using smartphone sensors and usage logging. To limit participant burden, time-varying reflective predictor variables (eg, self-control, demands, deliberation) are captured intermittently using self-report EMA (sets of questions administered together) with two types of prompting schedules (varying in prompting density): "measurement bursts" and "end-of-day (EOD) surveys." Measurement bursts (lasting 4 days each) occur once every 2 weeks and EOD surveys occur each night. Additionally, data from context-sensitive (CS)-EMA prompting will be used to verify accuracy of location via passive sensor (GPS) data. During the nonmeasurement burst periods, participants are prompted on the smartwatch to gather additional data on reflective and reactive variables and behaviors, and are asked CS questions on physical activity and sedentary behavior (via raw accelerometer data) using micro-EMA (µEMA) [31]. Details of each component are described below.

Participants

The study recruited young adults across the United States (N=246). Inclusion and exclusion criteria were assessed by self-report during the screening process. Inclusion criteria for the study were: (1) 18-29 years old living in the United States, (2) intention to engage in recommended levels of moderate-to-vigorous physical activity (MVPA) (≥150 minutes/week moderate or ≥75 minutes/week vigorous intensity) within the next 12 months, (3) use an Android-based smartphone as their only primary personal mobile device with no intention to switch to a non-Android phone, (4) able to speak and read English, and (5) plan to reside in a home with Wi-Fi connectivity during the study period. Exclusion criteria were (1) physical or cognitive disabilities that prevent participation; (2) health issues that limit physical activity; (3) any diagnosed sleep disorders; (4) unable to wear a smartwatch or answer EMA surveys at home, work, school, or another location where a substantial amount of time is spent; (5) spends more than 3 hours/day on a typical weekday or weekend day driving; (6) owns an Android phone version 6.0 (or older), or if the app will not function on the phone due to other technical issues; (7) currently owns and wears a smartwatch; (8) uses a pay-as-you-go data plan or data plan with less than 2 gigabytes of data per month; or (9) currently pregnant. Participants were recruited regardless of baseline activity level.

Ethics Approval

The study was approved by the Institutional Review Board at the University of Southern California (USC; HS-18-00605).

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The study was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments. All participants provided informed consent to have their deidentified data published in journals.

Recruitment, Screening, Consent, and Orientation

Due to health and safety concerns arising from the COVID-19 pandemic, all study procedures were conducted remotely. To recruit socioeconomically and racially/ethnically diverse young adults, we used a variety of recruitment methods, which broadly sampled young adults across the United States. Recruitment strategies included the following: (1) sending emails to individuals enrolled in a USC longitudinal cohort study of young adults [32]; (2) referrals from existing participants (word of mouth); and (3) contacting participants identified using ResearchMatch, a national health volunteer registry [33]. Potential participants filled out an online interest form to screen eligibility. For eligible and interested potential participants, a videoconference orientation and consent session over Zoom was then scheduled. This session involved reviewing all parts of the study, obtaining informed consent, and downloading our custom TIME study smartphone app onto the participant's smartphone (N=332). During the orientation session, participants received instructions on how to use the study app to complete EMA surveys. During the following week, individuals participated in their first 4-day EMA measurement burst period (further described below), during which the TIME app triggers surveys once per hour during the participant's waking hours. Participants who successfully completed at least 8 surveys per day during this first EMA measurement burst period were fully enrolled in the study (N=246). If compliance was below 8 surveys/day for the first measurement burst period, participants were unenrolled from the study. Participants who were fully enrolled received a smartwatch by mail within 1 week and were scheduled for a second orientation session for smartwatch setup and training.

Study App

EMA data are collected using our custom TIME app developed for Android smartwatches and smartphones. The app is downloaded directly to a participant's personal Android phone from the Google Play Store but is only available to authorized study participants. Once the participant receives the smartwatch by mail, the TIME app is downloaded to the watch paired with the smartphone.

Smartwatch

Participants are loaned a Fossil Sport Gen 4 or Gen 5 smartwatch. Participants are asked to wear the smartwatch on one wrist of their choice/comfort consistently and continuously over the study period, except for 1 hour per day when it should be charged by setting it on a provided charger. They are asked to develop a routine in which the smartwatch is fully charged every day, ideally at a consistent place and time such as during daily personal hygiene (eg, showering, bathing). Participants can use the smartwatch as they see fit throughout the study (eg, to get notifications from phone apps) if that use does not interfere with the TIME app's functionality. Participants were allowed to install health and fitness apps on their personal smartphones, but we asked that participants refrain from installing these apps onto the smartwatch to preserve the battery life of the watch. These apps use motion data and the heart rate sensor, which cause quicker battery drain that would increase perceived study burden by having to charge the watch more than once a day. However, 22% of participants reported installing health and fitness apps on the watch. We will be able to use data on smartwatch app installation as covariates in our analyses.

Data Collection Procedures

Ecological Momentary Assessment

Overview

Participants complete EMA surveys on the smartphone and µEMA questions on the smartwatch throughout the study during waking hours. The smartphone uses push notifications to prompt participants to complete EMA question sets with back-to-back multiple-choice questions; question sets require ~1-2 minutes to complete. If a response is not provided, up to two reprompts will be emitted at 5-minute intervals; when the second reprompt answer time expires, the EMA survey becomes inaccessible and is recorded as missed. Once a smartphone survey is started, it must be completed within 10 minutes. If a smartphone or smartwatch prompt occurs during an incompatible activity (eg, driving, sleep), participants are instructed to ignore it. The smartwatch prompts single µEMA questions. A µEMA question can be answered in ~3 seconds with a glance and tap. Each µEMA question on the smartwatch must be answered within 20 seconds; there are no reprompts. EMA data are captured intermittently using sampling schedules varying in prompting density as described below: (1) sleep-wake time, (2) measurement bursts, (3) EOD surveys, and (4) sensor-informed CS prompting. Examples of these questions are shown in Figure 2.

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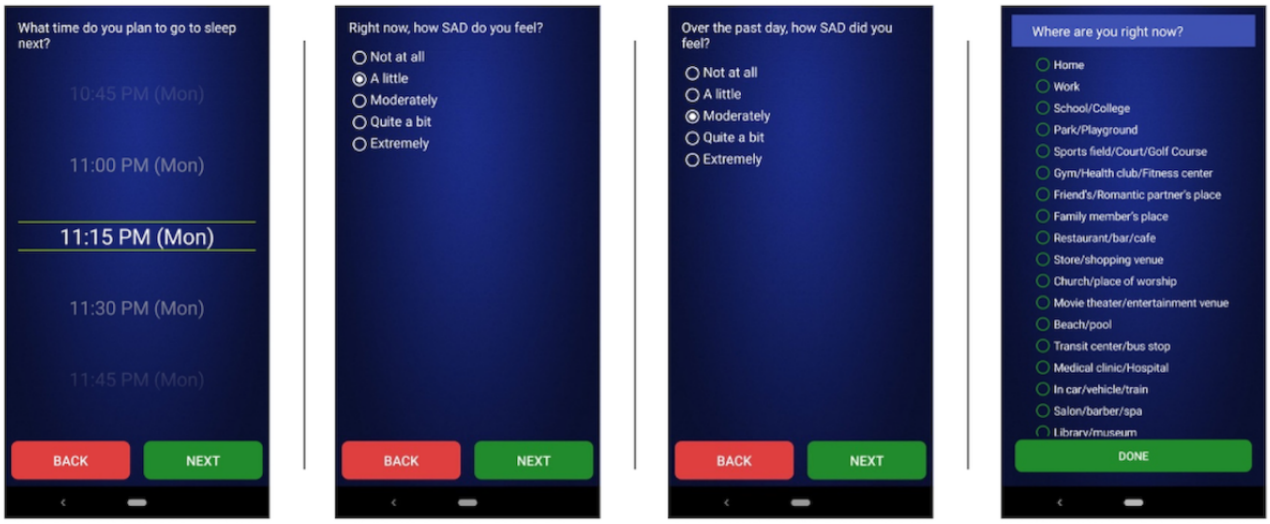
Figure 2. TIME app's ecological momentary assessment (EMA) interface, shown on a Google Pixel 3 phone. From left to right: example sleep time EMA measuring prospective sleep time, burst EMA question about momentary sadness, end-of-day EMA question about daily sadness, and context-sensitive location survey question assessing current location.



Sleep-Wake EMA

EMA prompting takes place only during waking hours to prevent sleep disruption; however, unlike most prior work using EMA, waking hours are adapted dynamically to match each participant's daily schedule. This outcome is achieved by asking participants to report their anticipated (ie, prospective) and actual (ie, retrospective) sleep/wake times each day. Sleep and wake times are assessed using short EMA surveys that are typically appended to other prompted surveys. During the EMA measurement burst days, the prospective sleep-wake questions are included in the first prompt of the day. Prospective sleep time questions are reassessed after 10 hours to capture potential changes in a participant's schedule throughout the day. The retrospective sleep-wake questions are only prompted once a day. On nonburst days, the sleep-wake EMA surveys are prompted on the smartphone without additional EMA questions. When the sleep and wake times are changed by the participants, the TIME app automatically updates the EMA prompting schedules.

EMA Measurement Bursts

Each EMA measurement burst consists of signal-contingent (ie, randomly prompted) question sets triggered multiple times per day, approximately once every hour during waking hours across 4 consecutive days. Within 1 hour, the prompting is restricted to between the 10th and 50th minute to ensure that two prompts from consecutive hours do not occur too close to each other. EMA measurement bursts last 4 days each and measurement bursts occur every 2 weeks, resulting in up to 26 bursts during the study period (104 total days). During the measurement burst periods, participants continue to wear the smartwatch but do not receive any µEMAs. EMA measurement bursts occur on randomly scheduled blocks of days, with at least 7 days in between each burst and guaranteeing two weekends and two weekdays within each burst. One day before the burst is set to begin, the TIME app notifies the participants about their upcoming burst period via a phone notification that gives participants a chance to snooze (ie, delay) the beginning of the burst period by 2 days. Participants can snooze each burst period only once.

To promote compliance, once an EMA question set is completed, the app displays a lighthearted "thank you" message. There are 250 different EMA thank you messages, and therefore they rarely repeat, providing novelty after each question set. In addition, 20% of the EMA burst surveys include a validation question; these questions are designed to be entertaining and provide novelty (rarely repeating), but with unambiguous answers so that they can be used to determine whether participants are paying attention to EMA questions and answering thoughtfully.

The hourly sampling schedule used in the study was piloted with 45 participants for 1 month (two burst periods) before starting the data collection described in this protocol. Feasibility of the schedule was demonstrated with compliance rates of 77.0% (SD 16.7, range 41.5%-100%) for burst 1 and 78.9% (SD 16.1, range 35.8%-100%) for burst 2, which are similar to rates found in other EMA studies with less frequent prompting schedules [34]. For this study, compliance is defined as the number of completed surveys divided by the number of prompted surveys.

End-of-Day EMA

Across the 12 months, an EMA question set is prompted on the smartphone at the end of each day asking participants to summarize experiences occurring that day and their plans for the next day. Participants respond to EOD EMA prompts during both burst and nonburst study periods. EOD EMA prompts are delivered 2 hours before a participant's anticipated sleep time. The question set remains accessible for 2 hours (up to the sleep time) or until it is answered via a persistent notification that can be clicked to access the EOD EMA survey. All EOD question sets ask about an individual's anticipated sleep time that same day and anticipated wake-up time the next day. If the sleep time is extended more than 1 hour past the current time, the participant may receive more EMA measurement burst prompts after the completion of the EOD EMA question.

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Once a week, on Sundays, the EOD EMA question sets include 28 additional unique questions asking about experiences over the past week, goals/intentions to engage in health behaviors in the upcoming week, and reactions to the COVID-19 pandemic.

Context-Sensitive EMA

On non-EMA measurement burst days, the smartphone also triggers sensor-informed CS-EMA surveys to gather data about the types of places where a participant is spending time. These surveys are prompted based on recorded information about a participant's current and prior locations, measured using the phone's location-sensing system. At the end of each day, a density-based clustering algorithm clusters that day's location measurements [35,36]. When clusters are found, they are inserted into a master cluster list for the participant. If the app detects that the participant has spent at least 5 minutes in a previously identified cluster, if the type of that location is not known with high reliability (based on prior CS-EMA surveys for location) and if the participant has not been asked to label the location within the last 2 hours, the participant will be prompted to describe the type of the current location (ie, "Where are you right now?"). This single question includes 21 types of common locations (eg, home, work, park/playground/trail, church/place of worship, in car/vehicle/train). Once a location cluster has been reliably identified, the app no longer triggers a CS-EMA prompt when that location is reencountered, unless 60 days have elapsed since the last label for the cluster was obtained, in which case the participant will be asked to reconfirm the location type. Participants self-report their locations to attach more meaningful labels to commonly visited locations than can be obtained from a map application programming interface (API). As location data represent a key reactive factor being tested in the analyses, the precision of the label justifies the additional user burden.

Micro-EMAs

Outside of EMA measurement burst periods (on 261 days during the 12-month study), participants are prompted with µEMAs (also known as microinteraction EMAs or micro-EMAs) [31] throughout the waking day. Each µEMA prompt includes one single question that can be read with a glance and answered with a quick, single tap (Figure 3). µEMA questions have simple categorical/ordinal answer options (eg, "yes/sort of/no") and are designed to be cognitively simple to answer (eg, Feeling stressed? Yes, Sort of, No). If the watch detects 10 minutes of continuous physical activity or 60 minutes of continuous sedentary behavior, sensor-triggered µEMA questions may be asked (eg, "physically active [x] min ago?" where "[x]" is the time difference between the prompt time and the middle of the window when the activity was detected). Additional details on the µEMA protocol and related study goals are described elsewhere [37].

Figure 3. Example microinteraction ecological momentary assessment question on the smartwatch.

Self-Report Online Electronic Questionnaires

Sociodemographic variables, mental health characteristics, health status, health behaviors, and other covariates are assessed at three time points (baseline, 6 months, 12 months) using online electronic questionnaires completed remotely on a computer, tablet, or smartphone. Questionnaire constructs include: general health [38], self-reported physical activity [39], usual lifestyle physical activities [40], team sports/activity classes [41], sedentary behavior [42], sleep problems [43], sleep disorders [44], diet [45], eating disorders [46], alcohol and substance use [47], acculturation [48], and demographics [38]. Participants

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receive an electronic link to the online questionnaire on REDCap (Research Electronic Data Capture) by email and are asked to complete the questionnaire within 7 days or before the end of the first burst period. Questionnaires take ~45-60 minutes to complete, and participants can stop midsurvey and return to the survey later to complete it.

At either the end of the 12-month period or when the participant is withdrawn or removed from the study, participants receive an email link to complete an additional 5-minute online end-of-study questionnaire about the acceptability of procedures and usability of the study app and smartwatch.

Exit Interview

At the end of the 12-month study period, participants complete a 30-45–minute interview on Zoom with study staff. Participants answer questions about the acceptability of study procedures, provide context to how they used their devices, and indicate how they interpreted and answered the study survey questions. This interview is recorded for transcription in subsequent analysis.

Measures

Overview

We will collect data on reflective processes (eg, self-control, attention, procrastination, deliberation ["trying to decide"], and intention) using intermittent self-report through EMA. Some reactive factors (eg, lack of deliberation ["not thought about it"], habit ["doing usual routine"], and affective motivation ["feel like doing it"]) will also be captured through EMA. Continuous, sensor-based passive monitoring of reactive factors (eg, location and screen/app use) will also occur using smartwatches and smartphones.

EMA Items

All EMA questions are presented in Multimedia Appendix 1. Both EMA bursts and EOD EMA assess the following *global* constructs at every prompt (ie, occurring 100% of the time) using items taken directly or modified from established measures: affective and feeling states, stress, attention, self-control, productivity, and habit. During EMA bursts, items start with "Right now..." to capture momentary reports. For the EOD EMA, items start with "Over the last day..." to capture daily summaries. Two additional EMA burst items assess health behaviors and social contexts that cannot be detected from sensors: "Over the past hour, I did the following things (choose all that apply)," and "In the past hour, I was with (in person and/or virtual)."

To reduce the question set length, only one of four possible *behavior-specific* construct modules (ie, physical activity, sleep, sedentary behavior, eating) is included in each EMA burst and EOD EMA question set; the module is randomly selected (see proportions in Multimedia Appendix 1).

Passive Monitoring

Reactive factors that may influence physical activity, sedentary time, and sleep are acquired continuously via passive sensing using the participants' smartwatch and smartphone sensors [49-51]. For any phone that permits it, each minute, the app collects light luminosity (measured in lux), ambient pressure (measured in hectopascal units), ambient relative humidity (measured as percentage), and temperature (measured in degrees Celsius). Once a day, using the UsageStats API in Android, the app captures the amount of time spent by the participant using different apps installed on the phone. Similarly, once an hour, the app saves the number of times different apps were opened (moved to the foreground) and closed (moved to the background). In addition, the app stores time-stamped data about phone use, such as phone unlocks, screen usage time, battery percentages, phone and watch charging events, and the notification frequency from other apps installed on the phone. The smartphone estimates the longitude and latitude of the participant each minute using the smartphone's location system, except for when the phone is turned off.

All participants in the study were informed about the type of passive data collected and consented to the procedures. Any identifiable data collected using the smartphone's location system are encrypted at the time of collection and only used in an identifiable way by the research team.

Motion Data

Motion data are collected using raw acceleration data processing, phone activity levels, and estimated step counts

Triaxial raw acceleration along the X, Y, and Z axes on both the smartphone and smartwatch is measured at a sampling rate of ~50 Hz using the embedded accelerometers. Smartwatch data are collected in the range of ±8 g; smartphone data sensitivity is based on the specific phone. The acceleration data are collected continuously except when the watch and/or phone are turned off. The area under the curve (AUC) of the summed 3-axis high-pass accelerometer signal is computed for 10-second epochs to provide a crude motion summary in real time on both the phone and the watch [34]. On the watch, this AUC value is used for sensor-triggered µEMA questions on physical activity and sedentary behavior.

The movement state of the smartphone (ie, the phone activity level) is captured each minute using Android's activity recognition API. Using the phone's motion sensors, an algorithm estimates if the user is "in vehicle," "on bicycle," "on foot," "running," "tilting," "still," "tilted," and "walking." The labels are not mutually exclusive, and thus the algorithm can report that the smartphone is "in vehicle" and "still" at the same time.

Once an hour, the number of steps recorded on the smartphone is collected using Android's built-in step counter. This built-in counter uses the inertial sensors (accelerometer and gyroscope) to estimate the step count when the phone is not turned off.

Data Processing Procedures

Motion Summary

Motion Independent Movement Summary (MIMS) units are computed using the raw acceleration data from the smartwatch after data collection. The watches reliably store raw accelerometer data at ~50 Hz. MIMS units are a device-independent summary of overall motion. The MIMS-unit algorithm is designed to allow for cross-monitor motion comparisons between research-grade devices such as actigraphs

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and consumer-grade devices such as the Fossil smartwatches used in this study [52]. MIMS units are computed with 1-second epochs, but can then be aggregated (eg, minute, hour, or day level). The SWaN (Sleep Wake and Nonwear) algorithm used in the study to summarize the raw accelerometer data has previously been used to summarize population-wide wrist-worn movement metrics in the NHANES data set [53]. Wrist-worn activity measurement may overestimate activity in response to large amounts of gesturing and underestimate activity for some activities such as cycling.

Smartwatch Sleep, Wear, and Sensor Nonwear

Sleep, wear, and sensor nonwear estimation is also computed after data collection using raw accelerometer data using the SWaN algorithm. SWaN classifies each 30-second window of the raw data into sleep, wear, and nonwear classes, each with some degree of certainty.

Smartwatch Activity Type

Finally, postprocessing using the watch accelerometer signal is used to estimate activity intensity (light, moderate, vigorous), posture (eg, sitting, standing, lying), and specific activities (eg, sitting and writing, walking, running). The algorithm classifies these activities for each 12.8-second window of raw data in the post data collection stages [54]. Estimates of MVPA will be developed using the passively collected smartwatch accelerometer data and these postprocessing algorithms.

Behavior Episode Categorization

For physical activity, labels will be assigned for each 1-minute interval, and any bout of MVPA ≥10 minutes will be considered a behavior episode based on the minimum recommended bout length for health benefits. Bouts of ≥120 minutes of sedentary time will be considered a behavior episode based on conferred health risks that start to emerge at this duration of prolonged sitting. Any period with ≥7 hours of sleep will be considered a behavior episode meeting the sleep guidelines for young adults.

Phase of Behavior Change Classification

Adoption versus maintenance phase will be a binary, time-varying variable assigned to each day in the study (starting on day 22) based on whether a participant has attained recommended levels of behavior/levels with conferred health benefits for ≥3 past weeks based on movement data collected from the smartwatch: adoption (not attained) or maintenance (attained). Alternative lengths of time (eg, 4 weeks, 6 weeks, 12 weeks) will be explored through sensitivity analyses. Thus, individuals can transition from adoption to maintenance or from maintenance to adoption throughout the study. The initial classification on day 22 will be cross-validated with the self-report stage of change measure, self-reported physical activity level from the International Physical Activity Questionnaire, and physical activity intention item from the baseline questionnaire

Data and Compliance Monitoring

During EMA measurement bursts, participants are shown their compliance (ie, number of prompted surveys and number of completed surveys) in real time via the persistent study notification. Study staff perform real-time remote monitoring of participant compliance of all the above data collection modes. On a weekly basis, staff review data uploaded to the study server and contact participants by email or text message in the case of missing data to encourage compliance and address technical issues. The smartphone app is aware of the status of the phone and watch (ie, if the watch is being worn and sending data, if survey responses are being received, if devices are being properly charged daily), and the smartphone automatically prompts participants via notifications to encourage proper watch use throughout the study. Study staff withdraw participants from the study due to technical or participant issues that lead to poor data integrity, missing data, or ongoing low compliance. To aid attrition, after completing 9 months in the study, participants were allowed more leniency in missing smartphone surveys. Participants are sent a birthday card and quarterly newsletters to keep them engaged in the study to maintain compliance with study procedures. Participants are given a number and instructed to text study staff with any questions, concerns, or technical issues.

Given that this is one of the first studies to collect intensive longitudinal data over the course of an entire 12-month period, with intensive (ie, hourly) within-day self-reported measurement, we made the intentional choice to prioritize representation of the subject instead of representation of the population. Our goal was to minimize noncompliance and missing data, as both lead to an inaccurate representation of an individual's daily life. Therefore, we decided to proactively remove participants from the study with low compliance given that this leads to biased data at the individual level. When recruiting for the study, we chose recruitment methods that would ensure a diverse sample, but we did not intend our sample to be representative of the entire population (given our intentional focus on those who could be compliant with the protocol). We acknowledge that our findings will not generalize to a broader population of young adults. However, our decision helps ensure that data will be generalizable to each individual and provide a reasonably accurate depiction of each individual's daily life across a 12-month period. This study is part of early phase work that aims to examine the feasibility of the intensive data collection methods.

Incentives

Participants can receive up to US $1260 for compliance with the study procedures. Each month (4-week period), participants can earn up to US $100, which includes US $20 for wearing the smartwatch at least 22 hours/day on at least 24 days and US $20 for answering at least 24 of the EOD EMA prompts. Participants receive US $10 for each EMA burst period they complete at least 8 prompts per day (2 EMA bursts per month; up to US $20). In addition, if a participant answers more than 11 EMA burst prompts on a given day, the participant receives a US $5 bonus per day (8 days per month; up to US $40/month). Participants are provided with their compensation electronically monthly. Participants who complete the 12-month data collection period may also keep their smartwatch at the end of the study.

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Analytic Approach

Overview

Data analyses will combine idiographic (person-specific, data-driven) and nomothetic (generalizable, theory-driven) approaches.

Idiographic Approach

To test idiographic effects, statistical machine learning (ML) models will identify specific combinations of reflective and reactive variables predicting behavior for each person. A reduced set of key variables (included in the ML algorithms demonstrating ≥80% accuracy for at least half of the sample) will be selected for continuation into nomothetic testing, given that multilevel statistical models can only handle a limited number of variables. ML will also identify frequently occurring reflective-reactive variable pairings to be tested in targeted multilevel statistical interactions in the nomothetic phase.

Nomothetic Approach

We will use generalized linear mixed models (GLMMs) for nonnormal dependent variables, which adjust for clustering within subjects, allow for varying measurement schedules, and incorporate random effects. We will generate between-subject and within-subject versions of the time-varying predictors and moderators, representing their deviations from the subject and grand mean, respectively. To examine the likelihood of a *behavior episode*, we will test a 3-level model (level 1, occasion; level 2, measurement burst; level 3, person), and to examine the likelihood of a *behavior lapse*, we will test a 2-level version of this model (level 1, occasion; level 2, person). To examine whether the phase of behavior change (adoption vs maintenance) moderates within-subject effects, we will add within-subject and between-subject product interaction terms for the following time-varying moderators (ie, coded at the day level): being in the adoption versus maintenance phase (binary) and duration of maintenance (continuous).

Sample Size Estimation

ML algorithm training and testing are most effective when benchmark data sets fully represent the complexity of the phenomena being modeled. Given the exploratory nature of the person-specific ILD modeling, we aim to collect as much data as possible from each individual for the longest time frame reasonable given what we believe, based on prior work [55-57], is an acceptable EMA burden. We will have continuous data on reactive factors and behavior for 12 months, and for the EMA data on reflective factors, we will have up to 1901 observations per person (n=365 EOD EMA prompts+16×96 burst EMA prompts).

For the multilevel modeling, our most stringent sample size requirements will be to test between-subject effects. In G*Power (ver. 3.1.9.2) software, a sample size of 210 people (after accounting for 30% attrition) will have statistical power >0.80 with a 5% type I error rate to detect small effect sizes (odds ratios of 1.55-1.66) in two-sided logistic regressions. Given that the hypothesized within-subject effects will have much larger level-1 sample sizes (equivalent to the number of observations nested within people), we should have sufficient power to detect small to very small effects for all the remaining associations.

Results

The study recruited young adults nationally (N=246). Rolling recruitment began in March 2020 and ended August 2021. Data collection will continue until August 2022.

Of the 332 participants who consented into the study, 51.5% (n=171) self-identified as a woman, 44.3% (n=147) as a man, and 4.2% (n=14) as nonbinary. Approximately half of the participants identified as nonwhite (n=184, 55.4%) and 26.0% (n=86) of participants identified as Hispanic or Latino. The mean age of participants was 23.6 (SD 3.2) years. Of the 290 participants who completed the baseline survey, 55.5% (n=161) were employed for wages, 49.3% (n=143) were students, and 13.5% (n=42) were out of work. Most participants lived at home with parents or guardians (135/290, 46.6%) or with their spouse or romantic partner (71/290, 24.5%). When describing their personal financial situation, 21.2% (61/290) of participants indicated that they “just meet” or “don’t meet” basic expenses.

Of the 246 participants fully enrolled in the study, 218 (88.6%) completed at least 3 months of data collection, 182 (74.0%) completed at least 6 months of data collection, and 148 (60.2%) completed at least 9 months of data collection to date. We expect that at least 50% of participants will complete the full 12 months of the study period.

Discussion

The TIME study will be one of the first studies to use wearable smartphone and smartwatch technology to collect continuous data on physical activity, sedentary behavior, sleep, and their determinants across a 12-month period. The study aims to predict within-subject variation in the likelihood of behavior “episodes” and “lapses” as a function of reflective and reactive factors. We hypothesize that compared to models including only reflective variables, models that also include reactive variables will more accurately predict physical activity, sedentary, and sleep behavior episodes and lapses. Furthermore, we hypothesize that reflective variables will be less predictive (and reactive variables will be more predictive) of behavior episodes and lapses during the maintenance (vs adoption) phase of behavior change. Finally, we hypothesize that individuals who exhibit greater influence of reactive (versus reflective) variables on within-subject variation in behavior will be more likely to maintain the behavior across 12 months (without a relapse). This study advances beyond existing multimodal data sets owing to its intensive, innovative design. Out study is designed to test a dual-process model using a multimeasurement burst design across 12 months and passive data collection of physical activity, sedentary behavior, and sleep across the 24-hour activity cycle. Other existing multimodal studies were either of shorter duration, collected fewer EMA data points per day and per year, and/or had a smaller sample size.

Use of mobile technology to gather data with greater specification across time, situations, behaviors, and people has the potential to lead to the development of new theories and

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models that better explain health behavior than common frameworks. A new framework could provide opportunities to engage with questions about temporal specificity, including whether explanatory factors and behavior are temporally synchronous (ie, co-occur), the time scales across which effects unfold (eg, minutes/hours), the directionality of the effects (ie, antecedents vs consequences), and whether there are differences in the strength of effects across time (ie, time-varying effects). This framework may also address situational specificity such as determining under what combinations of conditions, contexts, or exposures (eg, environmental, affective, biological) the explanatory factors have the greatest effects (ie, time-varying moderators). The framework might further address behavioral specificity such as identifying the factors that are more predictive for different types of behavior (eg, leisure vs travel physical activity, homework vs watching TV) and person specificity, including identifying the sets of factors that are more predictive for certain people. Specification in these domains could offer a dramatic shift in the way that theories are developed, and would follow recent calls from the National Institutes of Health for more personalized/precision approaches to medicine [58,59].

Additionally, this study may help researchers understand the methodological and computational requirements of intensively adaptive interventions [60] or just-in-time adaptive interventions [61,62], which aim to deliver personalized behavior change strategies under the conditions when they will be most effective. The TIME study could yield information about the (1) number and composition of variables, (2) duration of the observation period, and (3) time delay between antecedent and behavior to accurately predict behavior. The study might also provide insight into whether there are discernible patterns or commonalities among people in the sets of explanatory factors of individual behaviors. The ability to reliably put people in these larger "bins," if warranted, can (1) allow researchers to focus on developing a smaller number of intervention strategies targeting groups of people instead of separate interventions for each person, which can conserve resources and allow for greater efficiency; and (2) justify the foregoing of large and costly observation periods to determine unique sets of predictive factors for each individual prior to intervention development. Development of these targeted invention strategies is one of the many possible applications of ILD studies.

There are limitations of the study that must be acknowledged. Our use of GLMM and ML to perform data-driven analyses through running multiple models could be subject to overfitting and overgeneralization. Thus, the findings from this study should be interpreted with caution until they can be replicated in other studies. Additionally, our ML models will be limited by the diversity of the sample we have recruited and our results will lack generalizability to certain populations.

Overall, we anticipate that results from the TIME study will challenge current assumptions about, and yield new insights into, the fundamental structure and function of variables comprising health behavior theories, and eventually result in the development of more predictive models and personalized interventions targeting a wide variety of health behaviors.

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Conflicts of Interest

None declared.

Multimedia Appendix 1
Ecological momentary assessment questions presented in the TIME study.
[DOCX File , 41 KB - resprot_v11i7e36666_app1.docx]

References

1. Hill JO, Wyatt HR. Role of physical activity in preventing and treating obesity. J Appl Physiol 2005 Aug;99(2):765-770 [FREE Full text] [doi: 10.1152/japplphysiol.00137.2005] [Medline: 16020440]
2. Patel HSF, Hu FB. Short sleep duration and weight gain: a systematic review. Obesity 2008 Mar;16(3):643-653. [doi: 10.1038/oby.2007.118] [Medline: 18239586]
3. Thorp AA, Owen N, Neuhaus M, Dunstan DW. Sedentary behaviors and subsequent health outcomes in adults a systematic review of longitudinal studies, 1996-2011. Am J Prev Med 2011 Aug;41(2):207-215. [doi: 10.1016/j.amepre.2011.05.004] [Medline: 21767729]
4. Adams K, Leitzmann M, Ballard-Barbash R, Albanes D, Harris TB, Hollenbeck A, et al. Body mass and weight change in adults in relation to mortality risk. Am J Epidemiol 2014 Jan 15;179(2):135-144 [FREE Full text] [doi: 10.1093/aje/kwt254] [Medline: 24173550]
5. Al-Goblan AS, Al-Alfi MA, Khan M. Mechanism linking diabetes mellitus and obesity. Diabetes Metab Syndr Obes 2014;7:587-591. [doi: 10.2147/DMSO.S67400] [Medline: 25506234]

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6. Fan J, Song Y, Chen Y, Hui R, Zhang W. Combined effect of obesity and cardio-metabolic abnormality on the risk of cardiovascular disease: a meta-analysis of prospective cohort studies. Int J Cardiol 2013 Oct 12;168(5):4761-4768. [doi: 10.1016/j.ijcard.2013.07.230] [Medline: 23972953]
7. Zheng Y, Manson JE, Yuan C, Liang MH, Grodstein F, Stampfer MJ, et al. Associations of weight gain from early to middle adulthood with major health outcomes later in life. JAMA 2017 Jul 18;318(3):255-269 [FREE Full text] [doi: 10.1001/jama.2017.7092] [Medline: 28719691]
8. Zick C, Smith K, Brown B, Fan J, Kowaleski-Jones L. Physical activity during the transition from adolescence to adulthood. J Phys Act Health 2007 Apr;4(2):125-137. [doi: 10.1123/jpah.4.2.125] [Medline: 17570883]
9. Gordon-Larsen P, Nelson MC, Popkin BM. Longitudinal physical activity and sedentary behavior trends: adolescence to adulthood. Am J Prev Med 2004 Nov;27(4):277-283. [doi: 10.1016/j.amepre.2004.07.006] [Medline: 15488356]
10. Hayley AC, Skogen JC, Øverland S, Wold B, Williams LJ, Kennedy GA, et al. Trajectories and stability of self-reported short sleep duration from adolescence to adulthood. J Sleep Res 2015 Dec 14;24(6):621-628. [doi: 10.1111/jsr.12316] [Medline: 26172979]
11. Wood W, Neal DT. Behav Sci Policy 2016;2(1):71-83. [doi: 10.1353/bsp.2016.0008]
12. Fjeldsoe B, Neuhaus M, Winkler E, Eakin E. Systematic review of maintenance of behavior change following physical activity and dietary interventions. Health Psychol 2011 Jan;30(1):99-109. [doi: 10.1037/a0021974] [Medline: 21299298]
13. Riley WT, Rivera DE, Atienza AA, Nilsen W, Allison SM, Mermelstein R. Health behavior models in the age of mobile interventions: are our theories up to the task? Transl Behav Med 2011 Mar 24;1(1):53-71 [FREE Full text] [doi: 10.1007/s13142-011-0021-7] [Medline: 21796270]
14. Hagger M, Chatzisarantis N, Biddle S. A meta-analytic review of the theories of reasoned action and planned behavior in physical activity: Predictive validity and the contribution of additional variables. J Sport Exerc Psychol 2002;24(1):3-32. [doi: 10.1123/jsep.24.1.3]
15. Rothman AJ. Toward a theory-based analysis of behavioral maintenance. Health Psychol 2000 Jan;19(1S):64-69. [doi: 10.1037/0278-6133.19.suppl1.64] [Medline: 10709949]
16. Kwasnicka D, Dombrowski SU, White M, Sniehotta F. Theoretical explanations for maintenance of behaviour change: a systematic review of behaviour theories. Health Psychol Rev 2016 Sep;10(3):277-296 [FREE Full text] [doi: 10.1080/17437199.2016.1151372] [Medline: 26854092]
17. Strack F, Deutsch R. Reflective and impulsive determinants of social behavior. Pers Soc Psychol Rev 2004 Dec 21;8(3):220-247. [doi: 10.1207/s15327957pspr0803_1] [Medline: 15454347]
18. Chaiken S, Trope Y. Dual-process theories in social psychology. New York, NY: Guilford Press; 1999.
19. Evans JSBT. Dual-processing accounts of reasoning, judgment, and social cognition. Annu Rev Psychol 2008 Jan 01;59(1):255-278. [doi: 10.1146/annurev.psych.59.103006.093629] [Medline: 18154502]
20. Rosenstock IM, Strecher VJ, Becker MH. Social learning theory and the health belief model. Health Educ Quart 2016 Sep 04;15(2):175-183. [doi: 10.1177/109019818801500203]
21. Sheppard BH, Hartwick J, Warshaw PR. The theory of reasoned action: a meta-analysis of past research with recommendations for modifications and future research. J Consum Res 1988 Dec;15(3):325. [doi: 10.1086/209170]
22. Ajzen I. From intentions to actions: A theory of planned behavior. In: Kuhl J, Beckmann J, editors. Action Control. SSSP Springer Series in Social Psychology. Berlin, Heidelberg: Springer; 1985:11-39.
23. Bandura A. Social cognitive theory: an agentic perspective. Annu Rev Psychol 2001 Feb;52(1):1-26. [doi: 10.1146/annurev.psych.52.1.1] [Medline: 11148297]
24. Wood W, Labrecque J, Lin P, Rünger D. Habits in dual process models. In: Sherman JW, Gawraonski B, Trope Y, editors. Dual process theories of the social mind. New York, NY: Guilford Press; 2014:371-385.
25. Wood W, Quinn JM, Kashy DA. Habits in everyday life: thought, emotion, and action. J Person Soc Psychol 2002;83(6):1281-1297. [doi: 10.1037/0022-3514.83.6.1281]
26. Deutsch R, Strack F. Duality models in social psychology: from dual processes to interacting systems. Psychol Inq 2006 Jul;17(3):166-172. [doi: 10.1207/s15327965pli1703_2]
27. Rothman AJ, Sheeran P, Wood W. Reflective and automatic processes in the initiation and maintenance of dietary change. Ann Behav Med 2009 Dec 29;38(S1):S4-S17. [doi: 10.1007/s12160-009-9118-3] [Medline: 19787308]
28. Nahum-Shani I, Hekler EB, Spruijt-Metz D. Building health behavior models to guide the development of just-in-time adaptive interventions: A pragmatic framework. Health Psychol 2015 Dec;34S(Suppl):1209-1219 [FREE Full text] [doi: 10.1037/hea0000306] [Medline: 26651462]
29. Dunton GF, Atienza AA. The need for time-intensive information in healthful eating and physical activity research: a timely topic. J Am Diet Assoc 2009 Jan;109(1):30-35. [doi: 10.1016/j.jada.2008.10.019] [Medline: 19103320]
30. Spruijt-Metz D, Nilsen W. Dynamic models of behavior for just-in-time adaptive interventions. IEEE Pervasive Comput 2014 Jul;13(3):13-17. [doi: 10.1109/mprv.2014.46]
31. Intille S, Haynes C, Maniar D, Ponnada A, Manjourides J. µEMA: microinteraction-based ecological momentary assessment (EMA) using a smartwatch. Proc ACM Int Conf Ubiquitous Comput 2016 Sep;2016:1124-1128 [FREE Full text] [doi: 10.1145/2971648.2971717] [Medline: 30238088]

XSL•FO
RenderX

32. Leventhal AM, Strong DR, Kirkpatrick MG, Unger JB, Sussman S, Riggs NR, et al. Association of electronic cigarette use with initiation of combustible tobacco product smoking in early adolescence. JAMA 2015 Aug 18;314(7):700-707 [FREE Full text] [doi: 10.1001/jama.2015.8950] [Medline: 26284721]
33. Harris PA, Scott KW, Lebo L, Hassan N, Lightner C, Pulley J. ResearchMatch: a national registry to recruit volunteers for clinical research. Acad Med 2012 Jan;87(1):66-73 [FREE Full text] [doi: 10.1097/ACM.0b013e31823ab7d2] [Medline: 22104055]
34. Dunton GF, Dzubur E, Kawabata K, Yanez B, Bo B, Intille S. Development of a smartphone application to measure physical activity using sensor-assisted self-report. Front Public Health 2014;2:12. [doi: 10.3389/fpubh.2014.00012] [Medline: 24616888]
35. Ester M, Kriegel H, Sander J, Xu X. A density-based algorithm for discovering clusters in large spatial databases with noise. 1996 Presented at: KDD'96: Second International Conference on Knowledge Discovery and Data Mining; August 2-4, 1996; Portland, OR p. 226-231.
36. Schubert E, Sander J, Ester M, Kriegel HP, Xu X. DBSCAN Revisited, Revisited. ACM Trans Database Syst 2017 Aug 24;42(3):1-21. [doi: 10.1145/3068335]
37. Ponnada A, Wang S, Chu D, Do B, Dunton G, Intille S. Intensive longitudinal data collection using microinteraction ecological momentary assessment: pilot and preliminary results. JMIR Form Res 2022 Feb 09;6(2):e32772 [FREE Full text] [doi: 10.2196/32772] [Medline: 35138253]
38. Behavioral Risk Factor Surveillance System Survey Questionnaire. Centers for Disease Control and Prevention. URL: https://www.cdc.gov/brfss/questionnaires/pdf-ques/2018_BRFSS_English_Questionnaire.pdf [accessed 2022-06-21]
39. Craig CL, Marshall AL, Sjöström M, Bauman AE, Booth ML, Ainsworth BE, et al. International physical activity questionnaire: 12-country reliability and validity. Med Sci Sports Exerc 2003 Aug;35(8):1381-1395. [doi: 10.1249/01.MSS.0000078924.61453.FB] [Medline: 12900694]
40. Sallis JF, Haskell WL, Wood PD, Fortmann SP, Rogers T, Blair SN, et al. Physical activity assessment methodology in the Five-City Project. Am J Epidemiol 1985 Jan;121(1):91-106. [doi: 10.1093/oxfordjournals.aje.a113987] [Medline: 3964995]
41. Sallis JF, McKenzie TL, Conway TL, Elder JP, Prochaska JJ, Brown M, et al. Environmental interventions for eating and physical activity: a randomized controlled trial in middle schools. Am J Prev Med 2003 Apr;24(3):209-217. [doi: 10.1016/s0749-3797(02)00646-3] [Medline: 12657338]
42. Rosenberg DE, Sallis JF, Kerr J, Maher J, Norman GJ, Durant N, et al. Brief scales to assess physical activity and sedentary equipment in the home. Int J Behav Nutr Phys Act 2010 Jan 31;7:10 [FREE Full text] [doi: 10.1186/1479-5868-7-10] [Medline: 20181057]
43. Jenkins CD, Stanton BA, Niemcryk SJ, Rose RM. A scale for the estimation of sleep problems in clinical research. J Clin Epidemiol 1988;41(4):313-321. [doi: 10.1016/0895-4356(88)90138-2] [Medline: 3351539]
44. Sleep Disorders Questionnaire. Accelerating Change Transformation Team - Alberta Medical Association. URL: http://www.topalbertadoctors.org/download/2176/Sleep%20Disorders%20Questionnaire.pdf?_20180509164306 [accessed 2022-06-21]
45. Thompson FE, Midthune D, Kahle L, Dodd KW. Development and evaluation of the National Cancer Institute's Dietary Screener Questionnaire scoring algorithms. J Nutr 2017 Jun 10;147(6):1226-1233 [FREE Full text] [doi: 10.3945/jn.116.246058] [Medline: 28490673]
46. Fairburn CG, Beglin S. Eating Disorder Examination Questionnaire (EDE-Q6.0). In: Fairburn CG, editor. Cognitive behavior therapy and eating disorders. New York, NY: Guilford Press; 2008:309-313.
47. Pang RD, Farrahi L, Glazier S, Sussman S, Leventhal AM. Depressive symptoms, negative urgency and substance use initiation in adolescents. Drug Alcohol Depend 2014 Nov 01;144:225-230 [FREE Full text] [doi: 10.1016/j.drugalcdep.2014.09.771] [Medline: 25280962]
48. Norris AE, Ford K, Bova CA. Psychometrics of a brief acculturation scale for Hispanics in a probability sample of urban Hispanic adolescents and young adults. Hisp J Behav Sci 2016 Jul 25;18(1):29-38. [doi: 10.1177/07399863960181004]
49. Jankowska MM, Schipperijn J, Kerr J. A framework for using GPS data in physical activity and sedentary behavior studies. Exerc Sport Sci Rev 2015 Jan;43(1):48-56 [FREE Full text] [doi: 10.1249/JES.0000000000000035] [Medline: 25390297]
50. Zagalaz-Sánchez ML, Cachón-Zagalaz J, Sánchez-Zafra M, Lara-Sánchez A. Mini review of the use of the mobile phone and its repercussion in the deficit of physical activity. Front Psychol 2019 Jun 6;10:1307. [doi: 10.3389/fpsyg.2019.01307] [Medline: 31244720]
51. Turrisi TB, Bittel KM, West AB, Hojjatinia S, Hojjatinia S, Mama SK, et al. Seasons, weather, and device-measured movement behaviors: a scoping review from 2006 to 2020. Int J Behav Nutr Phys Act 2021 Feb 04;18(1):24 [FREE Full text] [doi: 10.1186/s12966-021-01091-1] [Medline: 33541375]
52. John D, Tang Q, Albinali F, Intille S. An open-source monitor-independent movement summary for accelerometer data processing. J Meas Phys Behav 2019 Dec;2(4):268-281 [FREE Full text] [doi: 10.1123/jmpb.2018-0068] [Medline: 34308270]

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53. Belcher B, Wolff-Hughes D, Dooley E, Staudenmayer J, Berrigan D, Eberhardt M, et al. US population-referenced percentiles for wrist-worn accelerometer-derived Activity. Med Sci Sports Exerc 2021 Nov 01;53(11):2455-2464. [doi: 10.1249/MSS.0000000000002726] [Medline: 34115727]
54. Tang QU, John D, Thapa-Chhetry B, Arguello DJ, Intille S. Posture and physical activity detection: impact of number of sensors and feature type. Med Sci Sports Exerc 2020 Aug;52(8):1834-1845 [FREE Full text] [doi: 10.1249/MSS.0000000000002306] [Medline: 32079910]
55. Dunton GF, Liao Y, Dzubur E, Leventhal AM, Huh J, Gruenewald T, et al. Investigating within-day and longitudinal effects of maternal stress on children's physical activity, dietary intake, and body composition: Protocol for the MATCH study. Contemp Clin Trials 2015 Jul;43:142-154 [FREE Full text] [doi: 10.1016/j.cct.2015.05.007] [Medline: 25987483]
56. Dunton GF, Dzubur E, Intille S. Feasibility and performance test of a real-time sensor-informed context-sensitive ecological momentary assessment to capture physical activity. J Med Internet Res 2016 Jun 01;18(6):e106 [FREE Full text] [doi: 10.2196/jmir.5398] [Medline: 27251313]
57. Dunton GF, Liao Y, Kawabata K, Intille S. Momentary assessment of adults' physical activity and sedentary behavior: feasibility and validity. Front Psychol 2012;3:260. [doi: 10.3389/fpsyg.2012.00260] [Medline: 22866046]
58. Collins FS, Varmus H. A new initiative on precision medicine. N Engl J Med 2015 Feb 26;372(9):793-795 [FREE Full text] [doi: 10.1056/NEJMp1500523] [Medline: 25635347]
59. Hamburg MA, Collins FS. The path to personalized medicine. N Engl J Med 2010 Jul 22;363(4):301-304. [doi: 10.1056/NEJMp1006304] [Medline: 20551152]
60. Riley WT, Serrano KJ, Nilsen W, Atienza AA. Mobile and wireless technologies in health behavior and the potential for intensively adaptive interventions. Curr Opin Psychol 2015 Oct 01;5:67-71 [FREE Full text] [doi: 10.1016/j.copsyc.2015.03.024] [Medline: 26086033]
61. Nahum-Shani I, Smith S, Spring BJ, Collins LM, Witkiewitz K, Tewari A, et al. Just-in-time adaptive interventions (JITAIs): an organizing framework for ongoing health behavior support. Technical Report No. 14-126. University Park, PA: The Methodology Center, Penn State; 2014.
62. Nahum-Shani I, Smith S, Spring B, Collins LM, Witkiewitz K, Tewari A, et al. Just-in-time adaptive interventions (JITAIs) in mobile health: key components and design principles for ongoing health behavior support. Ann Behav Med 2018 May 18;52(6):446-462 [FREE Full text] [doi: 10.1007/s12160-016-9830-8] [Medline: 27663578]

Abbreviations

API: application programming interface
AUC: area under the curve
CS: context-sensitive
EMA: ecological momentary assessment
EOD: end of day
GLMM: generalized linear mixed model
ILD: intensive longitudinal data collection
MIMS: Motion Independent Movement Summary
ML: machine learning
MVPA: moderate-to-vigorous physical activity
μEMA: microinteraction ecological momentary assessment
REDCap: Research Electronic Data Capture
SWaN: Sleep Wake and Non-wear algorithm
TIME: Temporal Influences on Movements and Exercise
USC: University of Southern California

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Protocol

Burnout and Associated Psychological Problems Among Teachers and the Impact of the Wellness4Teachers Supportive Text Messaging Program: Protocol for a Cross-sectional and Program Evaluation Study

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Abstract

Background: Stress, burnout, anxiety, and depression continue to be a problem among teachers worldwide. It is not presently known what the prevalence and correlates for these psychological problems are among teachers in Alberta and Nova Scotia. It is also not known if a supportive text message program (Wellness4Teachers) would be effective in reducing stress, burnout, anxiety, or depression symptoms among teachers.

Objective: The goal of this study is to evaluate the prevalence and correlates of stress, burnout, symptoms of anxiety, depression, and low resilience among elementary and high school teachers in Alberta and Nova Scotia, Canada. It also aims to determine if daily supportive text messages can help reduce the prevalence of these psychological problems in teachers.

Methods: This is a cross-sessional mixed methods study with data to be collected from subscribers of Wellness4Teachers using a web-based survey at baseline (onset of text messaging), 6 weeks, the program's midpoint (3 months), and end point (6 months). Teachers can subscribe to the Wellness4Teachers program by texting the keyword "TeachWell" to the program phone number. Outcome measures will be assessed using standardized rating scales and key informant interviews. Data will be analyzed with descriptive and inferential statistics using SPSS and thematic analysis using NVivo.

Results: The results of this study are expected 24 months after program launch. It is expected that the prevalence of stress, burnout, anxiety, depression, and low resilience among teachers in Alberta and Nova Scotia would be comparable to those reported in other jurisdictions. It is also expected that factors such as gender, number of years teaching, grade of teaching, and school type (elementary vs high school) will have an association with burnout and other psychological disorders among teachers. Furthermore, it is expected that Wellness4Teachers will reduce the prevalence and severity of psychological problems in teachers, and subscriber satisfaction will be high.

Conclusions: The Wellness4Teachers project will provide key information regarding prevalence and correlates of common mental health conditions in teachers in Alberta and Nova Scotia, as well as the impact of daily supportive text messages on these mental health parameters. Information from this study will be useful for informing policy and decision-making concerning psychological interventions for schoolteachers.

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KEYWORDS

burnout; stress; Wellness4Teachers; anxiety; depression; e-mental health; teachers; support; text message; mental health; SMS; high school; elementary school; prevalence; psychological intervention; school

Introduction

Background

Educators and the public alike see stress and burnout as a distinct problem of the teaching profession [1,2]. Burnout is defined as a state of emotional, mental, and physical exhaustion resulting from prolonged and lengthy stress at work [3,4], as well as a response to chronic emotional and interpersonal stressors. Burnout is defined by the 3 dimensions of emotional exhaustion, cynicism, and inefficacy [5]. Emotional exhaustion represents emotional depletion and loss of energy; depersonalization or cynicism is the interpersonal dimension of burnout and refers to a negative, callous, or excessively detached response to other people. Reduced accomplishment describes the self-evaluation dimension of burnout and refers to feelings of incompetence and a lack of achievement and productivity at work [5,6]. In a cross-sectional study, 33.3% of teachers reported high burnout while 27.6% were at risk for having moderate burnout [7]. Similarly, 34.9% of teachers indicated they might be threatened by burnout syndrome [8].

Literature shows that teachers experience considerable stress in the workplace resulting in higher burnout rates, which poses a health risk [7,9]. A recent study by Li et al [10] reported that 53.2 % of teachers identified work as a source of long-term stress, leading to burnout. The results of a transversal study conducted in Tunisia reported that most teachers (66.4%) acknowledged being stressed at work, and burnout syndrome was found in 21% of those teachers [3]. A systematic review indicated that burnout was an important predictor of both physical and psychological consequences, including insomnia, depressive symptoms, and mortality below the age of 45 years; hospitalization for mental disorders; and psychological ill-health symptoms [11]. Another study reported that physical illnesses are more common among individuals with burnout compared with those without (64% vs 54%; $P<.001$) with increased prevalence of diseases associated with severity of burnout [12]. A study finding also showed that high burnout was associated with a high level of emotional exhaustion, low personal accomplishment, and depersonalization, while low burnout was linked to high personal accomplishment [7]. The professional outcomes of burnout include job dissatisfaction and absenteeism [11]. Absence due to sickness was more prevalent among employees with burnout compared with those without burnout [13]. The level of satisfaction is a significant factor that impacts the mental and physical health of teachers as well as other workers. Those with low job satisfaction are more susceptible to experiencing burnout, high anxiety levels, depression, and low self-esteem [7,14]. A study also showed that participants who reported high social anxiety levels reported high burnout levels as well [15]. A survey conducted in Canada and the United States confirmed that workplace improvements could prevent adverse sequelae, improve health outcomes, and reduce health care expenditures [16]. Data on the prevalence of burnout and other psychological problems among teachers in Canada are limited in the literature. It has been suggested that this is because North American jurisdictions have been hesitant to recognize burnout as a clinical diagnosis, partly due to concerns about increasing requests for disability coverage [6].

The relationship between burnout and health exhibits complicated pattern in the sense that poor health contributes to burnout, and burnout contributes to poor health [17]. Burnout is a risk factor for poor physical and mental well-being, and it may adversely affect health [11,18]. There is increasing evidence that burnout as a stress response represents a risk factor not only for depression but also for cardiovascular and other somatic diseases [19]. Burnout is occupational-specific dysphoria, which is different from depression—a general mental illness [5]. Burnout is regarded as a stress-related state, and the rates of clinical depression increase with the severity of burnout [19]. Burnout is also job related and dependent on the situation or condition, while depression is more general and context - free [6]. Cross-sectional studies showed that there is a relationship between burnout and depression with greater risk of major depressive disorder (MDD) when burnout is severe [12]. Teachers with MDD also had higher levels of perceived stress, anxiety, disorder, and lower quality of life [20]; moreover, poor workplace environment was a factor associated with both increased anxiety and depressive symptoms [21]. The published results of a study reported a high prevalence of depression (49.1%) among teachers [22] as well as a relatively high prevalence of anxiety 68.0% [23].

In a longitudinal study, individual teachers who experienced an increase in the states of burnout had an increase in depression in comparison to those with decrease in burnout, which corresponded to less depression [7,24]. This was also observed in a study where 86% of the teachers who identified as burned-out met the criteria for a provisional diagnosis of depression [25].

The results of a study in Quebec, Canada found that the proportion of teachers who reported a high level of psychological distress was twice as high (40%) than that reported for a Quebec-wide sample (20%) [26], an indication that teachers in Canada are also prone to stress. The ability to be able to cope under stress and pressure is an important factor to reduce burnout. Self-efficacy is viewed as a significant personal resource associated with coping with stress, and teacher's self-efficacy was positively correlated with general self-efficacy but negatively with job burnout [27]. According to psychologists, resilience is the process of adapting well in the face of adversity, trauma, tragedy, threats, or significant sources of stress including workplace stressors [28]. Low resilience is predicted to reduce the individual's ability to cope with stress and therefore will lead to increased levels of burnout. Increased levels of job support, however, were a protective factor against emotional exhaustion [29]. A study's results also indicated that the prevalence of resilience was exclusively

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predicted by factors including the participant's level of trauma exposure, social support, and recent and past life stressors [30].

Elementary and high school teachers must constantly deal with students' discipline issues while at the same time ensuring the timely delivery of the curriculum. Teachers must also deal with their own personal and family day-to-day stressors while helping to support students under their care. This leads to heightened levels of occupational stress and amplified risk of mental disorders [1]. The stress of the job sometimes takes a toll on the teachers, giving rise to burnout, increased anxiety and depression, and sometimes reduced resilience [5,17,31]. Meditation is effective in improving resilience, psychological distress, fatigue, and burnout. Thus, teachers may benefit from in-school wellness programs that incorporate mindfulness and meditation [31]. Additionally, the quest for professional fulfillment is more challenging in schools with high discipline issues and poor classroom settings. Furthermore, in the last 2 years, the global pandemic has led to changes in the school system, including intermittent web-based learning, closure of schools, and cancellation of provincial exams, thus creating major uncertainties for both students and teachers. It is currently unknown if the additional stressors experienced from the pandemic impacts the levels of stress, anxiety, depression, burnout, and resilience in teachers in elementary and high schools. Given the aforementioned, teachers may benefit from in-school intervention and wellness programs to alleviate their stress and burnout. Meditation techniques such as mindfulness have been suggested to help teachers cope with stress and burnout. Mindfulness is the practice of bringing awareness to the here and now using a variety of methods [32], and it has been suggested as beneficial in coping with job-related stress and burnout in the teaching profession [33,34]. Mindfulness can also improve the interpersonal faculties of teachers' sense of efficacy and perceived stress [33], as well as reducing depression [34]. However, the nature of these programs requires focusing and concentration, and this can be challenging to pursue in the busyness of the school environment and especially when teachers are stressed or burnt-out. Thus, the teachers may not be in the position to complete these programs. As mentioned, these programs can be time-consuming and may require teachers to consciously set time apart to participate. In addition, mindfulness may not be easily accessible and scalable in all schools. Furthermore, mindfulness may not be suitable or convenient for some teachers. An innovative way to offer intervention to teachers is through mobile text technology.

Mobile text technology is a unique and innovative way that offers a convenient, low-cost, and easily accessible way of delivering psychological interventions to the general public with mental health problems [35]. Supportive text messages can be used to supplement mental health therapy and hence indirectly reduce waitlist and the number of days required to attend group-based or face-to-face therapy programs that span months and require a lot of human resources for their delivery. Text messages have been effectively used to support the mental health of the general Albertan population and was effective in reducing stress, anxiety, and depression [36,37]. Supportive text messaging has also been used to reduce depression and increase abstinence duration in alcohol use disorder [38,39]. It is currently unknown whether supportive text messages will be helpful in reducing stress, anxiety, and depression while improving resilience among elementary and high school teachers. Given the generally high psychological burden among teachers and the evidence of effectiveness of supportive text message interventions in the literature, we propose to use Wellness4Teachers, a supportive text message program to help reduce stress, burnout, anxiety, and depression and to improve resilience among teachers.

Wellness4Teachers Program

Wellness4Teachers is a self-subscription daily supportive text message intervention program designed to address stress, burnout, anxiety, and depression, and to build resilience and improve professional satisfaction in teachers. The Wellness4Teachers program is powered by the ResilienceNHope web-based application [40] and provided by the Global Psychological eHealth Foundation [41]. ResilienceNHope is an evidence-informed e–mental health program that incorporates cognitive behavioral therapy based on daily supportive messages (mobile text or email), weekly mental health literacy information, web-based mental health self-assessments, and other mental health resources to help address part of the mental health literacy and the psychological treatment gap for individuals and communities globally. The Wellness4Teachers application will deliver one-way (noninteractive) psychological intervention messages to mobile phones. Subscribers will be made aware of the noninteractive nature of the supportive messaging program through the welcome and introductory message they receive upon subscribing to the program. They will also be offered the phone number of the mental health crisis service for their province or region to call if they are in crisis. The daily supportive messages delivered through the Wellness4Teachers program were crafted by psychiatrists, mental health therapists, and psychologists based on the cognitive behavioral therapy principles. The messages were further reviewed by the lead author, who is an education specialist, before they were built into the Wellness4Teachers program. Different messages will be received daily from a bank of messages. Examples of the text messages are as follows:

> *Deep breathing is a skill. You may need to practice it often and for more than 5 minutes to feel calmer. When you are feeling stressed or tense, shrug your shoulders up to your ears, hold for 5 seconds, release and repeat 2 more times. https://www.youtube.com/watch?v=cOOd-wlMMRg.*
>
> *As a teacher, it is very important for your well-being to spend time talking, laughing, and sharing with your colleagues. If you feel overwhelmed, take time to do something kind for yourself such as a cup of tea, or nature walk.*
>
> *Visualize yourself coping with the current challenging student behavior or workload. See yourself confidently facing these challenges. You can do it! No matter the challenges.*

Teachers in both Alberta and Nova Scotia can subscribe to the Wellness4Teachers program by texting "TeachWell" to a designated phone number to be automatically registered to

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receive supportive text messages. Teachers will receive supportive text messages at no cost to themselves or their institutions and will not receive any reimbursement or incentives for participating. Wellness4Teachers supportive text messages will be delivered to subscriber cell phones at 12 PM Mountain Standard Time in Alberta and 9 AM Atlantic Standard Time in Nova Scotia each day, and subscribers will receive the daily messages for 6 months. Based on a 10% dropout rate recorded for the Text4Hope program [36,37], the dropout rate expected for the Wellness4Teachers program is less than 15% [42].

The effectiveness of the ResilienceNHope suite of programs have been evaluated and established through several randomized controlled clinical trials and evaluations of population level programs. In a randomized controlled trial (RCT) in Fort McMurray, Alberta, Canada, involving 73 patients diagnosed with MDD, the intervention group (n=35, 48%) received twice-daily supportive text messages for 3 months (intervention group) as part of their outpatient treatment, while the control group (n=38, 52%) received a single thank-you message (control group) every fortnight (20.8, SD 11.7 vs 24.9, SD 11.5, respectively; $F_{1,60}$=4.83; P=.03, η_p^2=0.07). The mean difference in the Beck Depression Inventory (BDI) score change was significant with an effect size (Cohen d) of 0.67 [43]. In an earlier RCT in Dublin, Ireland, 54 patients with MDD and comorbid alcohol use disorder were also randomized to receive either twice-daily supportive text messages (intervention group) or a thank-you text message (control group) for 3 months. After adjusting for baseline scores, there was a statistically significant difference in the 3-month BDI-II scores between the intervention and control groups (8.5, SD 8.0 vs 16.7, SD 10.3, respectively; $F_{1,49}$=9.54; P=.003, η_p^2=0.17. The mean difference in change BDI-II scores was –7.9 (95% CI –13.06 to –2.76; Cohen d=0.85) [39]. Subscribers of Text4Hope (launched in Alberta during the COVID-19 pandemic [44]), who had been enrolled for 6 weeks (intervention group) had a significantly lower prevalence of moderate-to-high stress (78.8% vs 88.0%); moderate-to-high anxiety symptoms (31.4% vs 46.5%); and moderate-to-high depression symptoms (36.8% vs 52.1%), suicidal ideation (16.9% vs 26.6%), and disturbed sleep (76.9% vs 85.1%) compared to new subscribers, respectively, during the same time period (control group) [45]. Furthermore, there were statistically significant reductions in both the prevalence and mean scores on standardized measures for stress, anxiety, and depression at 6 weeks and 3 months for subscribers to the Text4Hope program [36,37].

Study Aims

One goal of this study is to evaluate the prevalence and correlates of burnout, probable mental health disorders, and low resilience among elementary and high school teachers in Alberta and Nova Scotia, Canada. Another goal of this study is to determine if daily supportive text messages can help reduce the prevalence of burnout, stress, symptoms of anxiety, and depression, and improve resilience among elementary and high school teachers (Textbox 1).

Textbox 1. Study objectives.

Main objectives

- To determine the prevalence and correlates of burnout, moderate to high stress, likely generalized anxiety disorder, likely major depressive disorder, and low resilience among elementary and high school teachers in Alberta and Nova Scotia
- To determine if the daily supportive text messaging program, Wellness4Teachers, can reduce the prevalence and severity of stress, burnout, anxiety, and depression, and to improve resilience among elementary and high school teachers in Alberta and Nova Scotia
- To assess Wellness4Teachers program subscriber experience and satisfaction with the daily supportive text messaging program

Methods

Study Design

This study will use a mixed-methods quantitative and qualitative cross-sectional survey design. Quantitative data will be collected using web-based–administered questionnaires through the University of Alberta REDCap platform [46], a secure web application for building and managing web-based surveys and databases. Qualitative data will be collected through key informant interviews.

The web-based questionnaires will be designed to collect demographic, professional, and clinical variables including stress, burnout, anxiety, depression, and resilience. Follow-up surveys will also include subscriber experience and satisfaction questions. Teachers in Alberta and Nova Scotia will be invited to subscribe to the Wellness4Teachers program through an advertisement organized in collaboration with Alberta Teachers Association, the Alberta School Boards Association, the Nova Scotia School Boards Association, and the Nova Scotia Teachers Union. The web-based surveys will be distributed to subscribers upon enrollment, at 6 weeks, 3 months, and 6 months. Key informant interview questionnaire will be developed to assess and explore the factors that contribute to stress, burnout, anxiety, and depression among teachers, the impact of the Wellness4Teachers program on the levels of these mental health variables in subscribers, and subscriber satisfaction with the daily supportive text messaging program.

Ethics Approval

The study has approval from the University of Alberta Ethics Review Board (Pro00117558) and is currently seeking approval from the Dalhousie University Human Research Ethics Review Board. Consent to participate will be implied when participants complete and submit the web-based survey responses.

Study Setting

The study will occur in Alberta and Nova Scotia. Alberta is a province in Western Canada, with an estimated population of 4,067,175 in 2016 [47]. Elementary and high schools in Alberta are run by 61 school boards [48]. In 2013, Alberta's school

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jurisdictions employed approximately 35,000 full-time equivalent teachers. Alberta has more than 150 private school authorities, which operate about 180 schools and serve more than 38,000 students [49]. Nova Scotia is a province in Eastern Canada, with a population of 1 million residents in 2021, according to Statistics Canada [50]. Elementary and high schools in Nova Scotia are located in 8 school districts with 7 English-language school boards and 1 French–first language school board. Public schools in Nova Scotia are managed by the provincial department of education, called Education and Early Childhood Development. There were 372 public schools in Nova Scotia in the 2017-18 school year [51,52]. Nova Scotia also has more than 20 private or independent schools, many of which are in Halifax, the provincial capital [53]. There are more than 10,000 public school teachers in Nova Scotia, who are represented by the Nova Scotia Teachers Union [54].

Outcomes and Measures

Clinical outcomes will be assessed using validated screening scales for self-reported symptoms, including Perceived Stress Scale (PSS-10; a score of ≥10 indicates a likely moderate or high stress) [55], the 7-item GAD scale (GAD-7; a score of ≥10 indicates likely generalized anxiety disorder) [56], the Patient Health Questionnaire-9 (PHQ-9; a score ≥10 indicates likely MDD) [57], and the Brief Resilience Scale (BRS; mean scores ranging from 1.00 to 2.99 indicate low resilience, from 3.00 to 4.30 suggest normal resilience, and from 4.31 to 5.00 suggest high resilience) [58,59].Validated scales have been chosen to better understand self-reported symptoms and potential symptom severity and to screen for the likely presence of psychopathology. These scales are not intended as diagnostic tools but instead are to identify risk factors and early symptoms of potential mental disorders such as depression and anxiety disorders. In addition, we will assess burnout using the Maslach Burnout Inventory (MBI) [60]. The MBI-Educators Survey will be used in this case, which is a version of the original MBI for use with educators, including teachers, administrators, other staff members, and volunteers working in any educational setting [61]. The primary outcome measures will be prevalence of moderate-to-high stress, burnout, likely GAD, likely MDD, and low resilience at baseline in subscribers of Wellness4Teachers. Other primary outcome measures will be changes in prevalence of moderate-to-high stress, burnout, likely GAD, likely MDD, and low resilience as well as changes in mean scores on the PSS-10, MBI, GAD-7, PHQ-9, and the BRS from baseline to 6 weeks, 3 months, and 6 months. Secondary outcome measures will include sociodemographic, clinical, and professional correlates of moderate-to-high stress, burnout, likely MDD, likely GAD, and low resilience among subscribers of Wellness4Teachers at baseline. An exploratory outcome will be a measurement of the adoption of the Wellness4Teachers program by teachers in Alberta and Nova Scotia. This will be assessed by measuring the proportion of the target population (teachers in Alberta and Nova Scotia) who subscribe to the daily supportive text messages.

Sample Size Estimation

With a teacher population of approximately 45,000 in Alberta and Nova Scotia, using a web-based script [62], we estimate that the sample size needed for our prevalence estimates with a 95% CI and 3% margin of error for moderate-to-high stress, burnout, likely GAD, likely MDD, and low resilience among teachers in Alberta and Nova Scotia is 1043. Based on the response rates achieved for the Text4Hope and Text4Mood programs in Alberta [35,63,64], we expect a maximum of 20% survey completion rate for the Wellness4Teachers program. Thus, to achieve the 1043 completed surveys at baseline, we expect to enroll 5515 teachers on the Wellness4Teachers program within 12 months.

Statistical Analysis

Quantitative data from the surveys will be analyzed using SPSS (version 25, IBM Corp) [65]. Descriptive statistics will be provided for demographic, clinical, and burnout-related variables based on the province of residence. Cross-tabular analyses using the chi-square test will explore the differences between elementary and high school teachers with respect to demographic, clinical, and professional variables. Descriptive characteristics will be presented as numbers and percentages, and a 2-tailed $P \leq .05$ will be used to determine statistical significance for all analyses. We will use the chi-square test and logistic regression analysis to identify demographic, clinical, and work-related correlates of anxiety, depression, stress, low resilience, and burnout for elementary and high school teachers separately. Furthermore, we will assess the impact of the Wellness4Teachers program in reducing moderate-to-high stress, burnout, likely GAD, likely MDD, and improving resilience among Wellness4Teachers subscribers by assessing the mean changes in these parameters from baseline to 6 weeks, 3 months, and 6 months using the 2-tailed paired *t* test. To assess the effects of the intervention against a control group, we will choose a defined period of 3 months during the study period (eg, from the beginning of November 2022 to the end of January 2023) and compare the prevalence and mean scores on standardized scales for stress, burnout, anxiety, and depression at 6 weeks for subscribers who have received the daily supportive text messages for 6 weeks (intervention group) to the baseline prevalence and mean scores on the same scales for new subscribers during the period (control group). Surveys with more than 50% missing responses will be omitted from data analysis. For the included survey responses, there will be no imputation for missing data, and the analysis and results will be based on completed survey data.

We will analyze qualitative data (obtained by audio recording and transcribing responses from key informant interviews) using thematic analysis with NVivo (version 9; QSR International). The results will be reported as themes and subthemes supported by verbatim quotes.

Hypothesis

We hypothesize that the prevalence of stress, burnout, symptoms of anxiety and depression, as well as low resilience among teachers in Alberta and Nova Scotia would be comparable to those reported in other jurisdictions [8,66].

We also hypothesize that factors such as gender, sex, age, marital status, number of years teaching, grade of teaching, and school type (elementary vs high school) will have an association

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with burnout and other psychological disorders in teachers [67-72].

Finally, we hypothesize that the Wellness4Teachers program will reduce the prevalence and severity of stress, anxiety, depression, burnout, and low resilience symptoms among teachers by at least 20% [43]. This specific hypothesis is based on related research findings. In the 2 RCTs conducted in Ireland and Canada, there was a greater than 20% reduction in depression symptom scores in the intervention group compared to the control group [73,74]. Furthermore, for the Text4Hope program in Alberta, there was a greater than 20% reduction in anxiety symptom scores in subscribers at 6 weeks and 3 months [36,37].

Results

The Wellness4Teachers program is expected to be launched in September 2022 when the new academic year is scheduled to begin. Enrollment will last for approximately 1 year, and data collection will continue for another 6 months. Study results will be disseminated with stakeholders in the education sector in Alberta and Nova Scotia and globally through workshops, conference presentations, and peer-reviewed publications.

Discussion

Expected Findings

Stress, burnout, anxiety, and depression can have a significant impact on the health, lifestyle, psychological safety, and well-being of teachers, leading to low levels of resilience and reduced professional fulfilment. The psychological impact is likely to be more significant for those with prior mental health conditions or those who have been exposed to previous traumas. Mental health support for groups such as teachers require innovative techniques that can provide support for more teachers. This protocol outlines the use of mobile health technology as a convenient, cost-effective, and accessible means for implementing a psychological intervention for teachers who may be experiencing stress, burnout, anxiety, and depression, and improve their overall resilience.

The outcomes of this study will be evaluated with standardized and empirically validated questionnaires. The findings will contribute to knowledge on eHealth approaches in the education sector and will provide key information about the prevalence rates of stress, burnout, anxiety, depression, and low resilience as well as their correlates in teachers. The findings will also provide evidence of effectiveness for the use of daily supportive text messaging programs to address stress, burnout, anxiety, depression, and low resilience among teachers. Information from this study will thus be critical and useful for informing school policy and decision makers regarding psychological interventions for teachers, especially during the ongoing COVID-19 pandemic or similar stressful situations. We hope that the outcome of this study will promote the integration of supportive text messaging into many organizations' occupational health programs to provide readily available psychological support to individuals who need it, while at the same time improving their overall resilience and promoting professional fulfilment.

Limitations of the Study

First, the self-report scales used to assess mental health variables such as likely MDD, although standardized, are not meant to be diagnostic. Second, it is possible that participants' demographics in the study may not reflect the demographics of the teachers' population in Alberta or Nova Scotia, and therefore the study findings may not be generalizable to all teachers in the 2 provinces. Furthermore, web-based surveys with survey links delivered through text messages usually achieve a response rate of less than 20% [42,63,64,75-78], and therefore it is possible that we may not achieve our desired sample size. Lastly, the supportive text messages will be delivered for 6 months, and the outcome measures will be evaluated at 6 weeks, 3 months, and the end point of 6 months. It is unclear what the effects of the intervention would be if it were prolonged. It is also unclear if the benefits of the intervention would wane with the cessation of the daily supportive text messages. These limitations notwithstanding, this study is the first to examine the prevalence and correlates of stress, burnout, anxiety, and depression among teachers in the provinces of Alberta and Nova Scotia in Canada, aided by a text message program. This study is also the first globally to assess if daily supportive text messages delivered through the Wellness4Teachers program can reduce the prevalence and severity of stress, burnout, anxiety, and depression, and improve resilience among elementary and high school teachers. The findings would therefore be of interest to policy makers, especially those working in the education sector.

Conclusion

The outcome of this study will establish the prevalence and correlates of the common risk factors for psychological disorders under study in teachers in Alberta and Nova Scotia. The study will have a significant impact on the management of stress, burnout, anxiety, depression, and low resilience among teachers. If the findings are positive, the Wellness4Teachers program can be promoted as a tool to support the mental health of teachers in Canada and internationally. The study outcome will also compliment policy decision-making for health care resource allocation in support of the education sector.

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Conflicts of Interest

None declared.

References

1. Hillert A, Koch S, Lehr D. [Burnout phenomenon exemplified by the teaching profession: paradigms, findings and perspectives of profession-related therapy and prevention approaches]. Nervenarzt 2013 Jul;84(7):806-812. [doi: 10.1007/s00115-013-3745-4] [Medline: 23836330]
2. Chang M. An Appraisal Perspective of Teacher Burnout: Examining the Emotional Work of Teachers. Educ Psychol Rev 2009 Jun 30;21(3):193-218. [doi: 10.1007/s10648-009-9106-y]
3. Chennoufi L, Ellouze F, Cherif W, Mersni M, M'rad MF. [Stress and burnout among Tunisian teachers]. Encephale 2012 Dec;38(6):480-487. [doi: 10.1016/j.encep.2011.12.012] [Medline: 23200614]
4. Burnout. Psychology Today. 2021. URL: https://www.psychologytoday.com/us/basics/burnout [accessed 2022-07-06]
5. Maslach C, Schaufeli WB, Leiter MP. Job burnout. Annu Rev Psychol 2001 Feb;52(1):397-422. [doi: 10.1146/annurev.psych.52.1.397] [Medline: 11148311]
6. Maslach C, Leiter MP. Understanding the burnout experience: recent research and its implications for psychiatry. World Psychiatry 2016 Jun 05;15(2):103-111 [FREE Full text] [doi: 10.1002/wps.20311] [Medline: 27265691]
7. Méndez I, Martínez-Ramón JP, Ruiz-Esteban C, García-Fernández JM. Latent Profiles of Burnout, Self-Esteem and Depressive Symptomatology among Teachers. Int J Environ Res Public Health 2020 Sep 16;17(18):6760 [FREE Full text] [doi: 10.3390/ijerph17186760] [Medline: 32948075]
8. Ptáček R, Vnukova M, Raboch J, Smetackova I, Sanders E, Svandova L, et al. Burnout Syndrome and Lifestyle Among Primary School Teachers: A Czech Representative Study. Med Sci Monit 2019 Jul 05;25:4974-4981. [doi: 10.12659/msm.914205]
9. Belcastro P, Gold RS. Teacher stress and burnout: implications for school health personnel. J Sch Health 1983 Sep;53(7):404-407. [doi: 10.1111/j.1746-1561.1983.tb03148.x] [Medline: 6556388]
10. Li S, Li Y, Lv H, Jiang R, Zhao P, Zheng X, et al. The prevalence and correlates of burnout among Chinese preschool teachers. BMC Public Health 2020 Feb 03;20(1):160 [FREE Full text] [doi: 10.1186/s12889-020-8287-7] [Medline: 32013939]
11. Salvagioni DAJ, Melanda FN, Mesas AE, González AD, Gabani FL, Andrade SMD. Physical, psychological and occupational consequences of job burnout: A systematic review of prospective studies. PLoS One 2017 Oct 4;12(10):e0185781 [FREE Full text] [doi: 10.1371/journal.pone.0185781] [Medline: 28977041]
12. Ahola K, Honkonen T, Isometsä E, Kalimo R, Nykyri E, Aromaa A, et al. The relationship between job-related burnout and depressive disorders--results from the Finnish Health 2000 Study. J Affect Disord 2005 Sep;88(1):55-62. [doi: 10.1016/j.jad.2005.06.004] [Medline: 16038984]
13. Ahola K, Kivimäki M, Honkonen T, Virtanen M, Koskinen S, Vahtera J, et al. Occupational burnout and medically certified sickness absence: a population-based study of Finnish employees. J Psychosom Res 2008 Feb;64(2):185-193. [doi: 10.1016/j.jpsychores.2007.06.022] [Medline: 18222132]
14. Montgomery C, Rupp AA. A Meta-Analysis for Exploring the Diverse Causes and Effects of Stress in Teachers. Canadian Journal of Education / Revue canadienne de l'éducation 2005;28(3):458. [doi: 10.2307/4126479]
15. Vasilopoulos S. Job burnout and its relation to social anxiety in teachers of primary education. Hellenic Journal of Psychology 2012;9:18-44.
16. Wu S, Singh-Carlson S, Odell A, Reynolds G, Su Y. Compassion Fatigue, Burnout, and Compassion Satisfaction Among Oncology Nurses in the United States and Canada. ONF 2016 Jul 1;43(4):E161-E169. [doi: 10.1188/16.onf.e161-e169]
17. Bakker AB, Maslach C. Burnout at Work: A Psychological Perspective. London, England: Psychology Press; 2014.
18. Chesak SS, Khalsa TK, Bhagra A, Jenkins SM, Bauer BA, Sood A. Stress Management and Resiliency Training for public school teachers and staff: A novel intervention to enhance resilience and positively impact student interactions. Complement Ther Clin Pract 2019 Nov;37:32-38 [FREE Full text] [doi: 10.1016/j.ctcp.2019.08.001] [Medline: 31445365]
19. Bianchi R, Laurent E, Schonfeld IS. Burnout: An analysis of the status quo. International Journal of Stress Management 2019;26(01):36-45 [FREE Full text] [doi: 10.4414/sanp.2010.02136]
20. Besse R, Howard K, Gonzalez S, Howard J. Major Depressive Disorder and Public School Teachers: Evaluating Occupational and Health Predictors and Outcomes. Journal of Applied Biobehavioral Research 2015 Jun 01;20(2):71-83. [doi: 10.1111/jabr.12043]
21. Peele M, Wolf S. Predictors of anxiety and depressive symptoms among teachers in Ghana: Evidence from a randomized controlled trial. Soc Sci Med 2020 May;253:112957 [FREE Full text] [doi: 10.1016/j.socscimed.2020.112957] [Medline: 32251932]
22. Hadi AA, Naing NN, Daud A, Nordin R. Work related depression among secondary school teachers in Kota Bharu, Kelantan, Malaysia. International Medical Journal 2008;15(2):145-152.
23. Othman Z, Sivasubramaniam V. Depression, anxiety, and stress among secondary school teachers in Klang, Malaysia. International Medical Journal 2019;26(2):71-74.

XSL•FO
RenderX

24. Bianchi R, Schonfeld IS, Laurent E. Burnout-depression overlap: a review. Clin Psychol Rev 2015;36:28-41.
25. Schonfeld IS, Bianchi R. Burnout and Depression: Two Entities or One? J Clin Psychol 2016 Jan 09;72(1):22-37. [doi: 10.1002/jclp.22229] [Medline: 26451877]
26. Biron C, Brun J, Ivers H. Extent and sources of occupational stress in university staff. Work 2008;30(4):511-522. [Medline: 18725713]
27. Baka. [Norwegian Teacher Self-Efficacy Scale - Psychometric properties of the Polish version of the scale]. Med Pr 2017 Oct 17;68(6):743-755 [FREE Full text] [doi: 10.13075/mp.5893.00569] [Medline: 28857090]
28. Building your resilience. American Psychological Association. URL: https://www.apa.org/topics/resilience/building-your-resilience [accessed 2022-07-06]
29. Aronsson G, Theorell T, Grape T, Hammarström A, Hogstedt C, Marteinsdottir I, et al. A systematic review including meta-analysis of work environment and burnout symptoms. BMC Public Health 2017 Mar 16;17(1):264 [FREE Full text] [doi: 10.1186/s12889-017-4153-7] [Medline: 28302088]
30. Bonanno GA, Galea S, Bucciarelli A, Vlahov D. What predicts psychological resilience after disaster? The role of demographics, resources, and life stress. Journal of Consulting and Clinical Psychology 2007;75(5):671-682. [doi: 10.1037/0022-006x.75.5.671]
31. Valosek L, Wendt S, Link J, Abrams A, Hipps J, Grant J, et al. Meditation Effective in Reducing Teacher Burnout and Improving Resilience: A Randomized Controlled Study. Front. Educ 2021 Mar 4:1-6. [doi: 10.3389/feduc.2021.627923]
32. Stathas SA, Frazer C. Mindfulness: being present in the moment. International Journal of Childbirth Education. 2015. URL: https://scholarworks.waldenu.edu/cgi/viewcontent.cgi?article=1052&context=sn_pubs [accessed 2022-07-06]
33. Tarrasch R, Berger R, Grossman D. Mindfulness and Compassion as Key Factors in Improving teacher's Well Being. Mindfulness 2020 Feb 10;11(4):1049-1061. [doi: 10.1007/s12671-020-01304-x]
34. Cheng X, Zhang H, Cao J, Ma Y. The Effect of Mindfulness-Based Programs on Psychological Distress and Burnout in Kindergarten Teachers: A Pilot Study. Early Childhood Educ J 2021 Aug 18:1-11. [doi: 10.1007/s10643-021-01254-6]
35. Agyapong V. Cross-sectional survey evaluating Text4Mood: mobile health program to reduce psychological treatment gap in mental healthcare in Alberta through daily supportive text messages. BMC Psychiatry 2016;16(1):378. [doi: 10.26226/morressier.58c95390d462b8028d891cb0]
36. Agyapong VI, Hrabok M, Shalaby R, Vuong W, Noble JM, Gusnowski A, et al. Text4Hope: Receiving Daily Supportive Text Messages for 3 Months During the COVID-19 Pandemic Reduces Stress, Anxiety, and Depression. Disaster Med Public Health Prep 2021 Feb 08:1-5 [FREE Full text] [doi: 10.1017/dmp.2021.27] [Medline: 33551009]
37. Agyapong VIO, Hrabok M, Vuong W, Shalaby R, Noble JM, Gusnowski A, et al. Changes in Stress, Anxiety, and Depression Levels of Subscribers to a Daily Supportive Text Message Program (Text4Hope) During the COVID-19 Pandemic: Cross-Sectional Survey Study. JMIR Ment Health 2020 Dec 18;7(12):e22423 [FREE Full text] [doi: 10.2196/22423] [Medline: 33296330]
38. Agyapong VIO, Milnes J, McLoughlin DM, Farren CK. Perception of patients with alcohol use disorder and comorbid depression about the usefulness of supportive text messages. THC 2013 Jan 01;21(1):31-39. [doi: 10.3233/thc-120707]
39. Agyapong VI, Ahern S, McLoughlin DM, Farren CK. Supportive text messaging for depression and comorbid alcohol use disorder: single-blind randomised trial. J Affect Disord 2012 Dec 10;141(2-3):168-176. [doi: 10.1016/j.jad.2012.02.040] [Medline: 22464008]
40. Building resilience and inspiring hope in individuals and communities globally. ResilienceNHope. URL: https://www.resiliencenhope.org/ [accessed 2022-07-06]
41. Closing the psychological treatment and mental health literacy gaps globally. Global Psychological eHealth Foundation. URL: https://www.gpehealth.org/ [accessed 2022-07-06]
42. Shalaby R, Vuong W, Hrabok M, Gusnowski A, Mrklas K, Li D, et al. Gender Differences in Satisfaction With a Text Messaging Program (Text4Hope) and Anticipated Receptivity to Technology-Based Health Support During the COVID-19 Pandemic: Cross-sectional Survey Study. JMIR Mhealth Uhealth 2021 Apr 15;9(4):e24184 [FREE Full text] [doi: 10.2196/24184] [Medline: 33750738]
43. Agyapong VIO, Mrklas K, Suen VYM, Rose MS, Jahn M, Gladue I, et al. Supportive text messages to reduce mood symptoms and problem drinking in patients with primary depression or alcohol use disorder: protocol for an implementation research study. JMIR Res Protoc 2015 May 15;4(2):e55 [FREE Full text] [doi: 10.2196/resprot.4371] [Medline: 25979786]
44. Agyapong VIO, Hrabok M, Vuong W, Gusnowski A, Shalaby R, Mrklas K, et al. Closing the Psychological Treatment Gap During the COVID-19 Pandemic With a Supportive Text Messaging Program: Protocol for Implementation and Evaluation. JMIR Res Protoc 2020 Jun 22;9(6):e19292. [doi: 10.2196/19292]
45. Agyapong VIO, Shalaby R, Hrabok M, Vuong W, Noble JM, Gusnowski A, et al. Mental Health Outreach via Supportive Text Messages during the COVID-19 Pandemic: Improved Mental Health and Reduced Suicidal Ideation after Six Weeks in Subscribers of Text4Hope Compared to a Control Population. Int J Environ Res Public Health 2021 Feb 23;18(4):2157 [FREE Full text] [doi: 10.3390/ijerph18042157] [Medline: 33672120]
46. REDCap. Vanderbilt University. URL: https://redcap.vanderbilt.edu/ [accessed 2022-07-06]
47. Focus on Geography Series, 2016 Census. Statistics Canada. 2016. URL: https://www12.statcan.gc.ca/census-recensement/2016/as-sa/fogs-spg/Facts-can-eng.cfm?Lang=Eng&GK=CAN&GC=01&TOPIC=1 [accessed 2022-07-06]

XSL•FO
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48. Alberta Schools Board Association. URL: https://www.asba.ab.ca/ [accessed 2022-07-06]
49. Private schools. Government of Alberta. URL: https://www.alberta.ca/private-schools.aspx [accessed 2022-07-06]
50. A big day for Nova Scotia. Statistics Canada. URL: https://www.statcan.gc.ca/o1/en/plus/245-big-day-nova-scotia [accessed 2022-07-06]
51. Byrne S. Nova Scotia. London, UK: Faber and Faber; 2008.
52. Internationally Educated Teachers Multi-Stakeholder Work Group. URL: https://teach-in-novascotia.ca/overviewnovascotia/overviewnovascotiaeecd/ [accessed 2022-07-06]
53. Nova Scotia Overview: Alternatives to Public Education. Internationally Educated Teachers Multi-Stakeholder Work Group. 2022. URL: https://teach-in-novascotia.ca/overviewnovascotia/overviewnovascotiaalts/ [accessed 2022-07-06]
54. Nova Scotia teachers recognized for making a difference. Nova Scotia Teachers Union. 2015. URL: https://nstu.ca/the-nstu/communications/the-media-room/education-news?c=nova-scotia-teachers-recognized-for-making-a-difference [accessed 2022-07-06]
55. Cohen S, Kamarck T, Mermelstein R. A Global Measure of Perceived Stress. Journal of Health and Social Behavior 1983 Dec;24(4):385. [doi: 10.2307/2136404]
56. Spitzer RL, Kroenke K, Williams JBW, Löwe B. A brief measure for assessing generalized anxiety disorder: the GAD-7. Arch Intern Med 2006 May 22;166(10):1092-1097. [doi: 10.1001/archinte.166.10.1092] [Medline: 16717171]
57. Kroenke K, Spitzer RL, Williams JBW. The PHQ-9: validity of a brief depression severity measure. J Gen Intern Med 2001 Sep;16(9):606-613 [FREE Full text] [doi: 10.1046/j.1525-1497.2001.016009606.x] [Medline: 11556941]
58. Smith BW, Dalen J, Wiggins K, Tooley E, Christopher P, Bernard J. The brief resilience scale: assessing the ability to bounce back. Int J Behav Med 2008 Sep;15(3):194-200. [doi: 10.1080/10705500802222972] [Medline: 18696313]
59. Smith BW, Epstein EM, Ortiz JA, Christopher PJ, Tooley EM. The foundations of resilience: what are the critical resources for bouncing back from stress? In: Resilience in Children, Adolescents, and Adults. New York, US: Springer; 2013:167-187.
60. Maslach C, Jackson SE, Leiter M. Maslach burnout inventory. In: Evaluating Stress: A Book of Resources. Michigan, US: Scarecrow Education; 1997:191-218.
61. MBI: Educators Survey. Mind Garden. 2022. URL: https://www.mindgarden.com/316-mbi-educators-survey [accessed 2022-07-06]
62. Sample size calculator. SurveyMonkey. URL: https://www.surveymonkey.com/mp/sample-size-calculator [accessed 2022-07-06]
63. Nwachukwu I, Nkire N, Shalaby R, Hrabok M, Vuong W, Gusnowski A, et al. COVID-19 Pandemic: Age-Related Differences in Measures of Stress, Anxiety and Depression in Canada. Int J Environ Res Public Health 2020 Sep 01;17(17):6366 [FREE Full text] [doi: 10.3390/ijerph17176366] [Medline: 32882922]
64. Abba-Aji A, Li D, Hrabok M, Shalaby R, Gusnowski A, Vuong W, et al. COVID-19 Pandemic and Mental Health: Prevalence and Correlates of New-Onset Obsessive-Compulsive Symptoms in a Canadian Province. Int J Environ Res Public Health 2020 Sep 24;17(19):6986 [FREE Full text] [doi: 10.3390/ijerph17196986] [Medline: 32987764]
65. Release notes: IBM® SPSS® Statistics 28. IBM support. URL: https://www.ibm.com/support/pages/release-notes-ibm%C2%AE-spss%C2%AE-statistics-28 [accessed 2022-07-06]
66. Katsantonis I. Factors Associated with Psychological Well-Being and Stress: A Cross-Cultural Perspective on Psychological Well-Being and Gender Differences in a Population of Teachers. PEDAGOGICAL RES 2020;5(4):em0066. [doi: 10.29333/pr/8235]
67. Ali MF, Kundra S, Alam MA, Alam M. Investigating stress, anxiety, social support and sex satisfaction on physical education and sports teachers during the COVID-19 pandemic. Heliyon 2021 Aug;7(8):e07860 [FREE Full text] [doi: 10.1016/j.heliyon.2021.e07860] [Medline: 34485739]
68. Desouky D, Allam H. Occupational stress, anxiety and depression among Egyptian teachers. J Epidemiol Glob Health 2017 Sep;7(3):191-198 [FREE Full text] [doi: 10.1016/j.jegh.2017.06.002] [Medline: 28756829]
69. Gosnell NM, O'Neal CR, Atapattu R. Stress, mental health, and self-care among refugee teachers in Malaysia. Asian American Journal of Psychology 2021 Sep;12(3):176-192. [doi: 10.1037/aap0000249]
70. Bianchi R, Manzano-García G, Rolland J. Is Burnout Primarily Linked to Work-Situated Factors? A Relative Weight Analytic Study. Front Psychol 2020 Jan 13;11:623912 [FREE Full text] [doi: 10.3389/fpsyg.2020.623912] [Medline: 33519650]
71. Ratanasiripong P, Ratanasiripong NT, Nungdanjark W, Thongthammarat Y, Toyama S. Mental health and burnout among teachers in Thailand. JHR 2021 Jan 13;36(3):404-416. [doi: 10.1108/jhr-05-2020-0181]
72. Akın MA. An Investigation into Teacher Burnout in Relatıon To Some Varibles. IJPE 2019 Aug 02;15(4):47-65. [doi: 10.29329/ijpe.2019.203.4]
73. Agyapong V. Randomized controlled pilot trial of supportive text messages for patients with depression. BMC Psychiatry 2017;17(1):286. [doi: 10.26226/morressier.58c95390d462b8028d891cc4]
74. Agyapong VI, Juhás M, Mrklas K, Hrabok M, Omeje J, Gladue I, et al. Randomized controlled pilot trial of supportive text messaging for alcohol use disorder patients. J Subst Abuse Treat 2018 Nov;94:74-80. [doi: 10.1016/j.jsat.2018.08.014] [Medline: 30243421]

XSL•FO
RenderX

75. Nkire N, Mrklas K, Hrabok M, Gusnowski A, Vuong W, Surood S, et al. COVID-19 Pandemic: Demographic Predictors of Self-Isolation or Self-Quarantine and Impact of Isolation and Quarantine on Perceived Stress, Anxiety, and Depression. Front Psychiatry 2021 Feb 1;12:553468 [FREE Full text] [doi: 10.3389/fpsyt.2021.553468] [Medline: 33597900]
76. Lawal MA, Shalaby R, Chima C, Vuong W, Hrabok M, Gusnowski A, et al. COVID-19 Pandemic: Stress, Anxiety, and Depression Levels Highest amongst Indigenous Peoples in Alberta. Behav Sci (Basel) 2021 Aug 24;11(9):115 [FREE Full text] [doi: 10.3390/bs11090115] [Medline: 34562953]
77. Hrabok M, Nwachukwu I, Gusnowski A, Shalaby R, Vuong W, Surood S, et al. Mental Health Outreach via Supportive Text Messages during the COVID-19 Pandemic: One-week Prevalence and Correlates of Anxiety Symptoms. Can J Psychiatry 2021 Jan 02;66(1):59-61 [FREE Full text] [doi: 10.1177/0706743720969384] [Medline: 33131318]
78. Mrklas K, Shalaby R, Hrabok M, Gusnowski A, Vuong W, Surood S, et al. Prevalence of Perceived Stress, Anxiety, Depression, and Obsessive-Compulsive Symptoms in Health Care Workers and Other Workers in Alberta During the COVID-19 Pandemic: Cross-Sectional Survey. JMIR Ment Health 2020 Sep 25;7(9):e22408 [FREE Full text] [doi: 10.2196/22408] [Medline: 32915764]

Abbreviations

BDI: Beck Depression Inventory
BRS: Brief Resilience Scale
GAD: generalized anxiety disorder
MBI: Maslach Burnout Inventory
MDD: major depressive disorder
PHQ-9: Patient Health Questionnaire-9
PSS: Perceived Stress Scale
RCT: randomized controlled trial

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Protocol

The Roles of a Secondary Data Analytics Tool and Experience in Scientific Hypothesis Generation in Clinical Research: Protocol for a Mixed Methods Study

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Abstract

Background: Scientific hypothesis generation is a critical step in scientific research that determines the direction and impact of any investigation. Despite its vital role, we have limited knowledge of the process itself, thus hindering our ability to address some critical questions.

Objective: This study aims to answer the following questions: To what extent can secondary data analytics tools facilitate the generation of scientific hypotheses during clinical research? Are the processes similar in developing clinical diagnoses during clinical practice and developing scientific hypotheses for clinical research projects? Furthermore, this study explores the process of scientific hypothesis generation in the context of clinical research. It was designed to compare the role of VIADS, a visual interactive analysis tool for filtering and summarizing large data sets coded with hierarchical terminologies, and the experience levels of study participants during the scientific hypothesis generation process.

Methods: This manuscript introduces a study design. Experienced and inexperienced clinical researchers are being recruited since July 2021 to take part in this 2×2 factorial study, in which all participants use the same data sets during scientific hypothesis–generation sessions and follow predetermined scripts. The clinical researchers are separated into experienced or inexperienced groups based on predetermined criteria and are then randomly assigned into groups that use and do not use VIADS via block randomization. The study sessions, screen activities, and audio recordings of participants are captured. Participants use the think-aloud protocol during the study sessions. After each study session, every participant is given a follow-up survey, with participants using VIADS completing an additional modified System Usability Scale survey. A panel of clinical research experts will assess the scientific hypotheses generated by participants based on predeveloped metrics. All data will be anonymized, transcribed, aggregated, and analyzed.

Results: Data collection for this study began in July 2021. Recruitment uses a brief online survey. The preliminary results showed that study participants can generate a few to over a dozen scientific hypotheses during a 2-hour study session, regardless of whether they used VIADS or other analytics tools. A metric to more accurately, comprehensively, and consistently assess scientific hypotheses within a clinical research context has been developed.

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Conclusions: The scientific hypothesis–generation process is an advanced cognitive activity and a complex process. Our results so far show that clinical researchers can quickly generate initial scientific hypotheses based on data sets and prior experience. However, refining these scientific hypotheses is a much more time-consuming activity. To uncover the fundamental mechanisms underlying the generation of scientific hypotheses, we need breakthroughs that can capture thinking processes more precisely.

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KEYWORDS

clinical research; observational study; scientific hypothesis generation; secondary data analytics tool; think-aloud method

Introduction

A hypothesis is an educated guess or statement about the relationship between 2 or more variables [1,2]. Scientific hypothesis generation is a critical step in scientific research that determines the direction and impact of research investigations. However, despite its vital role, we do not know the answers to some basic questions about the generation process. Some examples are as follows: “Can secondary data analytics tools facilitate the process?” and “Is the scientific hypothesis generation process for clinical research questions similar to differential diagnosis questions?” Traditionally, the scientific method involves delineating a research question and generating a scientific hypothesis. After formulating a scientific hypothesis, researchers design studies to test the scientific hypothesis to determine the answers to research questions [1,3].

Scientific hypothesis generation and scientific hypothesis testing are distinct processes [1,4]. In clinical research, research questions are often delineated without the support of systematic data analysis and are not data driven [1,5,6]. Using and analyzing existing data to facilitate scientific hypothesis generation is considered ecological research [7,8]. An ever-increasing amount of electronic health care data is becoming available, much of which is coded. These data can be a rich source for secondary data analysis, accelerating scientific discoveries [9]. Thus, many researchers have been exploring data-driven scientific hypothesis generation guided by secondary data analysis [1,10]. This includes various fields, including genomics [4]. However, exactly how a scientific hypothesis is generated, even as shown by secondary data analysis in clinical research, is unknown. Understanding the detailed process of scientific hypothesis generation could improve the efficiency of delineating clinical research questions and, consequently, clinical research. Therefore, this study investigates the process of formulating scientific hypotheses guided by secondary data analysis. Using these results as a baseline, we plan to explore ways of supporting and improving the scientific hypothesis–generation process and to study the process of formulating research questions as long-term goals.

Electronic health record systems and related technologies have been widely adopted in both office-based physician practices (86% in 2019) [11] and hospitals (overall 86% in 2022), and types vary based on hospital types [12] across the United States. Thus, vast amounts of electronic data are continuously captured and available for analysis to guide future decisions, uncover new patterns, or identify new paradigms in medicine. Much of the data is coded using hierarchical terminologies, and some of these commonly used terminologies include the International Classification of Diseases, 9th Revision-Clinical Modification (ICD9-CM) [13] and 10th Revision-Clinical Modification (ICD10-CM) [14], Systematized Nomenclature of Medicine-Clinical Terms (SNOMED-CT) [15], Logical Observation Identifiers Names and Codes (LOINC) [16], RxNorm [17], Gene Ontology [18], and Medical Subject Headings (MeSH) [19]. We used the coded data sets by hierarchical terminologies *as examples* of existing data sets to facilitate and articulate the scientific hypothesis–generation process in clinical research, especially when guided by secondary data analyses. Algorithms [20,21] and a web-based secondary data analytics tool [22-25] were developed to use the coded electronic data (ICD9 or MeSH) in order to conduct population studies and other clinically relevant studies.

Arocha et al and Patel et al [26,27] studied the directionality of reasoning in scientific hypothesis–generation processes and evaluation strategies (of confirmation or disconfirmation) for solving a cardiovascular diagnostic problem by medical students (novice) and medical residents (experienced). The reasoning directions include forward (from evidence to a scientific hypothesis) and backward (from a scientific hypothesis to evidence). More experienced clinicians used their own underlying situational knowledge about the clinical condition, while the novices used the surface structure of the patient information during the diagnosis generation process. The studies by Patel et al [28,29] and Kushniruk et al [30] used inexperienced and experienced clinicians with different roles, levels of medical expertise, and corresponding strategies to diagnose an endocrine disorder. In these studies, expert physicians used more efficient strategies (integrating patient history and experts’ prior knowledge) to make diagnostic decisions [28,30,31]. All these studies focused on hypothesis generation in solving diagnostic problems. Their results set the groundwork for reasoning in the medical diagnostic process. Their findings regarding the generation of diagnostic hypotheses by experienced and inexperienced clinicians via different processes helped us formulate and narrow our research questions. Their methodology involved performing predefined tasks, recording “think-aloud” sessions, and transcribing and analyzing the study sessions. Making a diagnosis is a critical component of medicine and a routine task for physicians. In contrast, generating scientific hypotheses in clinical research focuses on establishing a scientific hypothesis or doing further searches to explore alternative scientific hypotheses for research. The difference between the 2 can be demonstrated by 2 enterprises. In clinical practice, the goal of generating a

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diagnostic hypothesis is to make decisions about patient care and the task is time constrained, while in scientific research, time is not similarly constrained and the task is to explore various scientific hypotheses to formulate and refine the final research question. In both making a medical diagnosis in clinical practice and scientific thinking, generating initial hypotheses depends on prior knowledge and experience [32,33]. However, in scientific thinking, analogies and associations play significant roles, in addition to prior knowledge, experience, and reasoning capability. Analogies are widely recognized as playing vital heuristic roles as aids to discovery [32,34], and these have been employed in a wide variety of settings and have had considerable success in generating insights and formulating possible solutions to existing problems.

This makes it essential to understand the scientific hypothesis–generation process in clinical research and to compare this process with generating clinical diagnoses, including the role of experience during the scientific hypothesis–generation process.

This study explores the scientific hypothesis–generation process in clinical research. It investigates whether a secondary data analytics tool and clinician experience influence the scientific hypothesis–generation process. We propose to use direct observations, think-aloud methods with video capture, follow-up inquiries and interview questions, and surveys to capture the participants' perceptions of the scientific hypothesis–generation process and associated factors. The qualitative data generated will be transcribed, analyzed, and quantified.

We aim to test the following study hypotheses:

1. Experienced and inexperienced clinical researchers will differ in generating scientific hypotheses guided by secondary data analysis.
2. Clinical researchers will generate different scientific hypotheses with and without using a secondary data analytics tool.
3. Researchers' levels of experience and use of secondary data analytics tools will interact in their scientific hypothesis–generation process.

In this paper, we used the term "research hypothesis" to refer to a statement generated by our research participants, the term "study hypothesis" to refer to the subject of our research study, and the term "scientific hypothesis" to refer to the general term "hypothesis" in research contexts.

Methods

Design

This manuscript introduces a study design and uses a mixed methods approach. The study includes assessment of direct observational, utility, and usability study designs. Surveys, interviews, semipredefined tasks, and capturing screen activities are also utilized. The modified Delphi method is also used in the study.

Ethics Approval

The study has been approved by the Institutional Review Board (IRB) of Clemson University, South Carolina (IRB2020-056).

Participants and Recruitment

Experienced and inexperienced clinical researchers, and a panel of clinical research experts, have been recruited for this study. The primary criterion used to distinguish subjects in the 3 groups is the level of their experience in clinical research. Table 1 summarizes the requirements for clinical researchers, expert panel members, and the computers that clinical researchers use during the study sessions. Participants are compensated for their time according to professional organization guidelines.

Table 1. Summary of the criteria for study participants and clinical research expert panel members.

Variable	Inexperienced clinical researchers[a]	Experienced clinical researchers[a]	A panel of clinical research experts
Participation in research hypothesis generation and study design	≤2 years	Leading role ≥5 and <10 years	Leading role ≥10 years
Participation in data analysis of study results	≤2 years	Leading role ≥5 and <10 years	Leading role ≥10 years
Publications in clinical research	Not required	≥5 as a leading author, including first, correspondence, or senior author for original studies	≥10 as a leading author, including at least one article in a high-impact journal in the past 5 years
Review experience in clinical research for conferences, journals, or grants	Not required	Not required	≥10 years
Internet connection	Required	Required	Required
Microphone	Required	Required	Not required
Software package for data analysis (eg, Microsoft Excel and R)	Required	Required	Not required
Tools to facilitate research hypothesis generation, if available	Required	Required	Not required

[a]If a participant has clinical research experience between 2 and 5 years, the decisive factor for the experienced group will be 5 publications for original studies as the leading author.

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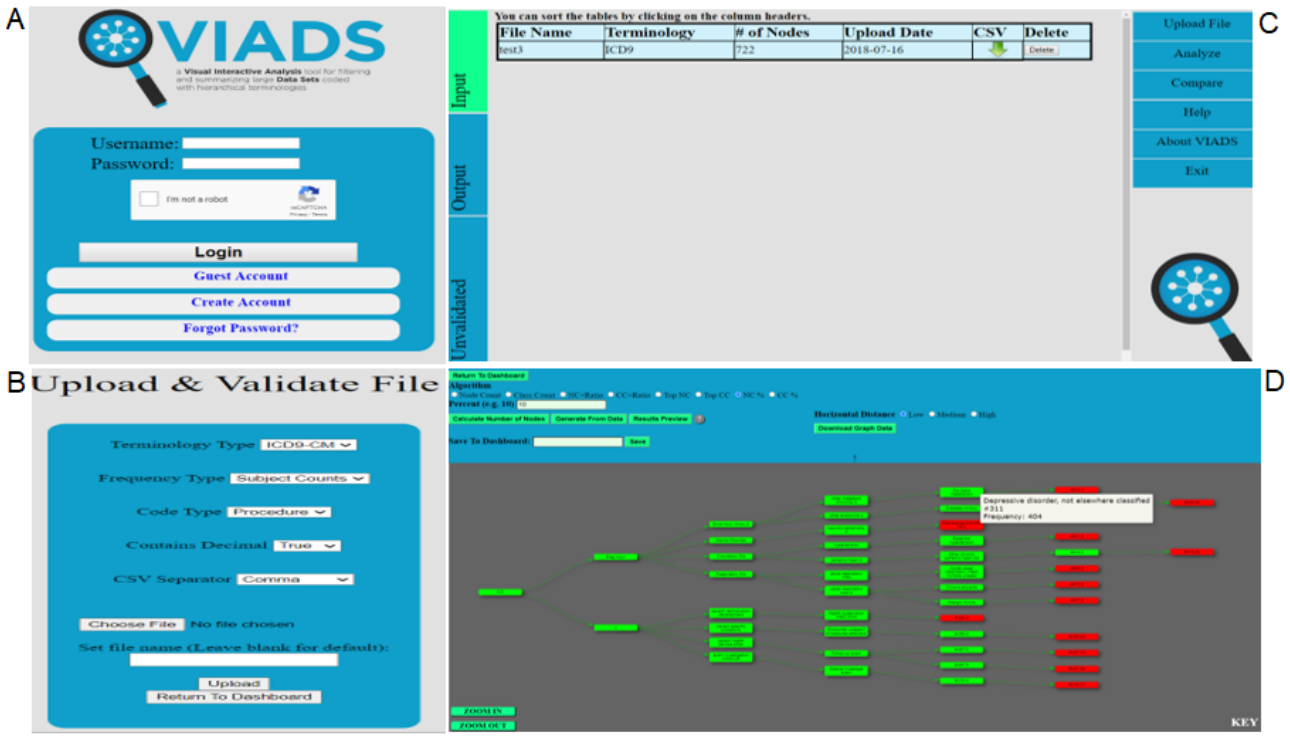
To recruit participants, invitational emails and flyers have been sent to collaborators, along with other communication means, including mailing lists, such as those of working groups of the American Medical Informatics Association, South Carolina Clinical & Translational Research Institute newsletters, and PRISMA health research newsletters, and Slack channels, such as National COVID Cohort Collaborative communities. All study sessions are conducted remotely via video conference software (Webex, Cisco) and recorded via a commercial software (BB FlashBack, Blueberry Software).

Introduction to VIADS

In this study, we have used VIADS as an example of a secondary data analytics tool. VIADS is a visual interactive analytical tool for filtering and summarizing large health data sets coded with hierarchical terminologies [22,23,35]. It is a cost-free web-based tool available for research and educational purposes. VIADS can be used by both registered users and guest users without registration. VIADS and the underlying algorithms were developed previously by the authors [20,21,24]. VIADS was designed to use codes and usage frequencies from terminologies with hierarchical structures to achieve the following objectives: (1) provide summary visualizations, such as graphs, of data sets; (2) filter data sets to ensure manageable sizes based on user selection of algorithms and thresholds; (3) compare similar data sets and highlight the differences; and (4) provide interactive, customizable, and downloadable features for the graphs generated from the data sets. VIADS is a useful secondary data analytics tool that can facilitate decision-making by medical administrators, clinicians, and clinical researchers. For example, VIADS can be used to track longitudinal data of a hospital over time and can explore trends and detect diagnosis trends and differences over time. VIADS can also be used to compare 2 similar medications and the medical events associated with the medications in order to provide detailed evidence to guide more precise clinical use of the medications [20]. This study provides evidence of the different information needs of physicians and nurses via the algorithms of VIADS [21]. Figure 1 shows example screenshots of VIADS.

Meanwhile, we recognize that VIADS can only accept coded clinical data and their associated use frequencies. Currently, VIADS can accept data sets coded using ICD9-CM, ICD10-CM, and MeSH. This can limit the types of scientific hypotheses generated by VIADS.

Figure 1. Selected screenshots of VIADS. (A) Homepage; (B) validation module; (C) dashboard; (D) a graph coded using International Classification of Diseases, 9th Revision-Clinical Modification (ICD9-CM) codes and generated by VIADS.



Preparation of Test Data Sets

We have prepared and used the same data sets for this study across different groups in order to reduce the potential biases introduced by different data sets. However, all data sets (ie, input files) used in VIADS are generally prepared by users within specific institutions. Table 2 summarizes the final format of data sets and the minimum acceptable sizes of data sets needed for analysis in VIADS. The current version of VIADS is designed to accept all data sets coded by the 3 types of terminologies (ICD9-CM, ICD10-CM, and MeSH) listed in Table 2. No identified patient information is included in the data sets used in VIADS, as the data sets contain only the node identification (ie, terminology code) and usage frequencies.

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Table 2. Acceptable formats and data set sizes in VIADS.

Data set[a] and graph node ID (code)	Usage frequency
ICD9-CM[b] data set	
300.00	2223
278.00	5567
… …[c]	…
ICD10-CM[d] data set	
O10.01	5590
E11.9	50,000
… …[c]	…
MeSH[e] data set	
A0087342	16,460
A0021563	4459
… …[c]	…

[a]Acceptable data set sizes for Web VIADS are as follows: patient counts ≥100 and event counts ≥1000.

[b]ICD9-CM: International Classification of Diseases, 9th Revision-Clinical Modification.

[c]There are many more codes in addition to the 2 examples provided.

[d]ICD10-CM: International Classification of Diseases, 10th Revision-Clinical Modification.

[e]MeSH: Medical Subject Headings.

The usage frequencies of the data sets used in VIADS can be either of the following: patient counts (the number of patients associated with specific ICD codes in the selected database) or event counts (the number of events [ICD codes or MeSH terms] in the selected database).

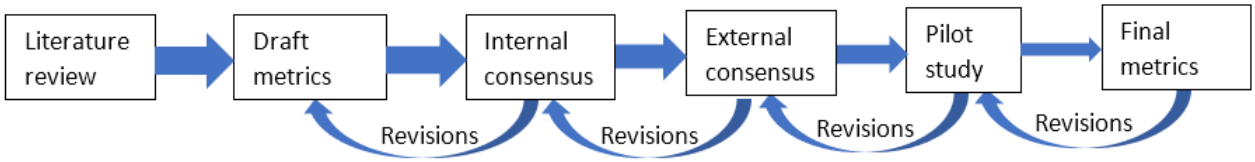
An ancestor-descendant table, which contains 1 row for each node and each of its distinct descendants, can calculate class counts easier and more accurately without counting the same node multiple times. These implementation details have been discussed in greater detail in prior publications [20,21].

A publicly accessible data source [36], including ICD9-CM codes, has been used to generate the needed input data sets. The patient counts are used as frequencies. Although ICD10-CM codes are now used in the United States, ICD9-CM data spanning the past several decades are available in most institutions across the country. Therefore, ICD9-CM codes have been used to obtain historical and longitudinal perspectives.

Instrument Development

Metrics have been developed to assess research hypotheses generated during the study sessions. The development process goes through iterative stages (Figure 2) via Qualtrics surveys, emails, and phone calls. First, a literature review is conducted to outline draft metrics. Then, the draft metrics are discussed and iteratively revised until all concerns are addressed. Next, the revised metrics are distributed to the entire research team for feedback. The internal consensus processes follow a modified Delphi method [37]. Modifications at this point primarily include transparent and open discussions conducted via email among the research team and anonymous survey responses received before and after discussions. The main difference between our modification and the traditional Delphi method is the transparent discussion among the whole team via emails between the rounds of surveys.

Figure 2. Development process for metrics to evaluate research hypotheses in clinical research.



The performance of scientific hypothesis–generation tasks will be measured using metrics that include the following qualitative and quantitative measures: validity, significance, clinical relevance, feasibility, clarity, testability, ethicality, number of total scientific hypotheses, and average time used to generate 1 scientific hypothesis. In an online survey, the panel of clinical research experts will assess the generated research hypotheses based on the metrics we have developed.

A survey (Multimedia Appendix 1) is administered for the first 4 groups at the end of the research hypothesis–generation study sessions (Figure 3). The groups that use VIADS also complete a modified System Usability Scale (SUS) questionnaire

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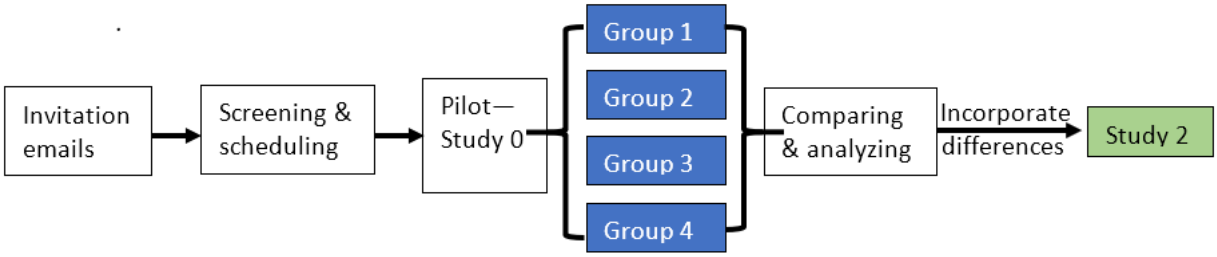
(Multimedia Appendix 2) evaluating the usability and utility of VIADS. The follow-up or inquiry questions and parameters generated during the think-aloud process used in Study 1 (Figure 3) are as follows:

- What are the needed but currently unavailable attributes that would help clinical researchers generate research hypotheses? The question is similar to a wish list of features facilitating research hypothesis generation.
- Follow-up questions clarify potential confusion during the think-aloud processes or enable meaningful inquiries when unexpected or novel questions emerge during observations [38]. However, these questions have been kept to a minimal level to avoid interrupting clinical researchers' thinking processes. This method complements the data from the think-aloud video captures.
- Can the list of items in Multimedia Appendix 3, which has been compiled from traditional clinical research textbooks [1-3,8,39] on scientific hypothesis generation and research question formulation, facilitate clinical researchers' research hypothesis generation when guided by secondary data analysis?

A survey will be developed based on the comparative results of the first 4 groups and administered at the end of Study 2. The identified differences from Study 1 will be the focus of the survey to determine whether these differences are helpful in Study 2.

Figure 3. Summary of the study procedures. Blue boxes indicate data collected in Study 1.



Study Design

Study 1 tests all 3 study hypotheses. If the study hypotheses are supported in Study 1, we will conduct a follow-up study (Study 2) to examine whether and how the efficiency or quality of research hypothesis generation may be improved or refined.

We will use the think-aloud method to conduct the following tasks: (1) observe the research hypothesis–generation process; (2) transcribe data, and analyze and assess if VIADS [22] and different levels of experience of clinical researchers influence the process; and (3) assess the interactions between VIADS (as an example of a secondary analytical tool) and the experience levels of the participants during the process. Figure 3 summarizes the Study 1 and Study 2 procedures.

Study 1

Experienced and inexperienced clinical researchers conduct research hypothesis–generation tasks using the same secondary data sets. The tasks are captured to describe participants' research hypothesis–generation processes when guided by analysis of the same data sets. VIADS is also used as an example of a secondary data analytics tool to assess participants' research hypothesis–generation processes. Accordingly, 2 control groups do not use VIADS, while 2 intervention groups do use it.

A pilot study, Study 0, was conducted in July and August 2021 for each group to assess the feasibility of using the task flow, data sets, screen capture, audio and video recordings, and study scripts. In Study 1, 4 groups are utilized. Table 3 summarizes the study design and participants in each group. The 4 groups will be compared in order to detect the primary effects of the 2 factors and their interactions after completing Study 1. After recruitment, the participants are separated into experienced or inexperienced groups based on predetermined criteria. Then, the participants are randomly assigned to a group that uses VIADS (3-hour session, with 1 hour to conduct VIADS training) or does not use VIADS (2-hour session) via block randomization.

Table 3. Design of Study 1 for assessment of the hypothesis–generation process in clinical research.

Variable	Number of experienced clinical researchers	Number of inexperienced clinical researchers
Not using VIADS	8 (Group 1)	8 (Group 2)
Using VIADS	8 (Group 3)	8 (Group 4)

We conduct 1 study session individually with each participant. The participants are given the same data sets from which to generate research hypotheses with or without VIADS during each study session. The same researcher observes the entire process and captures the process via think-aloud video recordings. Follow-up or inquiry questions from the observing researcher are used complementarily during each study session. The study sessions are conducted remotely via Webex. All screen activities are captured and recorded via BB FlashBack [40].

Study 2

If the results of Study 1 indicate group differences as expected (in particular, differences are found between experienced and inexperienced clinical researchers, along with differences between groups using VIADS and not using VIADS), Study 2

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will be conducted to examine whether the efficiency of the research hypothesis–generation process could be improved. Specifically, we will analyze for group differences, identify anything related to VIADS, and incorporate them into VIADS. Then, we will test whether the revised and presumably improved VIADS increases the efficiency or quality of the research hypothesis–generation process. In this process, the group that has the lowest performance in Study 1 will be invited to use the revised VIADS to conduct research hypothesis–generation tasks again with the same data sets. However, at least 8 months will be allowed to pass in order to provide an adequate wash-out period. This group's performance will be compared with that in Study 1.

If no significant difference can be detected between the groups using VIADS and not using VIADS in Study 1, we will use the usability and utility survey results to revise VIADS accordingly without conducting Study 2. If no significant difference can be detected between experienced and inexperienced clinical researchers, Study 2 will recruit both experienced and inexperienced clinical researchers as study participants. In this case, Study 2 will focus only on whether a revised version of VIADS impacts the research hypothesis–generation process and outcomes.

Data and Statistical Analysis

While conducting the given tasks, the qualitative data collected via the think-aloud method will be transcribed, coded, and analyzed according to the grounded theory [41,42], a classical qualitative data analysis method. This data analysis has not begun yet because data are still being collected. Combined analysis of discourse [30], video recordings of the study sessions, and screen activities will be conducted. The main components or patterns that we will focus on during analysis include potential nonverbal steps, sequential ordering among different components (such as prioritization of the use of either experience or data) across groups, seeking and processing evidence, analyzing data, generating inferences, making connections, formulating a hypothesis, searching for information needed to generate research hypotheses, and so forth. Ideally, based on video analyses and observations, we plan to develop a framework for the scientific hypothesis–generation process in clinical research, which is guided by secondary data analytics. Similar frameworks exist in education and learning areas [43], but do not currently exist in the field of clinical research.

The outcome variable used is based on the participants' performance in research hypothesis–generation tasks. The performance is measured by the quality (eg, significance and validity) and quantity of the research hypotheses generated through the tasks and the average time to generate 1 research hypothesis. At least three clinical research experts will assess each hypothesis using the scientific hypothesis assessment metrics that were developed for this study. The metrics include multiple items, each on a 5-point Likert scale. The details of the metrics are described in the Instrument Development section.

The data will be analyzed with a 2-tailed factorial analysis. We calculated the required sample size in G*Power 3.1.9.7 for a 2-way ANOVA. The sample size was 32 based on a confidence level of 95% (α=.05), effect size f=0.5, and power level of 0.8 (β=.20).

In Study 1, we will use descriptive statistics to report how many hypotheses were generated, average time spent per hypothesis, and how many hypotheses were evaluated for each participant. A 2-way ANOVA will be used to examine the main effects of VIADS and experience, as well as the interaction effect of the 2 factors. In the ANOVA, the outcome variable is the expert evaluation score. The follow-up survey data will be analyzed using correlations to examine the relationship between participants' self-rated creativity, the average time per hypothesis generation, the number of hypotheses generated, and the expert evaluation score. The SUS will be used to assess the usability of VIADS. Qualitative data from the SUS surveys will be used to guide revisions of VIADS after Study 1. Descriptive statistics will also be used to report the answers to other follow-up questions.

A *t* test will be conducted to determine whether the revised VIADS improves the performance of research hypothesis generation in Study 2.

Results

Overview

The study is a National Institutes of Health–funded R15 (Research Enhancement Award) project supported by the National Library of Medicine. We began collecting data in July 2021 via pilot studies, and here provide some preliminary results and summarize our early observations. The full results and analysis of the study will be shared in future publications when we complete the study.

Instruments

Based on a literature review, metrics were developed to assess research hypotheses [1,2,4,6-9,39]. Most of the dimensions used to evaluate clinical research hypotheses include clinical and scientific *validity*; *significance* (regarding the target population, cost, and future impact); *novelty* (regarding new knowledge, impact on practice, and new methodology); *clinical relevance* (regarding medical knowledge, clinical practice, and policies); *potential benefits and risks*; *ethicality*; *feasibility* (regarding cost, time, and the scope of the work); *testability*; *clarity* (regarding purpose, focused groups, variables, and their relationships); and *researcher interest level* (ie, willingness to pursue).

Multiple items were used to measure the quality for each dimension mentioned above. For each item, a 5-point Likert scale (1=strongly disagree, 5=strongly agree) was used for measurement. After internal consensus, we conducted external consensus and sought feedback from the external expert panel via an online survey [44]. The metrics are revised continuously by incorporating feedback. The expert panel will use our online survey [45] to evaluate research hypotheses generated by research participants during the study sessions.

We have developed the initial study scripts for Study 1 and have revised them after the pilot study sessions (Study 0). We have developed the screening survey for the recruitment process. The

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follow-up survey is administered after each study session, regardless of the group. The standard SUS survey [46,47] has been modified to add one more option in order to allow users to elaborate on what caused any dissatisfaction during the usability study.

Recruitment

Currently, we are recruiting all levels of participants, including inexperienced clinical researchers, experienced clinical researchers, and a panel of clinical research experts. Recruitment began in July 2021 with pilot study participants. To participate, anyone involved in clinical research can share their contact email address by filling out the screening survey [48]. So far, we have completed 16 study sessions with inexperienced clinical researchers who have either used or not used VIADS in Study 1.

Study 1

For this study, we are using data from the National Ambulatory Medical Care Survey (NAMCS) conducted by the Centers for Disease Control and Prevention [36]. The NAMCS is a publicly accessible data set of survey results related to clinical encounters in ambulatory settings. We processed raw NAMCS data (ICD9 codes and accumulated frequencies) from 2005 and 2015 to prepare the needed data sets for VIADS based on our requirements.

The experience level of the clinical researchers was determined by predetermined criteria. To determine which group a participant joins (inexperienced [groups 2 and 4] or experienced [groups 1 and 3] clinical researchers), we used the R statistical software package (blockrand [49]) to implement block randomization. The random blocks range from 2 to 6 participants.

Initial Observations

We have noticed that both forward [27] and backward reasoning had been used by participants during the study sessions. In addition, some participants did not start from data or a hypothesis. Instead, the reasoning started from the participant's focused (and often familiar) area of knowledge related to several ICD9 codes in the focus area being examined. The research hypotheses were then developed after examining the data on the focused area.

Many participants did not use any advanced analysis during the study sessions. However, they did use their prior experience and knowledge to generate research hypotheses based on the frequency rank of the provided data sets and by comparing the 2 years of data (ie, 2005 vs 2015).

Noticeably, VIADS can answer more complicated questions both systematically and more rapidly. However, we noticed that the training session required to enable use of VIADS increased participants' cognitive load. Cognitive load refers to the amount of working memory resources required during the task of thinking and reasoning. Without a comprehensive analysis, we cannot yet draw further conclusions about the potential effects of this cognitive load.

Discussion

Significance of the Study

A critical first step in the life cycle of any scientific research study is formulating a valid and significant research question, which can usually be divided into several scientific hypotheses. This process is often challenging and time-consuming [1,3,38,50]. Currently, there is limited practical guidance regarding generating research questions [38] beyond emphasizing that it requires long-term experience, observation, discussion, and exploration of the literature. A scientific hypothesis–generation process will eventually help to formulate relevant research questions. Our study aims to decipher the process of scientific hypothesis generation and determine whether a secondary data analytics tool can facilitate the process in a clinical research context. When combined with clinical researchers' experiences and observations, such tools can be anticipated to facilitate scientific hypothesis generation. This facilitation will improve the efficiency and accuracy of scientific hypothesis testing, formulating research questions, and conducting clinical research in general. We also anticipate that an explicit description of the scientific hypothesis–generation process with secondary data analysis may provide more feasible guidance for clinical research design newcomers (eg, medical students and new clinical investigators). However, we have not completed all study sessions, so we cannot yet analyze the collected data in order to draw meaningful conclusions.

Interpretation of the Study and Results

Participants have been observed to use analogical reasoning [51] both consciously and subconsciously; meanwhile, some participants verbally expressed that they avoided analogical reasoning intentionally to be more creative during the study sessions. The participants intentionally did not use the same pattern of statements for all the topics supported by the data sets. The way we organized the data sets seems to promote the participants to think systematically when using the data sets. For instance, the use frequencies of ICD9 codes were sorted from high to low in each data set. However, what would constitute the perfect balance between systematic structure and randomness during scientific hypothesis generation is unknown. Intuitively, both systematic reviews and random connections should be critical in generating novel ideas in general, regardless of academic settings or industrial environments. Concrete evidence is needed to draw any conclusions about the relationships between the 2 during scientific hypothesis generation with certainty. Additionally, the current version of VIADS can only accept coded data using ICD9-CM, ICD10-CM, and MeSH. This inevitably limits the types of hypotheses VIADS can generate. We also recognize that other more broadly used hierarchical terminologies, such as SNOMED CT, RxNorm, and LOINC, could provide additional valuable information related to more comprehensive aspects of clinical care. However, our current version of VIADS cannot use such information at this time.

Analyzing the research hypothesis–generation process may include several initial cognitive components. These components can consist of searching for, obtaining, compiling, and

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processing evidence; seeking help to analyze data; developing inferences using obtained evidence and prior knowledge; searching for external evidence, including literature or prior notes; seeking connections between evidence and problems; considering feasibility, testability, ethicality, and clarity; drawing conclusions; formulating draft research hypotheses; and polishing draft research hypotheses [1-3,8,39,52]. These initial components will be used to code the recorded think-aloud sessions to compare differences among groups.

We recognize that research hypothesis generation and the long refining and improving process matter most during the study sessions. Without technologies to capture what occurs cognitively during the research hypothesis–generation process, we may not be able to answer fundamental questions regarding the mechanisms of scientific hypothesis generation.

Establishing the evaluation metrics to assess research hypotheses is the first step and the critical foundation of the overall study. The evaluation metrics used will determine the quality measurements of the research hypotheses generated by study participants during the study sessions.

Research hypothesis evaluation is subjective, but metrics can help standardize the process to some extent. Although the metrics may not guarantee a precise or perfectly objective evaluation of each research hypothesis, such metrics provide a consistent instrument for this highly sophisticated cognitive process. We anticipate that a consistent instrument will help to standardize the expert panel's evaluations. Additionally, objective measures, such as the number of research hypotheses generated by the study participants and the average time each participant spends generating each research hypothesis, will be used in the study. The expert panel is therefore expected to provide more consistent research hypothesis evaluations with the combined metrics and objective measures.

Although developing metrics appears linear, as presented in Figure 2, the process itself is highly iterative. No revision occurs only once, and when we reflect on the first 3 stages of development, one observes that major revisions during the first 3 stages involve separating questions in the survey and refining the options for the questions. These steps reduce ambiguity.

Challenges

Many challenges have been encountered while conducting the research hypothesis–generation study sessions. These include the following:

1. What can be considered a research hypothesis? What will not be considered a research hypothesis? The response will determine which research hypotheses will be evaluated by the panel of clinical research experts.
2. How should the research hypothesis be measured accurately? Although we developed workable metrics, the metrics are not yet perfect.
3. How can we accurately capture thinking, reasoning, and networking processes during the research hypothesis–generation process? Currently, we use the think-aloud method. Although think-aloud protocols can capture valuable information about the thinking process, we recognize that not all processes can be articulated during the experiments, and not everyone can articulate their processes accurately or effectively.
4. What happens when a clinical researcher examines and analyzes a data set and generates a research hypothesis subconsciously?
5. How can we capture the roles of the external environment, internal cognitive capacity, existing knowledge base of the participant, and interactions between the individual and the external world in these dynamic processes?

When faced with challenges, we see opportunities for researchers to further explore and identify a clearer picture of research hypothesis generation in clinical research. We believe that the most pressing target is developing new technologies in order to capture what clinical researchers do and think when generating research hypotheses from a data set. Such technologies can promote breakthroughs in cognition, psychology, computer science, artificial intelligence, neurology, and clinical research in general. In clinical research, such technologies can help empower clinical researchers to conduct their tasks more efficiently and effectively.

Lessons Learned

We learned some important lessons while designing and conducting this study. The first lesson involved balancing the study design (straightforward or complicated) and conducting the study (feasibility). During the design stage, we were concerned that the 2×2 study design was too simple, even though we know it does not negatively impact the value of the research. We simply considered experience levels and whether the participants used VIADS in a very complicated cognitive process. However, even for such a straightforward design, only 1 experienced clinical researcher has volunteered so far. Thus, we will first focus on inexperienced clinical researchers. Even for study sessions involving inexperienced clinical researchers, considerable time is needed to determine strategies for coding and analyzing the raw data. In order to design a complicated experiment that answers more complex questions, we must consider balancing practical workload, recruitment reality, expected timeline, and researchers' desire to pursue a complex research question.

Recruitment is always challenging. Many of our panel invitations to clinical research experts either received no response or were rejected, which significantly delayed the study timeline, in addition to the effects of the COVID-19 pandemic. Furthermore, the IRB approval process was time-consuming, delaying our study when we needed to revise study documents. Therefore, the study timeline includes the IRB initial review and rereview cycles.

Future Work

The first step of a future direction for this project is to explore the feasibility of formulating research questions based on research hypotheses. In this project, we are looking for ways to improve the efficiency of generating research hypotheses. The next step will be to explore whether we can enhance the efficiency of formulating research questions.

A possible direction for future work is to develop tools to facilitate scientific hypothesis generation guided by secondary

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data analysis. We may explore automating the process or incorporating all positive attributes in order to guide the process better and improve efficiency and quality.

At the end of our experiments, we asked clinical researchers what facilitates their scientific hypothesis–generation process the most. Several of their responses included repeatedly reading academic literature and discussing with colleagues. We believe intelligent tools can undoubtedly improve both aspects of scientific hypothesis generation, namely, summarizing new publications of the chosen topic areas and providing conversational support to clinical researchers. This would be a natural extension of our studies.

An additional possible direction is to expand the terminologies that can be used by VIADS, for example, the addition of RxNorm, LOINC, and SNOMED CT can be considered in the future.

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Data Availability

A request for aggregated and anonymized transcription data can be made to the corresponding author, and the final decision on data release will be made on a case-by-case basis, as appropriate. The complete analysis and the results will be published in future manuscripts.

Conflicts of Interest

None declared.

Multimedia Appendix 1
Follow-up survey at the end of the hypothesis-generation tasks.
[PDF File (Adobe PDF File), 94 KB - resprot_v11i7e39414_app1.pdf]

Multimedia Appendix 2
VIADS System Usability Scale survey and utility questionnaire.
[PDF File (Adobe PDF File), 192 KB - resprot_v11i7e39414_app2.pdf]

Multimedia Appendix 3
List of items to consider during hypothesis generation.
[PDF File (Adobe PDF File), 59 KB - resprot_v11i7e39414_app3.pdf]

References

1. Supino PG, Borer JS. Principles of Research Methodology A Guide for Clinical Investigators. Berlin/Heidelberg, Germany: Springer; 2012.
2. Parahoo K. Nursing Research: Principles, Process and Issues. London, United Kingdom: Palgrave MacMillan Ltd; 1997.
3. Hulley SB, Cummings SR, Browner WS, Grady D, Newman TB. Designing clinical research. Philadelphia, PA: Wolters Kluwer; 2013.
4. Biesecker LG. Hypothesis-generating research and predictive medicine. Genome Res 2013 Jul 01;23(7):1051-1053 [FREE Full text] [doi: 10.1101/gr.157826.113] [Medline: 23817045]
5. Brian Haynes R. Forming research questions. J Clin Epidemiol 2006 Sep;59(9):881-886 [FREE Full text] [doi: 10.1016/j.jclinepi.2006.06.006] [Medline: 16895808]
6. Farrugia P, Petrisor B, Farrokhyar F, Bhandari M. Practical tips for surgical research: Research questions, hypotheses and objectives. Can J Surg 2010 Aug;53(4):278-281 [FREE Full text] [Medline: 20646403]
7. Hicks C. Research Methods for Clinical Therapists: Applied Project Design and Analysis. London, United Kingdom: Churchill Livingstone; 1999.
8. Glasser SP. Essentials of Clinical Research. Cham: Springer; 2014.
9. Spangler S. Accelerating Discovery Mining Unstructured Information for Hypothesis Generation. New York, NY: Chapman and Hall/CRC; 2016.
10. Cheng HG, Phillips MR. Secondary analysis of existing data: opportunities and implementation. Shanghai Arch Psychiatry 2014 Dec;26(6):371-375 [FREE Full text] [doi: 10.11919/j.issn.1002-0829.214171] [Medline: 25642115]

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11. Office-based Physician Electronic Health Record Adoption. Health IT. 2019. URL: https://www.healthit.gov/data/quickstats/office-based-physician-electronic-health-record-adoption [accessed 2022-06-27]
12. Adoption of Electronic Health Records by Hospital Service Type 2019-2021. Health IT. 2022. URL: https://www.healthit.gov/data/quickstats/adoption-electronic-health-records-hospital-service-type-2019-2021 [accessed 2022-06-27]
13. International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM). Centers for Diseases Control and Prevention. URL: https://www.cdc.gov/nchs/icd/icd9cm.htm [accessed 2022-06-27]
14. International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM). Centers for Diseases Control and Prevention. URL: https://www.cdc.gov/nchs/icd/icd-10-cm.htm [accessed 2022-06-27]
15. El-Sappagh S, Franda F, Ali F, Kwak K. SNOMED CT standard ontology based on the ontology for general medical science. BMC Med Inform Decis Mak 2018 Aug 31;18(1):76 [FREE Full text] [doi: 10.1186/s12911-018-0651-5] [Medline: 30170591]
16. Vreeman DJ, McDonald CJ, Huff SM. LOINC®: a universal catalogue of individual clinical observations and uniform representation of enumerated collections. IJFIPM 2010;3(4):273. [doi: 10.1504/ijfipm.2010.040211]
17. Liu S, Wei M, Moore R, Ganesan V, Nelson S. RxNorm: prescription for electronic drug information exchange. IT Prof 2005 Sep;7(5):17-23. [doi: 10.1109/mitp.2005.122]
18. Gene Ontology. URL: http://geneontology.org/ [accessed 2022-06-27]
19. Medical Subject Headings: MeSH. National Library of Medicine. URL: https://www.nlm.nih.gov/mesh/meshhome.html [accessed 2022-06-27]
20. Jing X, Cimino JJ. A complementary graphical method for reducing and analyzing large data sets. Methods Inf Med 2018 Jan 20;53(03):173-185. [doi: 10.3414/me13-01-0075]
21. Jing X, Cimino JJ. Graphical methods for reducing, visualizing and analyzing large data sets using hierarchical terminologies. AMIA Annu Symp Proc 2011;2011:635-643 [FREE Full text] [Medline: 22195119]
22. Jing X, Emerson M, Masters D, Brooks M, Buskirk J, Abukamail N, et al. A visual interactive analytic tool for filtering and summarizing large health data sets coded with hierarchical terminologies (VIADS). BMC Med Inform Decis Mak 2019 Feb 14;19(1):31 [FREE Full text] [doi: 10.1186/s12911-019-0750-y] [Medline: 30764811]
23. Emerson M, Brooks M, Masters D, Buskirk J, Abukamail N, Liu C, et al. Improved visualization of hierarchical datasets with VIADS. 2018 Presented at: AMIA Annual Symposium; November 3-7, 2018; San Francisco, CA.
24. Levine M, Osei D, Cimino JJ, Liu C, Phillips BO, Shubrook JH, et al. Performance comparison between two solutions for filtering data sets with hierarchical structures. J Comput Eng Inf Technol 2016 Jul 23;05(s1):f4147 [FREE Full text] [doi: 10.4172/2324-9307.S1-003]
25. Levine M, Osei D, Cimino JJ, Liu C, Phillips BO, Shubrook JH, et al. Performance comparison between two solutions for filtering data sets with hierarchical structures. 2015 Presented at: 8th Annual Mid-Atlantic Healthcare Informatics Symposium; October 23, 2015; Philadelphia, PA.
26. Arocha JF, Patel VL, Patel YC. Hypothesis generation and the coordination of theory and evidence in novice diagnostic reasoning. Med Decis Making 2016 Jul 01;13(3):198-211. [doi: 10.1177/0272989x9301300305]
27. Patel VL, Groen GJ, Arocha JF. Medical expertise as a function of task difficulty. Mem Cognit 1990 Jul;18(4):394-406. [doi: 10.3758/bf03197128] [Medline: 2381318]
28. Patel VL, Groen CJ, Patel YC. Cognitive aspects of clinical performance during patient workup: the role of medical expertise. Adv Health Sci Educ Theory Pract 1997;2(2):95-114. [doi: 10.1023/A:1009788531273] [Medline: 12386402]
29. Patel VL, Groen GJ. Knowledge based solution strategies in medical reasoning. Cognitive Sci 1986;10(1):91-116. [doi: 10.1207/s15516709cog1001_4]
30. Kushniruk A, Patel V, Marley A. Small worlds and medical expertise: implications for medical cognition and knowledge engineering. International Journal of Medical Informatics 1998 May;49(3):255-271. [doi: 10.1016/s1386-5056(98)00044-6]
31. Joseph G, Patel VL. Domain knowledge and hypothesis genenation in diagnostic reasoning. Med Decis Making 2016 Jul 02;10(1):31-44. [doi: 10.1177/0272989x9001000107]
32. The Cambridge Handbook of Thinking and Reasoning. Cambridge, United Kingdom: Cambridge University Press; 2005.
33. Patel VL, Arocha JF, Zhang J. Chapter 30: Thinking and Reasoning in Medicine. In: Holyoak KJ, Morrison RG, editors. The Cambridge Handbook of Thinking and Reasoning. Cambridge, United Kingdom: Cambridge University Press; 2005:727-750.
34. Kaufman DR, Patel VL, Magder SA. The explanatory role of spontaneously generated analogies in reasoning about physiological concepts. International Journal of Science Education 2007 Feb 25;18(3):369-386. [doi: 10.1080/0950069960180309]
35. Jing X, Emerson M, Gunderson D, Cimino JJ, Liu C, Shubrook J, et al. Architecture of a visual interactive analysis tool for filtering and summarizing large data sets coded with hierarchical terminologies (VIADS). AMIA Summits Transl Sci Proc 2018:444-445 [FREE Full text]
36. Datasets and Documentation. Centers for Disease Control and Prevention. URL: https://www.cdc.gov/nchs/ahcd/datasets_documentation_related.htm [accessed 2022-06-27]
37. Hohmann E, Cote MP, Brand JC. Research pearls: expert consensus based evidence using the Delphi method. Arthroscopy 2018 Dec;34(12):3278-3282. [doi: 10.1016/j.arthro.2018.10.004] [Medline: 30509437]

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38. Lipowski EE. Developing great research questions. Am J Health Syst Pharm 2008 Sep 01;65(17):1667-1670 [FREE Full text] [doi: 10.2146/ajhp070276] [Medline: 18714115]
39. Gallin JI, Ognibene FP. Principles and Practice of Clinical Research. Cambridge, MA: Academic Press; 2012.
40. FlashBack. URL: https://www.flashbackrecorder.com/ [accessed 2022-06-27]
41. Oates BJ. Researching Information Systems and Computing. Thousand Oaks, CA: SAGE Publications; 2006.
42. Friedman CP, Wyatt JC, Ash JS. Evaluation Methods in Biomedical and Health Informatics. Cham: Springer; 2022.
43. Moseley D, Baumfield V, Elliott J, Higgins S, Miller J, Newton DP, et al. Frameworks for Thinking: A Handbook for Teaching and Learning. Cambridge, United Kingdom: Cambridge University Press; 2005.
44. VIADS expert feedback on hypothesis evaluation matrix. Qualtrics. URL: https://clemson.ca1.qualtrics.com/jfe/form/SV_9n0zN4LaxXEA669 [accessed 2022-06-27]
45. VIADS hypothesis expert review. Qualtrics. URL: https://clemson.ca1.qualtrics.com/jfe/form/SV_0NvKpJChveqfKTz [accessed 2022-06-27]
46. Brooke J. SUS: A 'Quick and Dirty' Usability Scale. In: Jordan PW, Thomas B, McClelland IL, Weerdmeester B, editors. Usability Evaluation In Industry. Boca Raton, FL: CRC Press; 1996.
47. Brooke J. SUS: a retrospective. Journal of Usability Studies 2013;8(2):29-40 [FREE Full text] [doi: 10.5555/2817912.2817913]
48. VIADS Participants and Expert Panel Information Survey. Qualtrics. URL: https://clemson.ca1.qualtrics.com/jfe/form/SV_267ei2Fyhz89XIF [accessed 2022-06-27]
49. Snow G. blockrand: Randomization for Block Random Clinical Trials. R-project. URL: https://cran.r-project.org/web/packages/blockrand/index.html [accessed 2022-06-27]
50. Tully MP. Research: articulating questions, generating hypotheses, and choosing study designs. Can J Hosp Pharm 2014 Jan 06;67(1):31-34 [FREE Full text] [doi: 10.4212/cjhp.v67i1.1320] [Medline: 24634524]
51. Markman A, Wood K. Tools for Innovation. Oxford, United Kingdom: Oxford University Press; 2009.
52. Holyoak KJ, Morrison RG. The Oxford Handbook of Thinking and Reasoning. Oxford, United Kingdom: Oxford University Press; 2012.

Abbreviations

ICD: International Classification of Diseases
ICD9-CM: International Classification of Diseases, 9th Revision-Clinical Modification
ICD10-CM: International Classification of Diseases, 10th Revision-Clinical Modification
IRB: Institutional Review Board
LOINC: Logical Observation Identifiers Names and Codes
MeSH: Medical Subject Headings
NAMCS: National Ambulatory Medical Care Survey
SNOMED-CT: Systematized Nomenclature of Medicine-Clinical Terms
SUS: System Usability Scale

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Protocol

Sodium-Glucose Cotransporter-2 Inhibitor and Glucagon-Like Peptide-1 Receptor Agonist Combination Therapy in Type 2 Diabetes: Protocol for a Kidney End Points Real-world Study (COMBi-KID Study)

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Abstract

Background: Sodium-glucose cotransporter-2 inhibitors (SGLT2is) and glucagon-like peptide-1 receptor agonists (GLP-1RAs) are both considered to be part of standard care in the management of glycemia in type 2 diabetes. Recent trial evidence has indicated benefits on primary kidney end points for individual drugs within each medication class. Despite the potential benefits of combining SGLT2is and GLP-1RAs for glycemia management, according to national and international guideline recommendations, there is currently limited data on kidney end points for this drug combination.

Objective: The aims of the study are to assess the real-world effects of combination SGLT2i and GLP-1RA therapies for diabetes management on kidney end points, glycemic control, and weight in people with type 2 diabetes who are being treated with renin-angiotensin system blockade medication.

Methods: This retrospective cohort study will use the electronic health records of people with type 2 diabetes that are registered with general practices covering over 15 million people in England and Wales and are included in the Oxford-Royal College of General Practitioners Research and Surveillance Centre network. A propensity score–matched cohort of prevalent new users of SGLT2is and GLP-1RAs and those who have been prescribed SGLT2is and GLP-1RAs in combination will be identified. They will be matched based on drug histories, comorbidities, and demographics. A repeated-measures, multilevel, linear regression analysis will be performed to compare the mean change (from baseline) in estimated glomerular filtration rate at 12 and 24 months between those who switched to combined therapy and those continuing monotherapy with an SGLT2i or GLP-1RA. The secondary end points will be albuminuria, serum creatinine level, glycated hemoglobin level, and BMI. These will also be assessed for change at the 12- and 24-month follow-ups.

Results: The study is due to commence in March 2022 and is expected to be complete by September 2022.

Conclusions: Our study will be the first to assess the impact of combination SGLT2i and GLP-1RA therapy in type 2 diabetes on primary kidney end points from a real-world perspective.

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(JMIR Res Protoc 2022;11(7):e34206) doi:10.2196/34206

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KEYWORDS

type 2 diabetes; sodium-glucose cotransporter-2 inhibitor; glucagon-like peptide-1 receptor agonist; renal; kidney; electronic health records

Introduction

Background

Diabetes continues to be the leading cause of chronic kidney disease (CKD) and end-stage kidney disease (ESKD) requiring renal replacement therapy. Overall, about 40% of people with type 2 diabetes have evidence of diabetic kidney disease (DKD) [1-4]. For the last 2 decades, renin-angiotensin system (RAS) blockade medications (either angiotensin-converting enzyme inhibitors or angiotensin receptor blockers) have been considered—in addition to maximal glucose and blood pressure control—to be part of standard therapy for preventing or delaying the progression of DKD [1-4]. Yet, the incidence and prevalence of residual kidney disease, including CKD and ESKD, remain high and are associated with the high costs of care and dialysis [1-4]. Recent evidence from intervention outcome trials with sodium-glucose cotransporter-2 inhibitors (SGLT2is) and glucagon-like peptide-1 receptor agonists (GLP-1RAs) have indicated that these drugs individually have clear kidney benefits [1,5-15].

In cardiovascular outcome trials with SGLT2is and GLP-1Ras, which were used in the management of type 2 diabetes [1,5-15], several drugs from both classes showed benefits beyond glucose control, such as reducing the risk of heart failure and decreasing cardiovascular morbidity and mortality [1,5-15]. Moreover, it has been demonstrated that SGLT2is reduce the risk of new and worsening DKD [1,5-11]. There are also emerging data on kidney end points in GLP-1RA therapy trials, which have shown benefits on albumin excretion and reductions in estimated glomerular filtration rate (eGFR) decline [1,12-15].

Despite the potential benefits of combining SGLT2is and GLP-1RAs [16], according to guideline recommendations for the management of glycemia [17,18], there is currently limited data on kidney end points for this combination. This protocol describes our proposed study, which will explore whether combination SGLT2i and GLP-1RA therapy has additional kidney benefits when compared to treatment with either medication separately in real-world clinical practice.

Aims and Objectives

The aim of our study is to explore the real-world effectiveness of combining SGLT2i and GLP-1RA therapies in people with type 2 diabetes who are being treated with RAS blockade medication.

The primary objective is to assess the kidney effects (eGFR change) of combining SGLT2i and GLP-1RA therapies in the management of glycemia among people with type 2 diabetes who are being treated with RAS blockade medication. The secondary objectives are to assess the effects on albuminuria, glycemic control, and weight resulting from combining SGLT2i and GLP-1RA therapies among people with type 2 diabetes who are being treated with RAS blockade medication.

Methods

Study Design

Our study will be a retrospective observational cohort study that uses computerized medical records (CMRs) from general practices in England and Wales that contribute to the Oxford-Royal College of General Practitioners (RCGP) Research and Surveillance Centre (RSC) network.

Recruitment

The Oxford-RCGP RSC network is an established national database, is representative of patients attending primary care in England and Wales [19], and comprises CMR data from over 1800 urban and nonurban general practices. The Oxford-RCGP RSC database contains over 15 million patients, including over 900,000 people with diabetes, and includes demographic, coded diagnostic, laboratory test, and prescription data for men and women with diabetes in our study age band [19,20]. The size of the network has expanded considerably during the COVID-19 pandemic, and Oxford and the RCGP RSC are evolving into a major digital hub—the Oxford RCGP Clinical Informatics Digital Hub [21,22].

The primary data will be obtained from CMRs that use clinical codes. Until recently, the main terminology coding system that was used was the Read system (Read version 2 and Clinical Terms version 3). This has been replaced with the Systematized Nomenclature of Medicine Clinical Terms system, which uses clinical codes for diagnoses, prescriptions, investigations, and processes of care.

Data completeness in the RCGP RSC database is high for type 2 diabetes data due to the pay-for-performance incentive program for improving the coding of chronic diseases [20,23], the Quality and Outcomes Framework, and a dedicated team of practice liaison officers who are working closely with general practices and are able to provide feedback on coding. In addition to having high-quality data, the database also keeps its data up to date by performing updates every 3 to 10 days.

The Oxford-RCGP RSC network, as a national research platform [19-21,24], is also unique because there is no research license fee, and the network provides direct support for design-specific topics.

The study population will be adults with a diagnosis of type 2 diabetes, and we will identify this cohort by using a previously described 2-step ontological approach [20,24].

Inclusion Criteria

The inclusion criteria are as follows:

- Adults >40 to <80 years of age
- Diagnosed type 2 diabetes (>3 months)
- eGFR of >45 mL/min/1.73 m^2 (this is the lower eGFR limit on the product labels of SGLT2is for glycemia management) [25]

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- Current therapy (>3 months) to include an RAS blocker (either an angiotensin-converting enzyme inhibitor or an angiotensin receptor blocker)
- Current diabetes therapy (>3 months) to include either an SGLT2i (dapagliflozin, empagliflozin, ertugliflozin, or canagliflozin) or a GLP-1RA (exenatide, lixisenatide, liraglutide, dulaglutide, or semaglutide)
- A minimum of 1 baseline creatinine measurement within 24 months of study entry and 1 creatinine measurement during study follow-up (24 months)

Exclusion Criteria

The exclusion criterion is diagnosed type 1 diabetes.

Exposures

The primary exposures of interest in our study will be a current prescription for (1) an SGLT2i (excluding GLP-1RAs), (2) a GLP-1RA (excluding SGLT2is), or (3) a combination of an SGLT2i and GLP-1RA.

We will conduct a retrospective cohort study from the time of the coprescription of an SGLT2i and GLP-1RA combination, and paired groups for diabetes therapy will include patients taking SGLT2is (but not GLP-1RAs) and patients taking GLP-1RAs (but not SGLT2is). The follow-up time for each group will be 12 months (time window: +3 or −3 months) and 24 months (time window: +3 or −3 months) following the initiation of SGLT2i and GLP-1RA combination therapy, and comparator groups will include patients undergoing either SGLT2i monotherapy or GLP-1RA monotherapy.

The clinical and biochemistry variables that will be assessed include weight (kg), hemoglobin A_{1c} (HbA_{1c}; mmol/mol and %), the urine albumin-creatinine ratio (UACR), and the eGFR (mL/min/1.73 m^2), which are recorded as part of routine clinical care. Creatinine measurements will be used to calculate eGFRs via the CKD Epidemiology Collaboration equation [26,27].

Variables Adjusted in Matching

The variables that will be adjusted during the matching process include age, sex, ethnicity, weight, blood pressure, cardiovascular disease, medication persistence (*nonpersistence* is defined as a gap of ≥90 days in prescription [24]), diuretic or nonsteroidal anti-inflammatory drug use (>3 months), the duration of diabetes, HbA_{1c} level, eGFR, and the UACR.

Outcomes of Interest

Primary End Point

The primary end point will be eGFR (mL/min/1.73 m^2) change over time.

Secondary End Points

The secondary end points will include the following:

- UACR
- eGFR (mL/min/1.73 m^2) change over time for cohorts with a baseline eGFR of (1) ≥60 mL/min/1.73 m^2 and (2) 45 to 59 mL/min/1.73 m^2
- Serum creatinine level
- HbA_{1c} level
- Weight (BMI)

Statistical Analyses

The prevalent new-user design will proceed as follows. A cohort of all individuals who have been prescribed SGLT2is and/or GLP-1RAs will form a base cohort. As individuals can switch to combined SGLT2i and GLP-1RA therapy, we will identify an exposure set consisting of individuals who were exposed to either SGLT2is only or GLP-1RAs only prior to being prescribed combination therapy. The exposure set of individuals will constitute potential matches—participants who share the same drug histories, comorbidities, and demographics as those of given “switchers” (participants who switched to combined therapy). The prescription-based exposure sets will therefore provide equivalent points in the disease course with regard to comparator drug history and equivalent points at which confounder patient characteristics can be measured. A considerable computational challenge will arise when using estimated hazards as balancing scores in the matching process, given that there are approximately 3000 users of combined therapy in the Oxford-RCGP RSC data set. This will give rise to 3000 exposure sets with around 25,000 individuals. We will take (for sensitivity analyses) 10, 20, and 100 random prescription histories from each exposure set to estimate time-dependent propensity scores for switching therapies via conditional logistic regression (histories will be matched for each exposure set), whereby relative odds will be used to accurately estimate the corresponding relative hazards. The estimated propensity odds scores of the index “switchers” will be used to identify matched individuals (ie, participants with the closest matching variable values) from all members of the exposure set (not just the sampled members).

Summary statistics will be reported by using counts and percentages for categorical data, while means (with SDs) will be used to describe continuous data. We will report baseline demographics and comorbidities (using a chi-square test of independence for categorical variables and a Kruskal-Wallis test of difference for continuous variables) in the base cohort and in the matched cohort and adjudge whether good matching in the latter cohort has been achieved based on a standardized mean difference of <0.1 between groups. We will calculate and report mean changes (with SDs) in eGFR, albuminuria, serum creatinine level, HbA_{1c} level, and BMI between groups in the base cohort.

We will multiply impute (using the chained equations method) any missing data. A sensitivity analysis will be conducted on complete cases only. The primary analysis will include all participants. We will use a repeated-measures, multilevel, linear regression (with measurement occasions nested within individuals) to compare mean changes (from baseline) in eGFR at 12 and 24 months between those who switched to combined therapy and those on a single drug. A base model (containing only a cohort indicator) and a fully adjusted model (containing a cohort indicator together with all study variables) will be constructed and presented for inferences.

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Secondary end points (albuminuria, serum creatinine level, HbA_{1c} level, and BMI) will be similarly assessed for change at follow-ups.

The baseline eGFR will be a covariate, since we are using a repeated-measure regression for analyzing changes in eGFR from baseline to 12 and 24 months. Albuminuria, as a secondary outcome, will also be a covariate in the repeated-measure regression for analyzing changes from baseline to 12 and 24 months.

Power Calculation

We used G*Power to perform a power calculation for a repeated-measures ANOVA, basing our calculation on the results of a trial [13] where changes in eGFRs over 52 weeks were compared between drug groups. An absolute difference in eGFR reduction was measured at 2.7 mL/min/1.73 m^2 between drug groups. Given that an SE of 0.7 was reported for eGFR values in both groups and assuming a sample size of 384, we estimated a Cohen effect size (f_z) of approximately 0.19 (a moderate effect size) with 90% power at an α level of .05 for detecting a between-group effect of 0.10 (assuming a correlation of 0.5 between repeated measures). As such, we require a (total) sample size of 1032. Such a sample size is also sufficient for detecting group-by-time interaction effects of the same size.

Ethics Approval

The study proposal was approved by the Medical Sciences Interdivisional Research Ethics Committee, University Oxford, in August 2021 (approval number: R76885/RE001).

Results

The study is due to commence in March 2022 and is expected to be complete by September 2022.

Discussion

Study Implications

Our study will evaluate if combining 2 glucose-lowering drugs with established kidney benefits in randomized clinical trials and with differing mechanisms of action will have additive effects on kidney end points in real-world clinical practice.

Diabetes continues to be a leading cause of CKD and ESKD. Following the studies that were conducted 2 decades ago on the renal benefits of RAS blockers, these drugs are now considered part of standard therapy for preventing or delaying the progression of DKD [1]. The recent evidence for SGLT2i and GLP-1RA therapy with regard to their individual positive benefits on kidney end points has offered further individual drug options with renoprotective mechanisms in type 2 diabetes [5-15].

The mechanisms by which both drug classes influence kidney end points, such as reducing the risk and progression of albuminuria and slowing eGFR decline in type 2 diabetes, remain to be fully elucidated [28-30] Both drug groups favorably affect major risk factors for developing CKD by improving hyperglycemia, blood pressure, and weight loss. Further, trials reporting the effects of SGLT2is and GLP-1RAs on the progression of renal parameters have shown that these benefits occur independently of other clinical factors. Recent evidence indicates that GLP-1RAs have direct antiatherosclerotic influences on antioxidant, anti-inflammatory, and antifibrotic effects in diabetic kidneys [28]. By contrast, SGLT2is exert a hemodynamic effect, as well as specific, intrarenal, hemodynamic changes, that may protect glomeruli from high-pressure damage [29]. There is emerging physiological evidence for a combination effect [30].

Strengths and Limitations of the Study

The strengths of the study is that the Oxford-RCGP RSC database is derived from a large sample size with wide national coverage across primary care in England. The other benefits of the database include high data quality, with data dating back to 2004, which makes the database an ideal resource for the longitudinal follow-up of patient populations. The Oxford-RCGP RSC network also comprises a broadly representative population in terms of age, sex, and ethnicity when compared to England and Wales census data.

A limitation of the study is confounding. The prevalent new-user study design and time-conditional propensity score matching are used to address this, but there may be residual confounding due to unmeasured variables.

The process for considering an individual who is exposed to the medication of interest from the date of the first prescription (cohort entry) until the date of the last prescription plus 3 months is a potential limitation of the study. First, there is an assumption that the participants are taking the medication as prescribed, and second, the participants may have temporarily discontinued the medication during the presumed exposure period. Finally, the 3-month grace period relates to the longest prescription that a general practitioner can issue to a patient but is likely to be an overestimate in most cases.

Time-related biases are a potential limitation of the study. Time-lag bias may arise as a consequence of SGLT2i, GLP-1RA, and combination treatment not being initiated at the same time on the diabetes pathway. Consequently, the exposure groups may be at different stages of diabetes. We have attempted to address this by including the duration of diabetes and diabetic retinopathy—a microvascular complication of diabetes—in the propensity score.

Conclusions

There is emerging evidence from observational studies on the generalizability of cardiovascular outcome trials involving either SGLT2i monotherapy or GLP-1RA monotherapy to real-world clinical practice [31,32]. Our study will be one of the first studies to assess the effects of SGLT2i and GLP-1RA combination therapy in the management of type 2 diabetes and its effects on kidney end points from a real-world clinical perspective.

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Acknowledgments

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Conflicts of Interest

WH has had part of his academic salary funded by grant awards from Eli Lilly and Company, Novo Nordisk Ltd, and AstraZeneca UK Ltd. SdL is the director of the Royal College of General Practitioners Research and Surveillance Centre and holds or had recently held grants from EU Horizon 2020, European Association for Study of Diabetes Primary Care Diabetes Europe, Eli Lilly and Company, AstraZeneca, and Novo Nordisk Ltd through his university for investigator-led research in diabetes. DW has an ongoing consultancy contract with AstraZeneca. He has received payments from Amgen, Astellas, Bayer, Boehringer Ingelheim, Gilead, GlaxoSmithKline, Janssen, Mundipharma, Merck Sharp and Dohme, Napp, Tricida, and Zydus.

References

1. Rangaswami J, Bhalla V, de Boer IH, Staruschenko A, Sharp JA, Singh RR, American Heart Association Council on the Kidney in Cardiovascular Disease; Council on Arteriosclerosis, Thrombosis and Vascular Biology; Council on Cardiovascular and Stroke Nursing; Council on Clinical Cardiology; and Council on Lifestyle and Cardiometabolic Health. Cardiorenal protection with the newer antidiabetic agents in patients with diabetes and chronic kidney disease: A scientific statement from the American Heart Association. Circulation 2020 Oct 27;142(17):e265-e286 [FREE Full text] [doi: 10.1161/CIR.0000000000000920] [Medline: 32981345]
2. Alicic RZ, Rooney MT, Tuttle KR. Diabetic kidney disease: Challenges, progress, and possibilities. Clin J Am Soc Nephrol 2017 Dec 07;12(12):2032-2045 [FREE Full text] [doi: 10.2215/CJN.11491116] [Medline: 28522654]
3. Garlo KG, White WB, Bakris GL, Zannad F, Wilson CA, Kupfer S, et al. Kidney biomarkers and decline in eGFR in patients with type 2 diabetes. Clin J Am Soc Nephrol 2018 Mar 07;13(3):398-405 [FREE Full text] [doi: 10.2215/CJN.05280517] [Medline: 29339356]
4. Vistisen D, Andersen GS, Hulman A, Persson F, Rossing P, Jørgensen ME. Progressive decline in estimated glomerular filtration rate in patients with diabetes after moderate loss in kidney function-even without albuminuria. Diabetes Care 2019 Oct;42(10):1886-1894. [doi: 10.2337/dc19-0349] [Medline: 31221677]
5. Zinman B, Wanner C, Lachin JM, Fitchett D, Bluhmki E, Hantel S, EMPA-REG OUTCOME Investigators. Empagliflozin, cardiovascular outcomes, and mortality in type 2 diabetes. N Engl J Med 2015 Nov 26;373(22):2117-2128. [doi: 10.1056/NEJMoa1504720] [Medline: 26378978]
6. Wanner C, Inzucchi SE, Lachin JM, Fitchett D, von Eynatten M, Mattheus M, EMPA-REG OUTCOME Investigators. Empagliflozin and progression of kidney disease in type 2 diabetes. N Engl J Med 2016 Jul 28;375(4):323-334. [doi: 10.1056/NEJMoa1515920] [Medline: 27299675]
7. Neal B, Perkovic V, Mahaffey KW, de Zeeuw D, Fulcher G, Erondu N, CANVAS Program Collaborative Group. Canagliflozin and cardiovascular and renal events in type 2 diabetes. N Engl J Med 2017 Aug 17;377(7):644-657. [doi: 10.1056/NEJMoa1611925] [Medline: 28605608]
8. Wiviott SD, Raz I, Bonaca MP, Mosenzon O, Kato ET, Cahn A, DECLARE–TIMI 58 Investigators. Dapagliflozin and cardiovascular outcomes in type 2 diabetes. N Engl J Med 2019 Jan 24;380(4):347-357. [doi: 10.1056/NEJMoa1812389] [Medline: 30415602]
9. Mosenzon O, Wiviott SD, Cahn A, Rozenberg A, Yanuv I, Goodrich EL, et al. Effects of dapagliflozin on development and progression of kidney disease in patients with type 2 diabetes: an analysis from the DECLARE-TIMI 58 randomised trial. Lancet Diabetes Endocrinol 2019 Aug;7(8):606-617. [doi: 10.1016/S2213-8587(19)30180-9] [Medline: 31196815]
10. Perkovic V, Jardine MJ, Neal B, Bompoint S, Heerspink HJL, Charytan DM, CREDENCE Trial Investigators. Canagliflozin and renal outcomes in type 2 diabetes and nephropathy. N Engl J Med 2019 Jun 13;380(24):2295-2306. [doi: 10.1056/NEJMoa1811744] [Medline: 30990260]
11. Cannon CP, Pratley R, Dagogo-Jack S, Mancuso J, Huyck S, Masiukiewicz U, VERTIS CV Investigators. Cardiovascular outcomes with ertugliflozin in type 2 diabetes. N Engl J Med 2020 Oct 08;383(15):1425-1435. [doi: 10.1056/NEJMoa2004967] [Medline: 32966714]
12. Marso SP, Daniels GH, Brown-Frandsen K, Kristensen P, Mann JFE, Nauck MA, LEADER Steering Committee, LEADER Trial Investigators. Liraglutide and cardiovascular outcomes in type 2 diabetes. N Engl J Med 2016 Jul 28;375(4):311-322 [FREE Full text] [doi: 10.1056/NEJMoa1603827] [Medline: 27295427]
13. Tuttle KR, Lakshmanan MC, Rayner B, Busch RS, Zimmermann AG, Woodward DB, et al. Dulaglutide versus insulin glargine in patients with type 2 diabetes and moderate-to-severe chronic kidney disease (AWARD-7): a multicentre, open-label, randomised trial. Lancet Diabetes Endocrinol 2018 Aug;6(8):605-617. [doi: 10.1016/S2213-8587(18)30104-9] [Medline: 29910024]
14. Tuttle KR, Lakshmanan M, Rayner B, Zimmermann AG, Woodward B, Botros FT. CKD outcomes in type 2 diabetes and moderate-to-severe CKD treated with dulaglutide versus insulin glargine: award-7. Cochrane Library. 2018. URL: https://www.cochranelibrary.com/central/doi/10.1002/central/CN-02215884/full [accessed 2022-05-20]

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15. Mann JFE, Hansen T, Idorn T, Leiter LA, Marso SP, Rossing P, et al. Effects of once-weekly subcutaneous semaglutide on kidney function and safety in patients with type 2 diabetes: a post-hoc analysis of the SUSTAIN 1-7 randomised controlled trials. Lancet Diabetes Endocrinol 2020 Nov;8(11):880-893. [doi: 10.1016/S2213-8587(20)30313-2] [Medline: 32971040]
16. Jayasinghe KNU, Greener VJ, Feher MD. Combining SGLT2 inhibitor and GLP-1 agonist: exaggerated weight loss in a morbidly obese patient with type 2 diabetes. The British Journal of Diabetes 2016;16(3):138-139 [FREE Full text] [doi: 10.15277/bjd.2016.092]
17. Davies MJ, D'Alessio DA, Fradkin J, Kernan WN, Mathieu C, Mingrone G, et al. Management of hyperglycemia in type 2 diabetes, 2018. A consensus report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). Diabetes Care 2018 Dec;41(12):2669-2701 [FREE Full text] [doi: 10.2337/dci18-0033] [Medline: 30291106]
18. Type 2 diabetes in adults: management. National Institute for Health and Care Excellence. URL: http://www.nice.org.uk/guidance/ng28 [accessed 2022-05-05]
19. Correa A, Hinton W, McGovern A, van Vlymen J, Yonova I, Jones S, et al. Royal College of General Practitioners Research and Surveillance Centre (RCGP RSC) sentinel network: a cohort profile. BMJ Open 2016 Apr 20;6(4):e011092 [FREE Full text] [doi: 10.1136/bmjopen-2016-011092] [Medline: 27098827]
20. McGovern A, Hinton W, Correa A, Munro N, Whyte M, de Lusignan S. Real-world evidence studies into treatment adherence, thresholds for intervention and disparities in treatment in people with type 2 diabetes in the UK. BMJ Open 2016 Nov 24;6(11):e012801 [FREE Full text] [doi: 10.1136/bmjopen-2016-012801] [Medline: 27884846]
21. de Lusignan S, Bernal JL, Byford R, Amirthalingam G, Ferreira F, Akinyemi O, et al. Seasonal influenza surveillance and vaccine effectiveness at a time of co-circulating COVID-19: Oxford-Royal College of General Practitioners (RCGP) Research and Surveillance Centre (RSC) and Public Health England (PHE) protocol for winter 2020/21. JMIR Public Health Surveill. Preprint posted online on September 15, 2020 . [doi: 10.2196/preprints.24341]
22. de Lusignan S, Jones N, Dorward J, Byford R, Liyanage H, Briggs J, et al. The Oxford Royal College of General Practitioners Clinical Informatics Digital Hub: Protocol to develop extended COVID-19 surveillance and trial platforms. JMIR Public Health Surveill 2020 Jul 02;6(3):e19773 [FREE Full text] [doi: 10.2196/19773] [Medline: 32484782]
23. Langdown C, Peckham S. The use of financial incentives to help improve health outcomes: is the quality and outcomes framework fit for purpose? A systematic review. J Public Health (Oxf) 2014 Jun;36(2):251-258. [doi: 10.1093/pubmed/fdt077] [Medline: 23929885]
24. McGovern A, Hinton W, Calderara S, Munro N, Whyte M, de Lusignan S. A class comparison of medication persistence in people with type 2 diabetes: A retrospective observational study. Diabetes Ther 2018 Feb;9(1):229-242 [FREE Full text] [doi: 10.1007/s13300-017-0361-5] [Medline: 29302934]
25. Digital Medicines information Suite. MedicinesComplete. URL: http://www.medicinescomplete.com [accessed 2022-05-05]
26. Levey AS, Stevens LA, Schmid CH, Zhang YL, Castro AF3, Feldman HI, CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration). A new equation to estimate glomerular filtration rate. Ann Intern Med 2009 May 05;150(9):604-612 [FREE Full text] [doi: 10.7326/0003-4819-150-9-200905050-00006] [Medline: 19414839]
27. Cole NI, Liyanage H, Suckling RJ, Swift PA, Gallagher H, Byford R, et al. An ontological approach to identifying cases of chronic kidney disease from routine primary care data: a cross-sectional study. BMC Nephrol 2018 Apr 10;19(1):85 [FREE Full text] [doi: 10.1186/s12882-018-0882-9] [Medline: 29636024]
28. Dieter BP, Alicic RZ, Tuttle KR. GLP-1 receptor agonists in diabetic kidney disease: from the patient-side to the bench-side. Am J Physiol Renal Physiol 2018 Dec 01;315(6):F1519-F1525 [FREE Full text] [doi: 10.1152/ajprenal.00211.2018] [Medline: 30110568]
29. Dekkers CCJ, Gansevoort RT. Sodium-glucose cotransporter 2 inhibitors: extending the indication to non-diabetic kidney disease? Nephrol Dial Transplant 2020 Jan 01;35(Suppl 1):i33-i42 [FREE Full text] [doi: 10.1093/ndt/gfz264] [Medline: 32003836]
30. Goncalves E, Bell DSH. Combination treatment of SGLT2 inhibitors and GLP-1 receptor agonists: Symbiotic effects on metabolism and cardiorenal risk. Diabetes Ther 2018 Jun;9(3):919-926 [FREE Full text] [doi: 10.1007/s13300-018-0420-6] [Medline: 29623594]
31. Hinton W, Feher MD, Munro N, de Lusignan S. How generalizable are cardiovascular outcome trials of sodium-glucose co-transporter-2 inhibitors? A national database study: Study protocol. Diabetes Ther 2019 Jun;10(3):1163-1170 [FREE Full text] [doi: 10.1007/s13300-019-0620-8] [Medline: 31041781]
32. Hinton W, Feher M, Munro N, Walker M, de Lusignan S. Real-world prevalence of the inclusion criteria for the LEADER trial: Data from a national general practice network. Diabetes Obes Metab 2019 Jul;21(7):1661-1667 [FREE Full text] [doi: 10.1111/dom.13710] [Medline: 30900349]

Abbreviations

CKD: chronic kidney disease
CMR: computerized medical record
DKD: diabetic kidney disease

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eGFR: estimated glomerular filtration rate
ESKD: end-stage kidney disease
GLP-1RA: glucagon-like peptide-1 receptor agonist
HbA_{1c}: hemoglobin A_{1c}
RAS: renin-angiotensin system
RCGP: Royal College of General Practitioners
RSC: Research and Surveillance Centre
SGLT2i: sodium-glucose cotransporter-2 inhibitor
UACR: urine albumin-creatinine ratio

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Protocol

Feasibility and Impact of Integrating an Artificial Intelligence–Based Diagnosis Aid for Autism Into the Extension for Community Health Outcomes Autism Primary Care Model: Protocol for a Prospective Observational Study

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Abstract

Background: The Extension for Community Health Outcomes (ECHO) Autism Program trains clinicians to screen, diagnose, and care for children with autism spectrum disorder (ASD) in primary care settings. This study will assess the feasibility and impact of integrating an artificial intelligence (AI)–based ASD diagnosis aid (the *device*) into the existing ECHO Autism Screening Tool for Autism in Toddlers and Young Children (STAT) diagnosis model. The prescription-only Software as a Medical Device, designed for use in children aged 18 to 72 months at risk for developmental delay, produces ASD diagnostic recommendations after analyzing behavioral features from 3 distinct inputs: a caregiver questionnaire, 2 short home videos analyzed by trained video analysts, and a health care provider questionnaire. The device is not a stand-alone diagnostic and should be used in conjunction with clinical judgment.

Objective: This study aims to assess the feasibility and impact of integrating an AI-based ASD diagnosis aid into the ECHO Autism STAT diagnosis model. The time from initial ECHO Autism clinician concern to ASD diagnosis is the primary end point. Secondary end points include the time from initial caregiver concern to ASD diagnosis, time from diagnosis to treatment initiation, and clinician and caregiver experience of device use as part of the ASD diagnostic journey.

Methods: Research participants for this prospective observational study will be patients suspected of having ASD (aged 18-72 months) and their caregivers and up to 15 trained ECHO Autism clinicians recruited by the ECHO Autism Communities research team from across rural and suburban areas of the United States. Clinicians will provide routine clinical care and conduct best practice ECHO Autism diagnostic evaluations in addition to prescribing the device. Outcome data will be collected via a combination of electronic questionnaires, reviews of standard clinical care records, and analysis of device outputs. The expected study duration is no more than 12 months. The study was approved by the institutional review board of the University of Missouri-Columbia (institutional review board–assigned project number 2075722).

Results: Participant recruitment began in April 2022. As of June 2022, a total of 41 participants have been enrolled.

Conclusions: This prospective observational study will be the first to evaluate the use of a novel AI-based ASD diagnosis aid as part of a real-world primary care diagnostic pathway. If device integration into primary care proves feasible and efficacious, prolonged delays between the first ASD concern and eventual diagnosis may be reduced. Streamlining primary care ASD diagnosis

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could potentially reduce the strain on specialty services and allow a greater proportion of children to commence early intervention during a critical neurodevelopmental window.

Trial Registration: ClinicalTrials.gov NCT05223374; https://clinicaltrials.gov/ct2/show/NCT05223374

International Registered Report Identifier (IRRID): PRR1-10.2196/37576

(JMIR Res Protoc 2022;11(7):e37576) doi:10.2196/37576

KEYWORDS

autism spectrum disorder; diagnosis; artificial intelligence; primary care; machine learning; Software as a Medical Device; mobile phone

Introduction

Background

Autism spectrum disorder (ASD), a neurodevelopmental disorder impacting both communication and behavior, affects approximately 1 in every 44 children in the United States [1]. Targeted early intervention during a critical neurodevelopmental window is recommended to maximize long-term cognitive gains [2,3], adaptive behaviors [4-6], social and emotional functioning [7,8], and verbal fluency [8,9]. ASD evaluations have traditionally been managed in specialist settings; however, a rapid rise in prevalence rates over the past half century [10] has outpaced specialist capacity and led to prolonged wait times for diagnostic evaluations [10-13]. Currently, families in the United States may wait as long as 18 months between initial screening by their primary care clinician and diagnosis by a specialist [11].

Rising ASD prevalence rates, combined with specialist shortages, have contributed to significant diagnostic delays in the United States. Although ASD can be reliably diagnosed at as early as 18 months, the mean age of ASD diagnosis has remained >4 years since the Centers for Disease Control and Prevention began tracking prevalence rates [1,14-16]. The average 3 years delay from first parental concern to eventual diagnosis recorded in the literature is even longer for demographic groups that include girls, children of color, and children who are rural residing or of lower socioeconomic status [17-20]. An estimated 27% of children with ASD in the United States remain undiagnosed at the age of 8 years [20].

Given the importance of early diagnosis and intervention, the American Academy of Pediatrics has recommended that all children be screened in primary care at 18 and 24 months, in addition to whenever caregivers express concern [12]. When they feel confident, upon a failed screen, primary care clinicians are encouraged to make the ASD diagnosis themselves using the Diagnostic and Statistical Manual of Mental Disorders–fifth edition (DSM-5) criteria [12]. Alternatively, they can refer to specialists for further assessment. However, studies suggest that clinicians do not consistently screen or refer to these recommendations [21]. Currently, <1% of all ASD diagnoses are made by primary care clinicians in the United States [21,22].

The low rates of ASD diagnosis in primary care settings may be explained by several factors. Clinician–identified barriers include a lack of ASD-specific training and low self-efficacy in making the diagnosis, as well as time constraints that limit their ability to comprehensively evaluate, review results, and discuss treatment plans with families in primary care [23-26]. Complex presentations in children with ASD, including multiple overlapping comorbidities and a diverse spectrum of symptoms, can also confound the diagnosis [27]. Although diagnostic tools have been developed to support accurate evaluations [28], *gold standard* ASD diagnostic instruments with the highest validity [28-30] are typically poorly suited to use in primary care. This is because they are time intensive and typically require in-person delivery in a clinical facility and specialist training for reliable administration. Even when clinicians receive specialist training, primary care reimbursement rates may be insufficient to justify the effort [31].

Device Development

Diagnosis aids tailored specifically for use in primary care are urgently needed to streamline ASD evaluations and enhance primary care diagnostic capacity. In response to this need, an artificial intelligence (AI)–based Software as a Medical Device [32] was developed to support health care providers in diagnosing or ruling out ASD in children aged 18 to 72 months with concerns for developmental delay. The device is indicated for use by health care providers who have prescriptive authority in their state of practice. For the purposes of this study the device will be used exclusively by primary care Extension for Community Health Outcomes (ECHO) Autism clinicians. The device was developed using patient record data from thousands of children with diverse conditions, presentations, and comorbidities who were either diagnosed with ASD or confirmed not to have ASD based on standardized diagnostic tools [29,30] and representing both sexes across the supported age range. The underlying device algorithm was iteratively improved, supplemented with ASD expert input, and prospectively validated for over 7 years [33-38]. Key steps involved in device use are illustrated in Figure 1.

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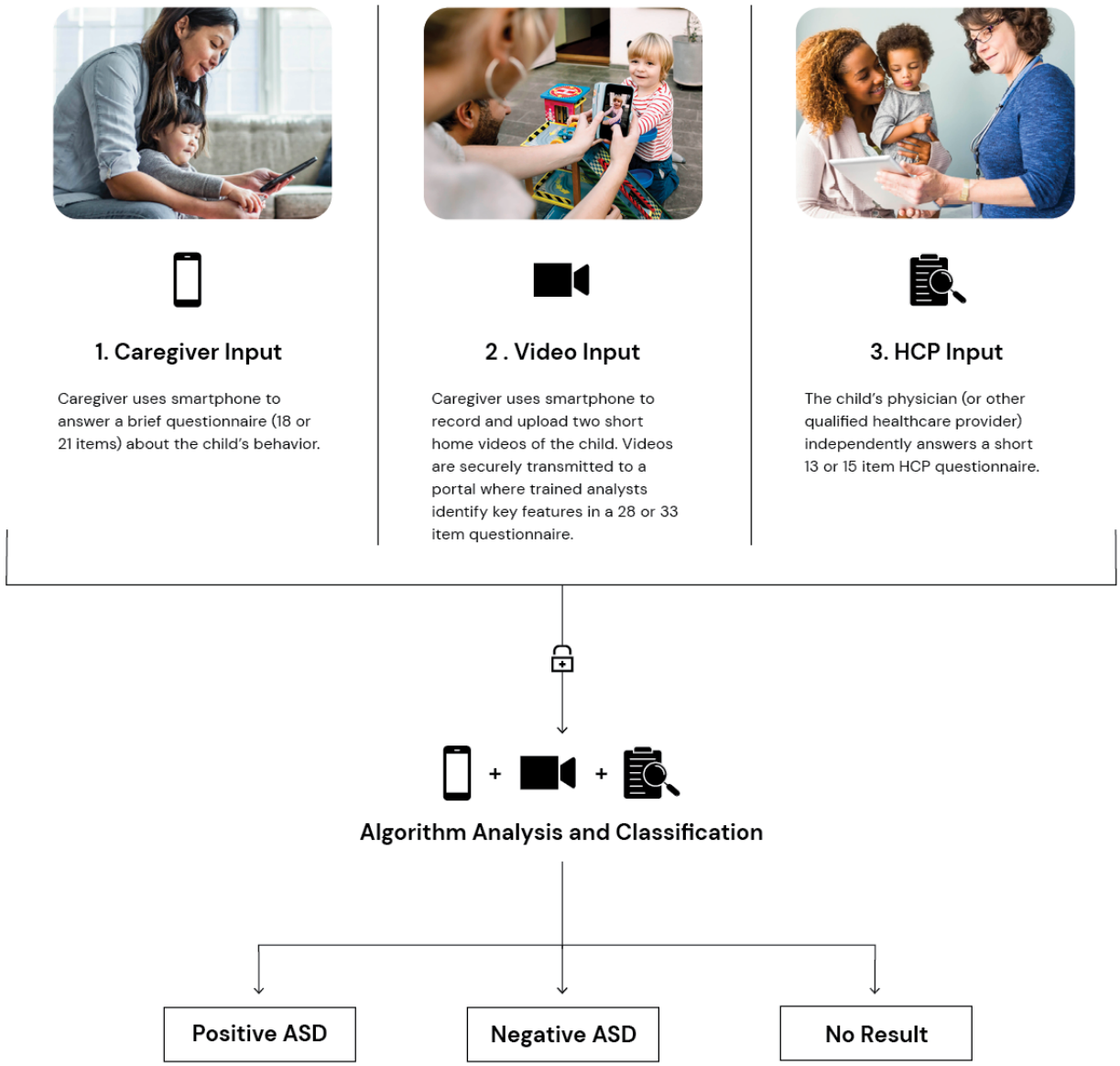
Figure 1. Overview of device use. ASD: autism spectrum disorder; HCP: health care provider.



The device integrates 3 independent inputs within its gradient-boosted decision tree algorithm: a brief caregiver questionnaire (completed via a mobile app), a video analyst questionnaire based on the analysis of 2 short home videos uploaded by the caregiver (completed in the video analyst portal), and a health care provider questionnaire (completed in the health care provider portal). The device evaluates inputs based on the predictive features that are most indicative of ASD. If the information provided is sufficiently granular, the device will provide an *ASD Positive* or *ASD Negative* output. When a highly predictive determination cannot be made, the device abstains from providing a result (*No Result* output). Following strong pivotal trial results [39], the device received Food and Drug Administration (FDA) marketing authorization on June 2, 2021 [40]. In a prospective, double-blinded multisite pivotal trial, the device was found to facilitate timely and accurate ASD diagnostic evaluation in nearly a third of the study cohort while minimizing false negatives to maintain clinical safety [39]. However, real-world evidence is needed to learn more about the utility and impact of the device in everyday US primary care settings.

The ECHO Autism Primary Care Model

ECHO Autism primary care [41,42] is a virtual learning program in which primary care clinicians receive guidance from ASD experts regarding best practices for ASD screening, identification, and management of medical and psychiatric comorbidities. The diagnostic component of the ECHO Autism primary care model involves training clinicians to conduct diagnostic assessments for ASD using the Screening Tool for Autism in Toddlers and Young Children (STAT), a level 2 ASD screener used as a diagnostic observational measure. The ECHO Autism STAT model provides training and mentorship to equip clinicians to diagnose ASD in cases that are clear and

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unambiguous and appropriately identify and refer complex cases for further assessment [43]. A 12-month pilot study with 18 participating clinicians was conducted using the ECHO Autism STAT model [43]. In this study, participating clinicians presented the results of their assessment to the ECHO Autism expert hub team for specialist input before guiding the diagnostic pathway to include either a diagnosis of ASD or a referral for further specialist evaluation. This pilot study showed that 73% of the participants reported acceptance of referrals for ASD diagnostic evaluations following program completion, and 80% reported an increase in the number of children with ASD in their caseloads. In addition, the pilot demonstrated a 2- to 6-month decrease in time to access services when compared with standard-of-care diagnostic pathways [41].

Study Objectives

The objective of this study is to assess the feasibility and impact of integrating the device into the existing primary care diagnostic pathway, the *ECHO Autism STAT model*.

Methods

Ethics Approval

The study was approved by the institutional review board of the University of Missouri-Columbia (institutional review board–assigned project number 2075722) and registered with ClinicalTrials.gov (NCT05223374).

Study Design

This prospective observational study was designed to obtain real-world evidence pertaining to the feasibility and impact of integrating the device into a primary care ASD diagnostic pathway. Demographic, clinical, and qualitative user experience data will be obtained from eligible participants. All decisions regarding patient care will be determined by the ECHO Autism clinicians, as the study is noninterventional. All clinical outcomes will be assessed by the ECHO Autism clinician, as in routine clinical practice.

Study Population

ECHO Autism Clinicians

Inclusion Criteria

Clinicians eligible for study participation will be practicing primary care physicians and nurse practitioners who are able to evaluate patients for ASD as part of their scope of practice. All clinicians must have received training in the ECHO Autism Communities diagnostic model from the University of Missouri ECHO Autism team before study enrollment.

Exclusion Criteria

Clinicians who are unable to evaluate patients with suspected ASD or who have not completed the ECHO Autism diagnostic training will be excluded from study enrollment.

ECHO Autism Program Recruitment

Starting in 2016, practicing primary care clinicians located in geographically diverse areas across Missouri were invited to participate in ECHO Autism STAT. Participants were identified through word of mouth, professional association listservs, and strategic recruitment from underserved locations. This program was a continuation of the existing ECHO Autism primary care program that started in 2015. A 2-day training was added focused on use of a direct behavior observation tool (STAT) and comprehensive diagnostic interviewing. The ECHO Autism STAT participants completed in-person training, regularly participated in ECHO Autism telementoring sessions, and achieved reliability with the certified trainer on the STAT observation. After completion of the training elements, these participants were eligible to bring diagnostic cases for discussion during the tele–ECHO Autism sessions. Only clinicians completing all elements of the ECHO Autism diagnostic training are eligible for participation in this study. Eligible clinician participants will be informed of the planned study, offered 2 sessions to ask questions about study participation, and consented through usual research procedures.

Patients and Caregivers

Inclusion and Exclusion Criteria

At the time of screening, patients must meet all of the inclusion criteria (Textbox 1) to be eligible for study enrollment. Patients who meet any of the exclusion criteria (Textbox 1) will not be eligible for enrollment in the study.

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Textbox 1. Inclusion and exclusion criteria.

Inclusion criteria

- Must be aged 18 to 72 months
- Must have developmental delay concerns expressed by caregivers, clinicians, or other community-based professionals
- The participating caregiver must speak English proficiently in the opinion of the clinician.
- Must be able to read, understand, sign, and date the informed consent form
- Must have a smartphone using either an iOS or Android operating system (as of June 2022, iOS 14 or 15 and Android 11 or 12, excluding Android Go, are supported; future updates are planned to ensure ongoing compatibility with new operating system versions as they are released)
- Must be willing to have the child videotaped as part of the device input
- Must meet device labeling requirements

Exclusion criteria

- Participants with a prior diagnosis of autism spectrum disorder rendered by a clinician
- Participants having any other medical, behavioral, or developmental condition that in the opinion of the clinician, may confound study data or assessments
- Participants whose age on the date of enrollment is outside the target age range
- Participants who have, to the best of their knowledge, been previously enrolled in any clinical study or survey involving the device or who have a caregiver who has been enrolled in any such study
- Participants whose medical records have been included in any internal device machine learning training or validation sets

Patient Recruitment

Participants will be recruited from the population of patients that the ECHO Autism clinician would see as part of their usual enhanced primary care practice. As part of routine practice, ECHO Autism clinicians receive referrals from external primary care clinicians, and when the referrals are received, families will be informed of the opportunity to participate in the study if deemed eligible. Participating clinicians or their designees will inform caregivers of children presenting with a concern for developmental delay about the study. Additional recruitment strategies such as social media, flyers, and email communication with community clinicians may be used as needed to reach recruitment goals.

Study Flow

Overview

This study is being conducted by the University of Missouri ECHO Autism Communities Research Team. Eligible caregivers of patients with a concern for developmental delay and ECHO Autism clinicians will complete the informed consent process before entering the study. Once enrolled, ECHO Autism clinicians will provide routine clinical care and conduct best practice ECHO Autism diagnostic evaluations with the addition of device prescriptions for patients suspected of having ASD. Patients will be followed up with routine clinical care on the schedule shown in Figure 2. Data will be collected at the end of the 3-month follow-up period. The clinician will complete a visit form for any interim visits that occur between visit 1 and the 3-month follow-up appointment.

The study flow is summarized in Figure 2 and described in detail in the following sections.

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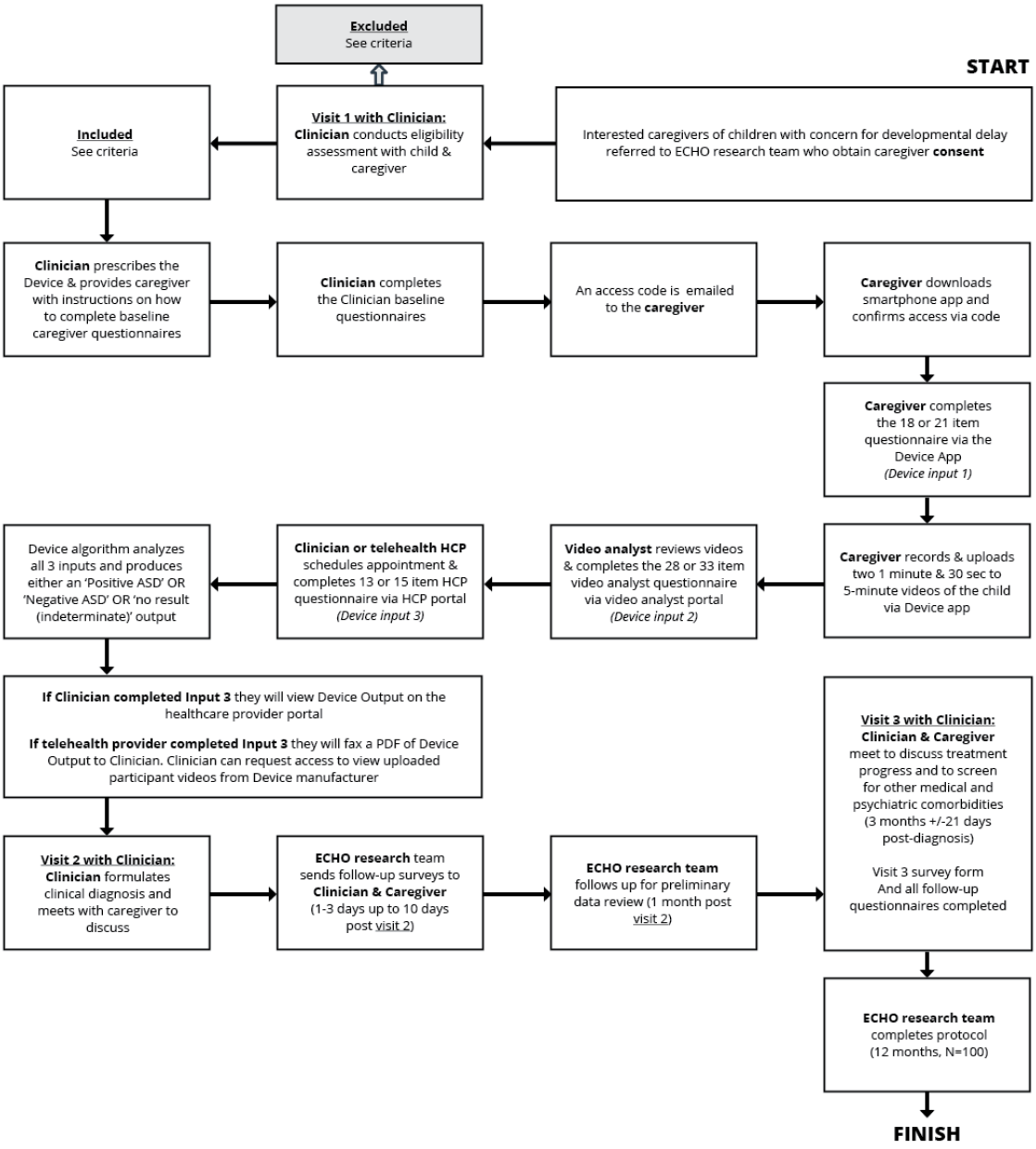
Figure 2. Study flow. ASD: autism spectrum disorder; ECHO: Extension for Community Health Outcomes; HCP: health care provider.



Visit 1: Eligibility Determination

An appointment is scheduled for a participant (patient) with concern for developmental delay and their caregiver. During the first clinic visit, the ECHO Autism clinician will observe the participant and conduct a DSM-5 interview to determine whether the participant requires further ASD evaluation.

Baseline Data Collection

The ECHO Autism clinician will connect the caregiver of any potential participant requiring further evaluation for ASD to the University of Missouri ECHO Autism Communities research team. Before visit 1, the research team will obtain consent from the family. The research team will provide instructions on how to complete the electronic study baseline caregiver questionnaires and download the device's caregiver app. The research team will also send electronic baseline ECHO Autism clinician questionnaires to the clinician to complete. The clinician will prescribe the device.

Device Completion

Once the device is prescribed by the clinician, the study sponsor will release the access code to the study team, who will then email it to the caregiver. The caregiver will download the mobile app to their smartphone and access the app using the code. The caregiver will then complete an 18- or 21-item age-dependent caregiver questionnaire (*device input 1*) and record and upload two 1.5-minute to 5-minute videos of the child on the mobile app. The uploaded videos will be remotely reviewed and scored on a 28- or 33-item video analyst questionnaire (*device input 2*) by a trained video analyst via the video analyst portal. The ECHO Autism clinician then has the option to *either* complete the health care provider questionnaire, which is a 13- or 15-item age-dependent questionnaire (*device input 3*), themselves or

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schedule the participant for a telehealth provider appointment, during which the questionnaire will be completed by the telehealth provider. The device algorithm then analyzes all 3 inputs and produces either a *positive ASD*, *negative ASD*, or *indeterminate/no result* output for the clinician to review.

Visit 2: Diagnostic Results Meeting

After the device output is received, the clinician will synthesize their diagnostic impressions (ie, in-person observation, DSM-5 interview, and questionnaires) and the device output to determine whether the participant meets the criteria for a diagnosis of ASD. The clinician may also request access to view the participant's videos when making a diagnosis. In cases where the clinician's judgment conflicts with the device output, the diagnostic determination of the clinician (who remains the decision-maker in the diagnostic process) takes precedence. This is consistent with the device's FDA market authorization status as a diagnosis aid intended to support health care providers in diagnosing ASD rather than as a stand-alone diagnostic device.

For participants whom the clinician determines as meeting the criteria of ASD, the clinician will deliver the diagnosis to the caregiver during visit 2. In addition, the clinician will schedule a 3-month follow-up visit. The research team will then send electronic postdiagnostic questionnaires to the caregiver and the clinician to be completed 1 to 3 (up to 10) days after visit 2.

Visit 3: Treatment Progress Meeting

The clinician will follow-up with the caregiver for 3 months (+21 or –21 days) after the participant receives an ASD diagnosis to discuss treatment progress and screen for any other medical and psychiatric comorbidities. The research team will send electronic postdiagnostic questionnaires to the caregiver and clinician to complete 1 to 3 (up to 10) days after this follow-up visit.

Interim Visit Forms

Clinicians will complete interim visit forms for any additional visits that may occur between study enrollment and the scheduled final 3-month follow-up visit.

Long-term Follow-up

Participants and their caregivers may be considered for enrollment if they choose to consent to an extension study to continue data collection related to long-term outcomes.

Number of Sites Enrolling Participants

Up to 15 University of Missouri ECHO Autism clinicians in both rural and suburban areas across the United States will be recruited.

Study Duration

Study enrollment is expected to take approximately 12 months. Patient participation will occur from the time the ECHO Autism clinician identifies a concern for ASD through +21 or −21 days of the 3-month follow-up visit.

Potential Risks and Benefits of Participation

There are no physical risks associated with participation in the study. Caregivers may feel some psychological discomfort when answering questions about their children's behaviors. Children might also feel some psychological discomfort when being filmed for the video analysis. Videos will be used to evaluate participants' behaviors as part of the diagnostic process. The videos will be captured within the mobile app, stored on Amazon's secure cloud service (Amazon S3), and analyzed by the device manufacturer through a secure web portal. By agreeing to participate in the study, participants will grant and release all rights, titles, and interests in the videos to the device manufacturer. Another potential risk is the possible release of sensitive medical, behavioral, or educational information. To mitigate the risk of releasing sensitive personal information, the device manufacturer will adhere to confidentiality protocols aligned with the US Health Insurance Portability and Accountability Act and FDA 21 Code of Federal Regulations Part 11, as well as other federal, national, and local laws and regulations, to protect the privacy of personal information. All content within the mobile app will be stored on Amazon S3 and analyzed by the device manufacturer through a secure web portal. When data are published, they will be anonymized in a manner that prevents the identification of specific caregivers or participants. To the best of the manufacturer's knowledge, there were no data or security breaches in any prior studies involving the device.

A potential benefit of the study is that device use could support ECHO Autism clinicians in identifying participants with ASD earlier than they would otherwise have been identified, thus enabling earlier therapy, which is known to positively affect long-term outcomes.

Participant Withdrawal or Termination

Participation is completely voluntary. Caregivers may withdraw consent for study participation at any time by informing the principal investigator or the study staff. The principal investigator may also withdraw a participant from the study if determined that further participation would not be in the participant's best interest. Participants may be discontinued by the study staff if determined unable to fully meet the requirements of participation, including the completion of study visits and necessary assessments. The reasons for discontinuation will be recorded for all participants. If lost to follow-up, the research team will attempt to contact the caregiver by telephone, followed by registered mail, to establish the reason for withdrawal as completely as possible.

Study Objectives

Primary Objective

The primary objective is to assess the time from the initial concern by the ECHO Autism clinician to diagnosis when using the device as part of the diagnostic pathway.

Secondary Objectives

Secondary objectives include the collection and analysis of data from both the ECHO Autism clinician and caregiver participants to learn about the information described in Textbox 2.

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Textbox 2. Data collected for secondary objectives.

Data collected for secondary objectives

- Patient outcomes correlating with time to initiating therapy following a positive autism spectrum disorder (ASD) diagnosis
- Distance from patient home to nearest ASD specialist center
- Level of clinician self-efficacy in using the device as part of the evaluation and diagnosis of children with suspected ASD
- Qualitative data on the following: caregiver satisfaction with the diagnostic process; time from caregiver concern to diagnosis; clinician certainty rating for diagnostic determination; clinician satisfaction with using the device as part of the Extension for Community Health Outcomes (ECHO) Autism diagnostic process; caregiver perception of the device with validated questionnaire; determination of whether the use of the device enhances the efficiency and feasibility of the ECHO Autism Communities diagnostic process; likelihood to recommend (clinician and caregiver); efficiency and feasibility of ECHO Autism Community–based diagnostic process, as measured by self-efficacy, certainty ratings, perceived barriers, and practice patterns questionnaires; percentage of positive outcomes correlating with shorter durations between diagnosis and treatment; percentage of caregivers who feel they received a high-quality evaluation; percentage of clinicians with increased self-efficacy in using the device as part of the diagnostic process; percentage of clinicians finding the device helpful in the diagnostic process; percentage of positive device perceptions from caregiver; barriers to app use for caregivers; clinician-perceived barriers to practice implementation of device
- Assessment of insurance coverage or reimbursement (although insurance will not be billed for this study)
- Amount of time required for clinicians to make a diagnosis
- Percentage of clinician participants reporting a positive change in practice flow because of using the device as part of their diagnostic process
- Percentage of patients for whom the device can provide a determinate result (ASD positive or negative)
- Summary of interventional treatments recommended by the clinician following diagnosis
- Changes in clinician clinical practice flow
- Change in quality of life measures
- Time associated with device use

Data Collection Instruments and Schedule of Assessments

Clinical History

Details of participants' clinical and medical histories will be reviewed and captured, including the description and timing of the initial concern for ASD.

Diagnostic Procedures

Diagnostic procedures will be completed according to the ECHO Autism Communities standard of care, as determined by the treating clinician in routine clinical practice. Details of any such procedure will be captured throughout the study, including the follow-up period after a participant has received diagnostic results.

Therapeutic Interventions

Any new therapeutic interventions recommended by the ECHO Autism clinician will be captured at time points 1, 2, and 3 and for any interim visit. Once a recommendation has been made, data will be collected during subsequent visits to indicate patient compliance with the recommendations.

All data collection instruments are listed and described in Textbox 3.

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Textbox 3. Data collection instruments.

Caregiver questionnaire (device input 1)

- This is not a stand-alone assessment. The caregiver questionnaire will be completed within the mobile caregiver app upon receipt of the access code following completion of the informed consent form. This is an 18- or 21-item questionnaire that collects details related to the caregiver's observations of the participant's developmental behaviors.

Video analyst questionnaire (device input 2)

- This is not a stand-alone assessment. Video analysts will answer a 28- or 33-item age-dependent questionnaire in the video analyst portal after viewing the 2 short video submissions uploaded by the caregiver. Video analysts will evaluate the observed behaviors by answering a series of multiple-choice questions evaluating phenotypic features of autism spectrum disorder (ASD) such as nonverbal and verbal communication, social interaction, unusual sensory interests or reactions, stereotypic or repetitive motor movements, use of objects, or speech on the combinative videos.

Health care provider questionnaire (device input 3)

- This is not a stand-alone assessment. The clinician or telehealth provider will schedule a visit with the caregiver and participant (which can be remote). During this visit, the participant must be available for observation. The clinician or telehealth vendor will complete the 13- or 15-item questionnaire within the health care provider portal. The questionnaire addresses aspects of the child's behavior and development.

Device output

- Device output is produced by the device summarizing findings after algorithmic analysis of the 3 device inputs and contains one of 3 possible results: positive ASD, negative ASD, or no result. It is to be used by the clinician as part of the Extension for Community Health Outcomes (ECHO) Autism Community–based diagnostic process.

Measure of processes of care

- This measure assesses the family's perceptions of the care they and their child receive within a particular setting. It is a means to assess the family-centered behaviors of clinicians. This is a validated measure that has been adapted for this study.

ECHO Autism caregiver presurvey

- This survey collects initial demographic information regarding each family and assesses the family's initial perception of the ECHO Autism clinician as they begin the diagnostic process.

ECHO Autism caregiver postdiagnostic survey

- This survey assesses the caregiver's satisfaction with the services they received.

ECHO Autism clinician preproject survey

- This survey measures the ECHO Autism clinician's self-efficacy, perceived barriers, and satisfaction with the current ECHO Autism standard-of-care procedure.

ECHO Autism clinician postproject survey

- This survey measures the self-efficacy, perceived barriers, and satisfaction with the use of the device as part of the ECHO Autism standard-of-care procedure.

ECHO Autism 3-month follow-up questionnaires

- The purpose of these questionnaires is to address the data points required for the study's secondary and exploratory objectives.

ECHO Autism interim visit form

- The purpose of the form is to summarize any visit from a research participant occurring between the time of concern and the 3-month follow-up visit.

Statistical Analyses

Statistical and Analytical Plans

Descriptive statistics will be used to summarize the data. Continuous variables will be summarized as n, mean, SD, median, minimum, and maximum values. Categorical variables will be summarized as participant counts and related percentages.

General Approach

All available data will be included in data listings and tabulations. Data will be summarized by participant counts and related percentages. In general, categorical data will be presented using counts and percentages, whereas continuous variables will be presented using mean, SD, median, minimum, and maximum values. Counts of observed and missing data will also be reported.

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Safety Analysis

Device- and procedure-related adverse effects will be tabulated and analyzed.

Sample Size

This is a prospective study with up to 100 patient participants determined eligible for an evaluation for ASD and up to 15 ECHO Autism clinicians who conduct assessments.

Results

Participant recruitment began in April 2022. As of June 2022, a total of 41 participants have been enrolled in the study. Data collection is anticipated to continue through 2022, with the data analysis and publication of findings being planned for 2023.

Discussion

Principal Findings

To our knowledge, this collaborative observational study will be the first to evaluate the use of a novel AI-based ASD diagnosis aid as part of a real-world primary care diagnostic pathway. It is anticipated that this study will provide valuable feasibility data regarding device integration into a primary care workflow. The study results may help clarify the length of time between initial clinician concern and diagnosis when an AI-based device is used as part of the evaluation process. The results may also provide insights into device performance outside of a research setting, including the percentage of primary care participants for whom it is able to provide a determinate ASD positive or negative result, and concordance between device output and clinical diagnostic determination. Qualitative user experience measures captured as part of the study are anticipated to shed light on the acceptability of the device to both families and clinicians and may help drive future product improvements.

Comparison With Previous Literature

Although to date, no previous AI-based ASD diagnosis aid primary care–focused studies have been conducted, there is literature supporting the feasibility of diagnosing and managing ASD in primary care settings. For example, a recent systematic review focused on training clinicians to diagnose and manage ASD in primary care [44] found that with appropriate training and support, primary care clinicians can render diagnostic decisions that closely align with specialty team assessments. The reviewed studies also reported reduced wait times for diagnosis when a proportion of evaluations were moved to the primary care setting.

Strengths and Limitations

Despite well-documented bottlenecks in ASD diagnosis and treatment initiation in the United States [11,45], to date, very few diagnostic tools have been designed to enhance primary care diagnostic capacity. The integration of the device into the ECHO Autism primary care diagnostic pathway in this study offers several potential benefits over existing tools [28-30]. As it was designed with primary care use in mind, the device is more time-efficient than existing instruments and does not require specialist training to administer. For example, in the pivotal trial, the total time burden associated with device use was <30 minutes (median time for caregiver questionnaire completion was 4 minutes and 56 seconds; median time for video analyst scoring from the time video review began to submission of scores was 10 minutes and 54 seconds; self-reported time for health care providers to complete their questionnaire was approximately 10 minutes) [39].

The device is also amenable to remote administration. Caregivers will complete their questionnaires and upload videos remotely using an app on their mobile phones. Video analysts will receive inputs and upload questionnaire outputs remotely through an analyst portal. Pivotal trial data showed no evidence of performance degradation in cases where health care providers completed their questionnaires remotely versus in person. Remote administration may support diagnostic access for families residing in rural and remote locations, as well as families without access to transportation. Remote administration is also useful during public health emergencies such as the COVID-19 pandemic.

Compared with other ASD assessment instruments where the child is observed in a clinical setting, the device leverages home videos that provide naturalistic data about the child's behavior outside of the clinical setting. These data may help to overcome some of the challenges clinicians and caregivers have described capturing typical child behavior within time-limited clinical encounters [46]. For example, in the clinical setting, the child may become overly reactive to changes in the environment or may not display the behaviors of concern they exhibit at home. Without a picture of the child's typical behavior, it can be challenging for the clinician to make a confident diagnostic assessment.

The device was also trained on a large and diverse data set in terms of race and ethnicity, socioeconomic status, and gender. Although the pivotal trial was not powered for statistical inference on these covariates, our initial analysis indicated no evidence of inconsistent device performance across these variables [39]. This finding is encouraging and points to the potential of the device to address some of the well-documented disparities in current diagnostic approaches whereby girls and African American and Hispanic children are misdiagnosed more often, as well as diagnosed at a later age, on average, than other groups [47,48].

The device itself and the overall study design have several constraints and limitations. Device use requires access to a smartphone and wireless internet, which not all low-income American families have [49]. In addition, the device is only available in English. Thus, many culturally and linguistically diverse potential participants will be excluded from the study. Selection bias may also be a concern in this study. For example, parents with a higher number of concerns about their child's development may be more motivated to enroll in the study and complete all device inputs than parents with milder concerns. Attrition is another concern in this study as participation involves multiple steps and engagement over a 3-month period. Given the multiple steps involved, it is possible that study completers may end up representing a more motivated cohort

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than study leavers. The clinicians who will be recruited into the trial may also represent a biased sample, as by enrolling in ECHO training, they have already demonstrated an interest in enhancing their knowledge of developmental disabilities. In addition, owing to the ECHO Autism curriculum training they receive, clinicians may have more experience and background in ASD diagnosis than other primary care clinicians. In other settings, clinicians with less interest in ASD may be less motivated or confident in using the device and may be less willing to diagnose in the primary care setting.

Future Directions

The study follows participants for a total of 3 months. Additional follow-up studies are recommended to assess the stability of device performance over a longer period. For the purposes of this study, the sponsors will cover the device cost and associated clinician fees. However, if the device were to become a standard tool in primary care settings, it is unknown to what extent insurance companies would accept and reimburse these costs. Questions also remain regarding whether and how families with no health insurance can access the device. We recommend that future device studies be conducted in populations who have not completed the ECHO Autism diagnostic training program. Such research could help answer important questions about the feasibility of device use in primary care clinician populations with less ASD-specific knowledge and training.

Conclusions

If device integration into primary care practice proves feasible and efficacious, it may support clinicians in diagnosing more children in the primary care setting and reducing current delays between the first ASD concern and eventual diagnosis. Streamlining primary care ASD diagnosis could potentially reduce strain on specialist services by allowing for the diagnosis of less ambiguous cases in primary care and quicker referral of complex cases to relevant specialist teams. Ultimately, we hope that decreasing the time to diagnosis and age of diagnosis through enhanced primary care capacity will allow a greater proportion of children to commence early intervention during a critical neurodevelopmental window.

Acknowledgments

This study is sponsored by Cognoa Inc.

Conflicts of Interest

KS has received consulting fees from Cognoa, is on the Medical Advisory Board for Quadrant Biosciences, and provides research support for Autism Speaks. SL-M, JS, CS, and ST are employees of Cognoa and have Cognoa stock options. ST additionally receives consulting fees for Cognito Therapeutics, volunteers as a board member of the American Academy of Pediatrics-Orange County Chapter and American Academy of Pediatrics California, is a paid adviser for MI10 LLC, and owns stock for NTX, Inc, and HandzIn.

References

1. Maenner MJ, Shaw KA, Bakian AV, Bilder DA, Durkin MS, Esler A, et al. Prevalence and Characteristics of Autism Spectrum Disorder Among Children Aged 8 Years - Autism and Developmental Disabilities Monitoring Network, 11 Sites, United States, 2018. MMWR Surveill Summ 2021 Dec 03;70(11):1-16 [FREE Full text] [doi: 10.15585/mmwr.ss7011a1] [Medline: 34855725]
2. Ben Itzchak E, Zachor DA. Who benefits from early intervention in autism spectrum disorders? Res Autism Spectrum Disorders 2011 Jan;5(1):345-350. [doi: 10.1016/j.rasd.2010.04.018]
3. Flanagan H, Perry A, Freeman N. Effectiveness of large-scale community-based Intensive Behavioral Intervention: a waitlist comparison study exploring outcomes and predictors. Res Autism Spectrum Disorders 2012 Apr;6(2):673-682. [doi: 10.1016/j.rasd.2011.09.011]
4. Smith T, Klorman R, Mruzek DW. Predicting outcome of community-based early intensive behavioral intervention for children with autism. J Abnorm Child Psychol 2015 Oct 17;43(7):1271-1282. [doi: 10.1007/s10802-015-0002-2] [Medline: 25778537]
5. Dawson G, Rogers S, Munson J, Smith M, Winter J, Greenson J, et al. Randomized, controlled trial of an intervention for toddlers with autism: the Early Start Denver Model. Pediatrics 2010 Jan;125(1):e17-e23 [FREE Full text] [doi: 10.1542/peds.2009-0958] [Medline: 19948568]
6. Baker-Ericzén M, Stahmer A, Burns A. Child demographics associated with outcomes in a community-based pivotal response training program. J Positive Behav Interv 2016 Aug 13;9(1):52-60. [doi: 10.1177/10983007070090010601]
7. Mazurek MO, Kanne SM, Miles JH. Predicting improvement in social–communication symptoms of autism spectrum disorders using retrospective treatment data. Res Autism Spectrum Disorder 2012 Jan;6(1):535-545. [doi: 10.1016/j.rasd.2011.07.014]
8. MacDonald R, Parry-Cruwys D, Dupere S, Ahearn W. Assessing progress and outcome of early intensive behavioral intervention for toddlers with autism. Res Dev Disabil 2014 Dec;35(12):3632-3644. [doi: 10.1016/j.ridd.2014.08.036] [Medline: 25241118]

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9. Vivanti G, Dissanayake C, Victorian ASELCC Team. Outcome for children receiving the early start denver model before and after 48 months. J Autism Dev Disord 2016 Jul 28;46(7):2441-2449. [doi: 10.1007/s10803-016-2777-6] [Medline: 27020055]
10. Elsabbagh M, Divan G, Koh Y, Kim YS, Kauchali S, Marcín C, et al. Global prevalence of autism and other pervasive developmental disorders. Autism Res 2012 Jun 11;5(3):160-179 [FREE Full text] [doi: 10.1002/aur.239] [Medline: 22495912]
11. Gordon-Lipkin E, Foster J, Peacock G. Whittling down the wait time: exploring models to minimize the delay from initial concern to diagnosis and treatment of autism spectrum disorder. Pediatr Clin North Am 2016 Oct;63(5):851-859 [FREE Full text] [doi: 10.1016/j.pcl.2016.06.007] [Medline: 27565363]
12. Hyman S, Levy S, Myers S, Council on Children With Disabilities, Section on Developmental and Behavioral Pediatrics. Identification, evaluation, and management of children with autism spectrum disorder. Pediatrics 2020 Jan;145(1):e20193447. [doi: 10.1542/peds.2019-3447] [Medline: 31843864]
13. Bridgemohan C, Bauer N, Nielsen B, DeBattista A, Ruch-Ross H, Paul L, et al. A workforce survey on developmental-behavioral pediatrics. Pediatrics 2018 Mar;141(3):e20172164. [doi: 10.1542/peds.2017-2164] [Medline: 29453235]
14. Baio J, Wiggins L, Christensen DL, Maenner MJ, Daniels J, Warren Z, et al. Prevalence of autism spectrum disorder among children aged 8 years - autism and developmental disabilities monitoring network, 11 sites, United States, 2014. MMWR Surveill Summ 2018 Apr 27;67(6):1-23 [FREE Full text] [doi: 10.15585/mmwr.ss6706a1] [Medline: 29701730]
15. van 't Hof M, Tisseur C, van Berckelear-Onnes I, van Nieuwenhuyzen A, Daniels A, Deen M, et al. Age at autism spectrum disorder diagnosis: a systematic review and meta-analysis from 2012 to 2019. Autism 2021 May;25(4):862-873 [FREE Full text] [doi: 10.1177/1362361320971107] [Medline: 33213190]
16. Pierce K, Gazestani VH, Bacon E, Barnes CC, Cha D, Nalabolu S, et al. Evaluation of the diagnostic stability of the early autism spectrum disorder phenotype in the general population starting at 12 months. JAMA Pediatr 2019 Jun 01;173(6):578-587 [FREE Full text] [doi: 10.1001/jamapediatrics.2019.0624] [Medline: 31034004]
17. Delobel-Ayoub M, Ehlinger V, Klapouszczak D, Maffre T, Raynaud J, Delpierre C, et al. Socioeconomic disparities and prevalence of autism spectrum disorders and intellectual disability. PLoS One 2015 Nov 5;10(11):e0141964 [FREE Full text] [doi: 10.1371/journal.pone.0141964] [Medline: 26540408]
18. Oswald D, Haworth S, Mackenzie B, Willis J. Parental report of the diagnostic process and outcome: ASD compared with other developmental disabilities. Focus Autism Other Dev Disabl 2015 Jun 09;32(2):152-160. [doi: 10.1177/1088357615587500]
19. Wiggins LD, Durkin M, Esler A, Lee L, Zahorodny W, Rice C, et al. Disparities in documented diagnoses of autism spectrum disorder based on demographic, individual, and service factors. Autism Res 2020 Mar 23;13(3):464-473 [FREE Full text] [doi: 10.1002/aur.2255] [Medline: 31868321]
20. Shattuck PT, Durkin M, Maenner M, Newschaffer C, Mandell DS, Wiggins L, et al. Timing of identification among children with an autism spectrum disorder: findings from a population-based surveillance study. J Am Academy Child Adolescent Psychiatry 2009 May;48(5):474-483. [doi: 10.1097/chi.0b013e31819b3848]
21. Monteiro SA, Dempsey J, Berry LN, Voigt RG, Goin-Kochel RP. Screening and referral practices for autism spectrum disorder in primary pediatric care. Pediatrics 2019 Oct 12;144(4):e20183326. [doi: 10.1542/peds.2018-3326] [Medline: 31515298]
22. Rhoades RA, Scarpa A, Salley B. The importance of physician knowledge of autism spectrum disorder: results of a parent survey. BMC Pediatr 2007 Nov 20;7(1):37 [FREE Full text] [doi: 10.1186/1471-2431-7-37] [Medline: 18021459]
23. Carbone P, Norlin C, Young P. Improving early identification and ongoing care of children with autism spectrum disorder. Pediatrics 2016 Jun;137(6):e20151850. [doi: 10.1542/peds.2015-1850] [Medline: 27244841]
24. Fenikilé T, Ellerbeck K, Filippi M, Daley C. Barriers to autism screening in family medicine practice: a qualitative study. Prim Health Care Res Dev 2014 Nov 4;16(04):356-366. [doi: 10.1017/s1463423614000449]
25. Self T, Parham D, Rajagopalan J. Autism spectrum disorder early screening practices. Commun Disorder Q 2014 Dec 30;36(4):195-207. [doi: 10.1177/1525740114560060]
26. Mazurek MO, Harkins C, Menezes M, Chan J, Parker RA, Kuhlthau K, et al. Primary care providers' perceived barriers and needs for support in caring for children with autism. J Pediatr 2020 Jun;221:240-5.e1. [doi: 10.1016/j.jpeds.2020.01.014] [Medline: 32143927]
27. Lai M, Kassee C, Besney R, Bonato S, Hull L, Mandy W, et al. Prevalence of co-occurring mental health diagnoses in the autism population: a systematic review and meta-analysis. Lancet Psychiatry 2019 Oct;6(10):819-829. [doi: 10.1016/s2215-0366(19)30289-5]
28. Falkmer T, Anderson K, Falkmer M, Horlin C. Diagnostic procedures in autism spectrum disorders: a systematic literature review. Eur Child Adolesc Psychiatry 2013 Jun 16;22(6):329-340. [doi: 10.1007/s00787-013-0375-0] [Medline: 23322184]
29. Lord C, Rutter M, Le Couteur A. Autism diagnostic interview-revised: a revised version of a diagnostic interview for caregivers of individuals with possible pervasive developmental disorders. J Autism Dev Disord 1994 Oct;24(5):659-685. [doi: 10.1007/bf02172145]
30. (ADOS®-2) Autism Diagnostic Observation Schedule™, Second Edition. WPS Publish. URL: https://www.wpspublish.com/ados-2-autism-diagnostic-observation-schedule-second-edition [accessed 2021-12-14]

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31. Kaufman NK. Rethinking "gold standards" and "best practices" in the assessment of autism. Appl Neuropsychol Child 2022 Aug 27;11(3):529-540. [doi: 10.1080/21622965.2020.1809414] [Medline: 32847428]
32. Software as a Medical Device (SaMD). U.S. Food & Drug Administration. URL: https://www.fda.gov/medical-devices/digital-health-center-excellence/software-medical-device-samd [accessed 2021-12-12]
33. Abbas H, Garberson F, Liu-Mayo S, Glover E, Wall DP. Multi-modular AI approach to streamline autism diagnosis in young children. Sci Rep 2020 Mar 19;10(1):5014 [FREE Full text] [doi: 10.1038/s41598-020-61213-w] [Medline: 32193406]
34. Abbas H, Garberson F, Glover E, Wall D. Machine learning approach for early detection of autism by combining questionnaire and home video screening. J Am Med Inform Assoc 2018 Aug 01;25(8):1000-1007 [FREE Full text] [doi: 10.1093/jamia/ocy039] [Medline: 29741630]
35. Levy S, Duda M, Haber N, Wall DP. Sparsifying machine learning models identify stable subsets of predictive features for behavioral detection of autism. Mol Autism 2017 Dec 19;8(1):65 [FREE Full text] [doi: 10.1186/s13229-017-0180-6] [Medline: 29270283]
36. Tariq Q, Daniels J, Schwartz J, Washington P, Kalantarian H, Wall D. Mobile detection of autism through machine learning on home video: a development and prospective validation study. PLoS Med 2018 Nov;15(11):e1002705 [FREE Full text] [doi: 10.1371/journal.pmed.1002705] [Medline: 30481180]
37. Wall DP, Dally R, Luyster R, Jung J, Deluca TF. Use of artificial intelligence to shorten the behavioral diagnosis of autism. PLoS One 2012 Aug 27;7(8):e43855 [FREE Full text] [doi: 10.1371/journal.pone.0043855] [Medline: 22952789]
38. Kosmicki JA, Sochat V, Duda M, Wall DP. Searching for a minimal set of behaviors for autism detection through feature selection-based machine learning. Transl Psychiatry 2015 Mar 24;5(2):e514 [FREE Full text] [doi: 10.1038/tp.2015.7] [Medline: 25710120]
39. Megerian JT, Dey S, Melmed RD, Coury DL, Lerner M, Nicholls CJ, et al. Evaluation of an artificial intelligence-based medical device for diagnosis of autism spectrum disorder. NPJ Digit Med 2022 May 05;5(1):57 [FREE Full text] [doi: 10.1038/s41746-022-00598-6] [Medline: 35513550]
40. Cognoa receives FDA marketing authorization for first-of-its-kind Autism Diagnosis Aid. Cognoa. URL: https://cognoa.com/cognoa-receives-fda-marketing-authorization-for-first-of-its-kind-autism-diagnosis-aid/ [accessed 2021-10-10]
41. Mazurek M, Brown R, Curran A, Sohl K. ECHO Autism. Clin Pediatr (Phila) 2017 Mar;56(3):247-256. [doi: 10.1177/0009922816648288] [Medline: 27169714]
42. Sohl K, Mazurek M, Brown R. ECHO Autism: using technology and mentorship to bridge gaps, increase access to care, and bring best practice autism care to primary care. Clin Pediatr (Phila) 2017 Jun;56(6):509-511. [doi: 10.1177/0009922817691825] [Medline: 28497714]
43. Mazurek M, Curran A, Burnette C, Sohl K. ECHO Autism STAT: accelerating early access to autism diagnosis. J Autism Dev Disord 2019 Jan;49(1):127-137. [doi: 10.1007/s10803-018-3696-5] [Medline: 30043354]
44. Guan X, Zwaigenbaum L, Sonnenberg L. Building capacity for community pediatric autism diagnosis: a systemic review of physician training programs. J Dev Behav Pediatr 2021 Dec 15;43(1):44-54. [doi: 10.1097/dbp.0000000000001042]
45. Bishop-Fitzpatrick L, Kind AJ. A scoping review of health disparities in autism spectrum disorder. J Autism Dev Disord 2017 Nov 29;47(11):3380-3391 [FREE Full text] [doi: 10.1007/s10803-017-3251-9] [Medline: 28756549]
46. Nazneen N, Rozga A, Romero M, Findley AJ, Call NA, Abowd GD, et al. Supporting parents for in-home capture of problem behaviors of children with developmental disabilities. Pers Ubiquit Comput 2011 May 1;16(2):193-207. [doi: 10.1007/s00779-011-0385-1]
47. Constantino JN, Abbacchi AM, Saulnier C, Klaiman C, Mandell DS, Zhang Y, et al. Timing of the diagnosis of autism in African American children. Pediatrics 2020 Sep 24;146(3):e20193629 [FREE Full text] [doi: 10.1542/peds.2019-3629] [Medline: 32839243]
48. Yingling ME, Hock RM, Bell BA. Time-lag between diagnosis of autism spectrum disorder and onset of publicly-funded early intensive behavioral intervention: do race-ethnicity and neighborhood matter? J Autism Dev Disord 2018 Feb 28;48(2):561-571. [doi: 10.1007/s10803-017-3354-3] [Medline: 29080927]
49. Mobile Fact Sheet. Pew Research Center. URL: https://www.pewresearch.org/internet/fact-sheet/mobile/ [accessed 2021-12-11]

Abbreviations

AI: artificial intelligence
ASD: autism spectrum disorder
DSM-5: Diagnostic and Statistical Manual of Mental Disorders–fifth edition
ECHO: Extension for Community Health Outcomes
FDA: Food and Drug Administration
STAT: Screening Tool for Autism in Toddlers and Young Children

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Protocol

Key Stakeholder Barriers and Facilitators to Implementing Remote Monitoring Technologies: Protocol for a Mixed Methods Analysis

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Abstract

Background: The implementation of novel digital solutions within the National Health Service has historically been challenging. Since the start of the COVID-19 pandemic, there has been a greater push for digitization and for operating remote monitoring solutions. However, the implementation and widespread adoption of this type of innovation have been poorly studied.

Objective: We aim to investigate key stakeholder barriers and facilitators to implementing remote monitoring solutions to identify factors that could affect successful adoption.

Methods: A mixed methods approach will be implemented. Semistructured interviews will be conducted with high-level stakeholders from industry and academia and health care providers who have played an instrumental role in, and have prior experience with, implementing digital solutions, alongside the use of an adapted version of the Technology Acceptance Model questionnaire.

Results: Enrollment is currently underway, having started in February 2022. It is anticipated to end in July 2022, with data analysis scheduled to commence in August 2022.

Conclusions: The results of our study may highlight key barriers and facilitators to implementing digital remote monitoring solutions, thereby allowing for improved widespread adoption within the National Health Service in the future.

Trial Registration: ClinicalTrials.gov NCT05321004; https://clinicaltrials.gov/ct2/show/NCT05321004

(JMIR Res Protoc 2022;11(7):e38437) doi:10.2196/38437

KEYWORDS

implementation science; health plan implementation; mobile health; health care industry; stakeholder; barriers; remote monitoring; implementation; digitization; digital solutions

Introduction

Advancements in digital technologies, alongside increasing digitization in other industries and the global pandemic of COVID-19, have accelerated the adoption of novel health care pathways worldwide, with health care delivery transitioning beyond the traditional face-to-face model [1,2]. Telemedicine has gained long overdue exposure during a complicated crisis; since the onset of the pandemic, digital modalities have become critical in moderating exposure risk to health care staff, reducing community spread, and delivering quality health care remotely to exposed or infected individuals [3,4].

Remote monitoring solutions are being established internationally to allow individuals to continue living at home rather than in expensive hospital facilities, using noninvasive digital technologies (eg, wearable sensors) to collect health data

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and support health care provider assessment and clinical decision-making [5-9].

Wearable sensors, including patches, smart watches, clothing, and bands, can continuously register vital parameters (eg, heart rate, respiratory rate, blood pressure, oxygen saturation, and temperature) [10-14]. With the advances in technology miniaturization, sensors have become increasingly portable, unobtrusive, lightweight, and waterproof, offering an emerging solution to the continuous remote monitoring of vital signs. It is predicated that continuous monitoring will offer an opportunity for earlier clinical intervention through the earlier recognition of clinical deterioration, thereby improving patient care and patient outcomes, although it remains unclear whether the need for continuous monitoring for ambulatory patients is clinically meaningful [15].

Patient attitudes toward continuous remote monitoring in acute settings have been previously studied [16-18]. Although the work lacks external validity and has inherent selection bias, an insight into barriers and facilitators of continuous remote monitoring has been provided. More recently, a study reported favorable staff perceptions on the use of remote monitoring technologies in an acute surgical ward. Despite this however, the same cohort found no clinical benefit with varied engagement from health care staff, suggesting the need for the further exploration of implementation issues [19,20]. Within the United Kingdom, widespread digital transformations are facilitated by National Health Service (NHS) Digital—a nondepartmental public body created by statute that delivers large health informatics programs [21,22].

Digitally ready services, mature services, and data-enabled services are three ambitions listed by NHS England that form the basis of a digital framework for supporting digitization [23]. In addition, NHS England has supported virtual ward implementation, further indicating the future push toward digitization [24]. Therefore, there is a pressing need to understand key stakeholder perceptions to ensure the successful implementation of such services.

As such, our study aims to investigate key stakeholder perspectives, at the organizational level, on implementing remote monitoring solutions, given the pandemic, in the NHS to identify factors that could affect successful execution and adoption.

Methods

Study Design

A mixed methods approach will be implemented; semistructured interviews will be conducted with high-level stakeholders from industry, academia, and health care providers who have played an instrumental role in, and have prior experience with, implementing digital solutions. These individuals will be identified through their notable work with remote monitoring in health care (eg, authors of impactful research in the literature, major digital technology companies, and experts recommended by peers). The purpose of the interviews will be to highlight barriers and facilitators to the implementation process. This will allow for a road map to be created for the future deployment of digital solutions. In conjunction, questionnaires will be undertaken to determine the perceived technological acceptance of new remote monitoring systems.

Ethics Approval

All recruited participants will provide informed consent. Ethical approval for this study was granted by the Imperial College London's Science, Engineering and Technology Research Ethics Committee (reference number: 20IC6331). The trial will be performed in accordance with good clinical practice guidelines and the Declaration of Helsinki. Patient data will be anonymized to ensure privacy. The storage and handling of personal data will comply with the General Data Protection Regulation.

Questionnaires

An adapted version of the Technology Acceptance Model (TAM) questionnaire will be used (Multimedia Appendix 1). This version was previously validated, and it demonstrated acceptably high Cronbach α values [25]. The proposed theoretical framework (information technology acceptance) was adapted from Chau and Hu [26], comprising individual context, technological context, and organizational context. Gagnon et al [25] adapted this further with the inclusion of the theories of interpersonal behavior and reasoned action, building on the TAM proposed by Davis [25-29]. As such, individual context consists of compatibility (factors that affect the acceptance of a new technology) and attitude (a perception of an individual toward adopting a technology), and technological context consists of the perceived usefulness and perceived ease of use of technologies, alongside habits of individuals. Lastly, organization context consists of facilitators and subjective norms; the latter can be described as *social* (an individual's perception toward a behavior) or *descriptive* (the behaviors of others).

Semistructured Interviews

All participants will be invited to take part in semistructured interviews conducted by the lead researcher (FI). A structured topic guide was created (Multimedia Appendix 1) by following a literature review that drew heavily from a model proposed by Simblett et al [30]. The guide highlights the following five key areas for determining the likelihood of engagement with remote monitoring technology by stakeholders: health status, usability, convenience/accessibility, perceived utility, and motivation. Data collection will be an iterative process; emerging recurring concepts will be incorporated into the interview guide for further exploration with remaining participants. Interviews will then be recorded, anonymized, and transcribed verbatim before being entered into NVivo 12 (QSR International) for analysis.

Statistical Analysis

Frequency distributions will be used to show responses to the TAM questionnaire. Responses will be recorded by using a 7-point Likert scale ("strongly disagree" to "strongly agree"). Analyses will be performed by using R Studio (RStudio, PBC).

Transcribed interviews will be analyzed by using a broadly deductive approach [31], with the adapted topic guide described by Simblett et al [30], which will form the basis for the initial predefined coding framework. This will be undertaken by two independent researchers to determine barriers and facilitators

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[31]. An iterative process of coding and data indexing will occur, ensuring that key aspects are not missed from the predefined coding framework. Subsequent emerging themes will be summarized thereafter. The results will be discussed until consensus is reached. Interviews will be analyzed until data saturation is achieved.

Results

Enrollment is currently underway, having started in February 2022. It is anticipated to end in July 2022, with data analysis scheduled to occur in August 2022.

Discussion

Our study has the potential to identify barriers and facilitators of implementing remote monitoring solutions within an NHS trust. It will lay a road map based on the collated experiences of key stakeholders for the future deployment of remote monitoring solutions, thereby improving widespread adoption.

Indeed, a recent study highlighted the effectiveness of such solutions in patients with COVID-19, although the study noted the limited number of high-quality trial designs, which were heterogenous in nature [32]. The pandemic has resulted in heightened interest in public health research with models for implementing pulse oximetry. Given this digital acceleration, further research into implementation strategies are of growing importance [33,34].

Our study will be limited to the implementation of remote monitoring solutions, and the findings may not be generalizable to other digital solutions nor to other health care settings. Moreover, nonprobabilistic sampling may result in selection bias. Despite this, our use of semistructured interviews to capture stakeholder perceptions may yield pertinent considerations for the pragmatic implementation of remote monitoring, and the broad heterogenous sample of key stakeholders we hope to include may identify issues that are generalizable to the implementation of other technologies—an area of paucity within the current literature and an area of growing importance, given the favorable patient attitudes toward continuous remote monitoring [16-18]. Lastly, the viewpoints of end users will not be examined in this study, as this has been done elsewhere [19,35]. As such, a top-down view has been provided herein.

In conclusion, the results of our study could offer insight into highlighting key barriers and facilitators to implementing digital remote monitoring solutions, thereby allowing for improved widespread adoption within the NHS in the future.

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Data Availability

The data sets used and/or analyzed during the study will be available from the corresponding author on reasonable request.

Authors' Contributions

FMI drafted the manuscript. Significant amendments were made by MJ, MW, SK, HA, and AD. All authors approved the final manuscript.

Conflicts of Interest

AD is chair of the Health Security initiative, and HA is chief scientific officer at Flagship Pioneering UK Ltd. Flagship Pioneering had no role in the development, conduct, or analysis of the study.

Multimedia Appendix 1
Modified Technology Acceptance Model questionnaire and semistructured interview questions.
[PDF File (Adobe PDF File), 94 KB - resprot_v11i7e38437_app1.pdf]

References

1. Watson AR, Wah R, Thamman R. The value of remote monitoring for the COVID-19 pandemic. Telemed J E Health 2020 Sep;26(9):1110-1112. [doi: 10.1089/tmj.2020.0134] [Medline: 32384251]
2. Mehrotra A, Chernew ME, Linetsky D, Hatch H, Cutler DA, Schneider EC. The impact of the COVID-19 pandemic on outpatient visits: Changing patterns of care in the newest COVID-19 hot spots. The Commonwealth Fund. 2020 Aug 13. URL: https://www.commonwealthfund.org/publications/2020/aug/impact-covid-19-pandemic-outpatient-visits-changing-patterns-care-newest [accessed 2020-09-19]
3. Xu S, Li Y. Beware of the second wave of COVID-19. Lancet 2020 Apr 25;395(10233):1321-1322 [FREE Full text] [doi: 10.1016/S0140-6736(20)30845-X] [Medline: 32277876]

XSL•FO
RenderX

4. WHO coronavirus (COVID-19) dashboard. World Health Organization. URL: https://covid19.who.int/?gclid=CjwKCAjw2Jb7BRBHEiwAXTR4jTyiJ83RwLwaLTHzkxD3tqRLxDjbB8GqAxU09OFw-RB3F3Q0P4URcRoC46sQAvD_BwE [accessed 2020-09-19]
5. Martirosyan M, Caliskan K, Theuns DAMJ, Szili-Torok T. Remote monitoring of heart failure: benefits for therapeutic decision making. Expert Rev Cardiovasc Ther 2017 Jul;15(7):503-515. [doi: 10.1080/14779072.2017.1348229] [Medline: 28656875]
6. Annis T, Pleasants S, Hultman G, Lindemann E, Thompson JA, Billecke S, et al. Rapid implementation of a COVID-19 remote patient monitoring program. J Am Med Inform Assoc 2020 Aug 01;27(8):1326-1330 [FREE Full text] [doi: 10.1093/jamia/ocaa097] [Medline: 32392280]
7. Ford D, Harvey JB, McElligott J, King K, Simpson KN, Valenta S, et al. Leveraging health system telehealth and informatics infrastructure to create a continuum of services for COVID-19 screening, testing, and treatment. J Am Med Inform Assoc 2020 Dec 09;27(12):1871-1877 [FREE Full text] [doi: 10.1093/jamia/ocaa157] [Medline: 32602884]
8. O'Carroll O, MacCann R, O'Reilly A, Dunican EM, Feeney ER, Ryan S, et al. Remote monitoring of oxygen saturation in individuals with COVID-19 pneumonia. Eur Respir J 2020 Aug 13;56(2):2001492 [FREE Full text] [doi: 10.1183/13993003.01492-2020] [Medline: 32616588]
9. Medina M, Babiuch C, Card M, Gavrilescu R, Zafirau W, Boose E, et al. Home monitoring for COVID-19. Cleve Clin J Med. Epub ahead of print 2020 Jun 11 [FREE Full text] [doi: 10.3949/ccjm.87a.ccc028] [Medline: 32409432]
10. Joshi M, Ashrafian H, Aufegger L, Khan S, Arora S, Cooke G, et al. Wearable sensors to improve detection of patient deterioration. Expert Rev Med Devices 2019 Feb;16(2):145-154. [doi: 10.1080/17434440.2019.1563480] [Medline: 30580650]
11. Iqbal MH, Aydin A, Brunckhorst O, Dasgupta P, Ahmed K. A review of wearable technology in medicine. J R Soc Med 2016 Oct;109(10):372-380 [FREE Full text] [doi: 10.1177/0141076816663560] [Medline: 27729595]
12. Hentschel MA, Haaksma ML, van de Belt TH. Wearable technology for the elderly: Underutilized solutions. Eur Geriatr Med 2016 Sep;7(5):399-401. [doi: 10.1016/j.eurger.2016.07.008]
13. Chan M, Estève D, Fourniols JY, Escriba C, Campo E. Smart wearable systems: current status and future challenges. Artif Intell Med 2012 Nov;56(3):137-156. [doi: 10.1016/j.artmed.2012.09.003] [Medline: 23122689]
14. Appelboom G, Camacho E, Abraham ME, Bruce SS, Dumont EL, Zacharia BE, et al. Smart wearable body sensors for patient self-assessment and monitoring. Arch Public Health 2014 Aug 22;72(1):28 [FREE Full text] [doi: 10.1186/2049-3258-72-28] [Medline: 25232478]
15. Tarassenko L, Hann A, Young D. Integrated monitoring and analysis for early warning of patient deterioration. Br J Anaesth 2006 Jul;97(1):64-68 [FREE Full text] [doi: 10.1093/bja/ael113] [Medline: 16707529]
16. Downey CL, Brown JM, Jayne DG, Randell R. Patient attitudes towards remote continuous vital signs monitoring on general surgery wards: An interview study. Int J Med Inform 2018 Jun;114:52-56. [doi: 10.1016/j.ijmedinf.2018.03.014] [Medline: 29673603]
17. Weenk M, Bredie SJ, Koeneman M, Hesselink G, van Goor H, van de Belt TH. Continuous monitoring of vital signs in the general ward using wearable devices: Randomized controlled trial. J Med Internet Res 2020 Jun 10;22(6):e15471 [FREE Full text] [doi: 10.2196/15471] [Medline: 32519972]
18. Tran VT, Riveros C, Ravaud P. Patients' views of wearable devices and AI in healthcare: findings from the ComPaRe e-cohort. NPJ Digit Med 2019 Jun;2:53 [FREE Full text] [doi: 10.1038/s41746-019-0132-y] [Medline: 31304399]
19. Joshi M, Archer S, Morbi A, Ashrafian H, Arora S, Khan S, et al. Perceptions on the use of wearable sensors and continuous monitoring in surgical patients: Interview study among surgical staff. JMIR Form Res 2022 Feb 11;6(2):e27866 [FREE Full text] [doi: 10.2196/27866] [Medline: 35147503]
20. Iqbal FM, Joshi M, Fox R, Koutsoukou T, Sharma A, Wright M, et al. Outcomes of vital sign monitoring of an acute surgical cohort with wearable sensors and digital alerting systems: A pragmatically designed cohort study and propensity-matched analysis. Front Bioeng Biotechnol 2022 Jun 27;10:895973 [FREE Full text] [doi: 10.3389/fbioe.2022.895973] [Medline: 35832414]
21. About NHS Digital. NHS Digital. URL: https://digital.nhs.uk/about-nhs-digital [accessed 2020-09-19]
22. NHS Digital annual report and accounts 2019 to 2020. NHS Digital. URL: https://digital.nhs.uk/about-nhs-digital/corporate-information-and-documents/nhs-digital-s-annual-reports-and-accounts/nhs-digital-annual-report-and-accounts-2019-20/annual-report-and-accounts [accessed 2020-09-19]
23. A digital framework for allied health professionals. NHS England. 2019. URL: https://www.england.nhs.uk/wp-content/uploads/2019/04/a-digital-framework-for-allied-health-professionals.pdf [accessed 2022-07-15]
24. Supporting information: Virtual ward including hospital at home. NHS England. 2022. URL: https://www.england.nhs.uk/publication/supporting-information-virtual-ward-including-hospital-at-home/ [accessed 2022-06-07]
25. Gagnon MP, Orruño E, Asua J, Abdeljelil AB, Emparanza J. Using a modified technology acceptance model to evaluate healthcare professionals' adoption of a new telemonitoring system. Telemed J E Health 2012;18(1):54-59 [FREE Full text] [doi: 10.1089/tmj.2011.0066] [Medline: 22082108]
26. Chau PYK, Hu PJ. Examining a model of information technology acceptance by individual professionals: An exploratory study. J Manag Inf Syst 2014 Dec 23;18(4):191-229. [doi: 10.1080/07421222.2002.11045699]

XSL•FO
RenderX

27. Davis FD. Perceived usefulness, perceived ease of use, and user acceptance of information technology. MIS Q 1989 Sep;13(3):319. [doi: 10.2307/249008]
28. Fishbein MA, Ajzen I. Belief, Attitude, Intention and Behaviour: An Introduction to Theory and Research. Reading, MA: Addison-Wesley; 1975.
29. Triandis HC. Values, attitudes, and interpersonal behavior. Nebr Symp Motiv 1980;27:195-259. [Medline: 7242748]
30. Simblett S, Greer B, Matcham F, Curtis H, Polhemus A, Ferrão J, et al. Barriers to and facilitators of engagement with remote measurement technology for managing health: Systematic review and content analysis of findings. J Med Internet Res 2018 Jul 12;20(7):e10480 [FREE Full text] [doi: 10.2196/10480] [Medline: 30001997]
31. Braun V, Clarke V. Using thematic analysis in psychology. Qual Res Psychol 2006 Jan;3(2):77-101. [doi: 10.1191/1478088706qp063oa]
32. Alboksmaty A, Beaney T, Elkin S, Clarke JM, Darzi A, Aylin P, et al. Effectiveness and safety of pulse oximetry in remote patient monitoring of patients with COVID-19: a systematic review. Lancet Digit Health 2022 Apr;4(4):e279-e289 [FREE Full text] [doi: 10.1016/S2589-7500(21)00276-4] [Medline: 35337644]
33. Golinelli D, Boetto E, Carullo G, Nuzzolese AG, Landini MP, Fantini MP. Adoption of digital technologies in health care during the COVID-19 pandemic: Systematic review of early scientific literature. J Med Internet Res 2020 Nov 06;22(11):e22280 [FREE Full text] [doi: 10.2196/22280] [Medline: 33079693]
34. Whitelaw S, Mamas MA, Topol E, Van Spall HGC. Applications of digital technology in COVID-19 pandemic planning and response. Lancet Digit Health 2020 Aug;2(8):e435-e440 [FREE Full text] [doi: 10.1016/S2589-7500(20)30142-4] [Medline: 32835201]
35. Joshi M, Archer S, Morbi A, Arora S, Kwasnicki R, Ashrafian H, et al. Short-term wearable sensors for in-hospital medical and surgical patients: Mixed methods analysis of patient perspectives. JMIR Perioper Med 2021 Apr 22;4(1):e18836 [FREE Full text] [doi: 10.2196/18836] [Medline: 33885367]

Abbreviations

NHS: National Health Service
NIHR: National Institute for Health and Care Research
TAM: Technology Acceptance Model

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Protocol

Adapting and Developing an Academic and Community Practice Collaborative Care Model for Metastatic Breast Cancer Care (Project ADAPT): Protocol for an Implementation Science–Based Study

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Abstract

Background: Metastatic breast cancer (MBC) remains incurable despite significant treatment advances. Coordinating care for patients with MBC can be challenging given the various treatment options, available clinical trials, and frequent need for ancillary services. To optimize MBC care, we designed a project for adapting and developing an academic and community practice collaborative care model for MBC care (Project ADAPT), based on the Ending Metastatic Breast Cancer for Everyone (EMBRACE) program developed at Dana Farber Cancer Institute.

Objective: We aim to describe the implementation science–based study design and innovative components of Project ADAPT.

Methods: Project ADAPT uses the Dynamic Adaptation Process informed by the Exploration, Preparation, Implementation, Sustainment framework. Washington University School of Medicine (WUSM) partnered with 3 community hospitals in the St. Louis region covering rural and urban settings. The exploration and preparation phases provide patient and provider feedback on current referral practices to finalize the approach for the implementation phase. At the implementation phase, we will enroll patients with MBC at these 3 community sites to evaluate potential collaborative care at WUSM and assess the impact of this collaborative care model on referral satisfaction and acceptability for patients with MBC and their providers. Patients may then return to their community site for care or continue to receive part of their care at WUSM. We are incorporating virtual and digital health strategies to improve MBC care coordination in order to minimize patient burden.

Results: The exploration phase is ongoing. As of August 2021, we have recruited 21 patient and provider participants to complete surveys of the current collaborative care process at WUSM. Using a 2-tailed paired *t* test, 44 patients (including 10 patients from the exploration phase) and 32 oncologists are required to detect an effect size of 0.5 with 80% power at a level of significance of .05. Throughout this phase and in preparation for the implementation phase, we have iteratively updated and refined our surveys for the implementation phase based on testing of our data collection instruments. Our partner sites are in various stages of the

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single institutional review board (IRB) approval process. We have ongoing engagement with all partner sites, which has helped solidify our participant recruitment strategies and design patient-friendly recruitment materials. In addition, we have included a patient advocate on the research team. Members of the research team have launched a single IRB Support Network at WUSM to create a repository of the single IRB procedures in order to streamline the partner site onboarding process and facilitate enhanced collaboration across institutions.

Conclusions: With this robust model, we expect that patients with MBC will receive optimal care regardless of geographical location and the model will improve patient and provider experiences when navigating the health system.

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KEYWORDS

metastatic breast cancer; care coordination; Project ADAPT; referral process; implementation science; oncology; community practice; academic institutions; breast cancer; cancer; breast; implementation; science

Introduction

Background

As of 2019, there were over 3.8 million breast cancer survivors in the United States, with this number projected to increase substantially by 2030 [1]. Excluding skin cancers, breast cancer is the most common cancer type and accounts for 30% of new cancer diagnoses in the United States [2,3]. In 2021, breast cancer incidence was expected to be 284,200 in the United States, with a 0.5% annual increase [3]. Although mortality rates have declined, the projected number of deaths from breast cancer in 2021 was over 44,000, and nearly all these deaths were due to metastatic breast cancer (MBC), which has a median survival of about 3 years [3,4]. Breast cancer incidence is higher in urban populations than among those living in rural settings [5]. However, this rural-urban disparity has been attributed to lower mammography screening rates, due to limited access to health care services in rural settings and low socioeconomic status [6,7], impacting this population's ability to obtain quality care and making the diagnosis of breast cancer at later stages more likely [8]. When viewed at the population level, these barriers often explain the observed gap in breast cancer incidence between urban and rural populations [7].

Despite significant advances in treatment, there is no cure for MBC [9-12]. Current treatment options are palliative in nature with the goal of extending survival and improving quality of life, but are frequently encumbered by care coordination challenges [9,11,13]. Even with national guidelines for the treatment of MBC and subtype-specific MBC, which encourage participation in clinical trials [14-16], there is not always a clear sequence of treatments or an accessible clinical trial available for patients, particularly those in rural settings [9,17-19]. Additionally, there is often a need for ancillary supportive care services for patients with MBC [17,19]. The complexities involved in the routine care of patients with MBC can lead to underutilization or overutilization of care; missed opportunities to improve cancer outcomes, including cancer-specific survival and treatment-related symptoms; and undue patient and care delivery burden. Therefore, there is a need for coordinated care models that cater to the increasing prevalence of patients with MBC in the United States [20].

Limitations of Current Care Models

Patients with MBC usually choose to receive cancer care near their homes. Treatment may be at a community or academic center. However, while many patients live near academic centers, a considerable number of patients also travel to academic centers for treatment or second opinions, clinical trial options, and ancillary services not available at their local community practice [21]. Effective coordination and communication between the referring provider and oncologists at academic centers are needed to maximize the benefits of these consultations. When coordination is lacking, patients may be seen at an academic center when they are not candidates for a clinical trial or when a relevant trial is unavailable. Treatment plans may also be delayed if certain medical records or up-to-date test results are unavailable. In addition, patients are often not referred due to referring physicians' lack of access to real-time clinical trial options at an academic cancer center or their concern for patient burden, including financial responsibility, health insurance limitations, and transportation cost [17,19,22]. Given these referral barriers, communication is often limited to a phone call or email between individual physicians, which is not always a secure, reliable, or organized approach. This way of communication also inhibits collaborative consultations for patients who may benefit from a multidisciplinary review of their case. Therefore, existing communication media and channels lack efficiency and create barriers to eliciting a second opinion or screening patients potentially eligible for clinical trials. Ultimately, a lack of consistent uniform coordination and communication among physicians is likely to result in decreased patient satisfaction and potentially missed opportunities to improve patient outcomes [13].

Addressing physician-level barriers to referring patients, such as physicians' lack of awareness of available trials, concern of losing patients, and lack of time [23], is imperative to adequate patient care. Additionally, current referral practices encompassing preappointment communication regarding available trials, required testing and records, patient functional status, and preferences must be honed among academic and referring community centers. A collaborative care model can improve workflow, minimize patient burden, improve care delivery and communication between physicians, and ultimately

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enhance the referral process between academic and community cancer centers [22].

In this protocol paper, we describe the implementation science study design of a project for adapting and developing an academic and community practice collaborative care model for MBC care (*Project ADAPT*). This project evaluates clinical health service utilization (eg, access and utilization of clinical trials, virtual consult/telemedicine, and genomic testing), and the fidelity and adoption of a coordinated care intervention between academic and community settings. This model can then be tested on a larger scale, with a more significant number of community partners, to evaluate its impact on additional outcomes, including quality of life, and progression-free and overall survival, among patients with MBC.

Methods

Study Development

EMBRACE Program

Project ADAPT originated from a review of the Ending Metastatic Breast Cancer for Everyone (EMBRACE) clinical program at the Dana Farber Cancer Institute (DFCI) [24]. The DFCI research team explicitly designed the EMBRACE program for MBC to (1) enhance the longitudinal care of patients with MBC; (2) develop a robust, seamless, collaborative care model between the DFCI and referring providers; and (3) improve the quality of life and satisfaction with care among patients with MBC. To accomplish these goals, EMBRACE created a clinical flow model that identifies patients with MBC seen at the DFCI (either newly diagnosed or recently seen at the DFCI), streamlines and coordinates the initial consultation, facilitates treatment at the DFCI or collaborative care between institutions, and coordinates reconsultations at the DFCI on disease progression. This process enables ongoing contact with the patient and between providers, and leverages the expertise of providers and health care administrators to achieve this care coordination for MBC [24].

Most medical oncologists at the DFCI who completed the initial baseline survey reported moderate satisfaction with the initial consultation and stated that access to the referring provider's email was extremely important. They expressed dissatisfaction with the current approach of accessing the emails of referring providers. In addition, among referring providers, most reported difficulty in referring patients to academic institutions for clinical trials. Patients who completed the baseline survey at the DFCI strongly desired all aspects of information on their cancer and treatment [24].

With similar challenges in our local institution and community, and with this intervention in mind, we adapted existing knowledge and tools from EMBRACE into the design and implementation of a care model for the patients, providers, and local community cancer sites in and around St. Louis, Missouri by engaging several community practices and experts in implementation science and medical oncology. We named this intervention *Project ADAPT*.

Project ADAPT

Disparities in breast cancer stage at diagnosis have been observed in the St. Louis region among medically underserved patients and have been attributed to barriers in the referral pathway to Siteman Cancer Center (SCC), the only National Cancer Institute (NCI)-designated comprehensive cancer center within a 240-mile radius of St. Louis [25]. SCC comprises physicians and researchers from Washington University School of Medicine (WUSM), Barnes-Jewish Hospital, and St. Louis Children's Hospital. Thus, SCC provides several vital resources for cancer research in the St. Louis metropolitan area and extends throughout the catchment area. Approximately 10%-15% of patients referred via private health care practices presented at late stages (stages III and IV) compared with about 40% of patients referred via Safety Net clinics, a referral system used by community clinics that cater primarily to uninsured and underinsured locals [25]. A collaborative care model has the potential to address these disparities. Existing collaborative care challenges identified by the research team include the need for (1) efficient and reliable communication between the referring community and accepting academic providers; (2) optimal timing of genomic testing to aid in decision-making for next-line therapies and access to clinical trials; and (3) minimizing patient burden (eg, excess travel and unnecessary in-person appointments).

The goal of *Project ADAPT* is to implement a multilevel collaborative model between academic and referring community oncology practices to accelerate the translation of evidence into practice to improve MBC management and the patient referral process. This multilevel model for coordinated care leverages the clinical expertise of oncologists at both the academic and partner institutions managing patients with MBC, the numerous clinical trials available at SCC, and the unique NCI Community Oncology Research Program (NCORP) resources at the community partner centers. Employing the single institutional review board (IRB) structure through the WUSM, *Project ADAPT* extends existing SCC partnerships in the St. Louis region to develop a sustainable collaborative care model [26]. To achieve this goal, we have the following specific objectives: (1) assess patients' satisfaction and acceptability of the academic and community collaborative care model for their MBC care; (2) evaluate providers' (academic oncologists and referring oncology providers) satisfaction and acceptability of the collaborative care model with the referral and management processes of MBC patients; and (3) evaluate the implementation of the adapted EMBRACE program using fidelity and adoption measures.

To accelerate the translation of evidence-informed MBC management across multiple systems into practice, we are using the dynamic adaptation process (DAP) to adapt EMBRACE to reflect the characteristics and context of the St. Louis regional care environment [27,28]. This approach builds upon the EMBRACE evidence-informed practice and modifies the intervention to fit the proposed collaborative environment of St. Louis. This adaptation includes the 4-phase Exploration, Preparation, Implementation, Sustainment (EPIS) model for multilevel program design [27,28]. This innovative implementation science framework allows us to assess our

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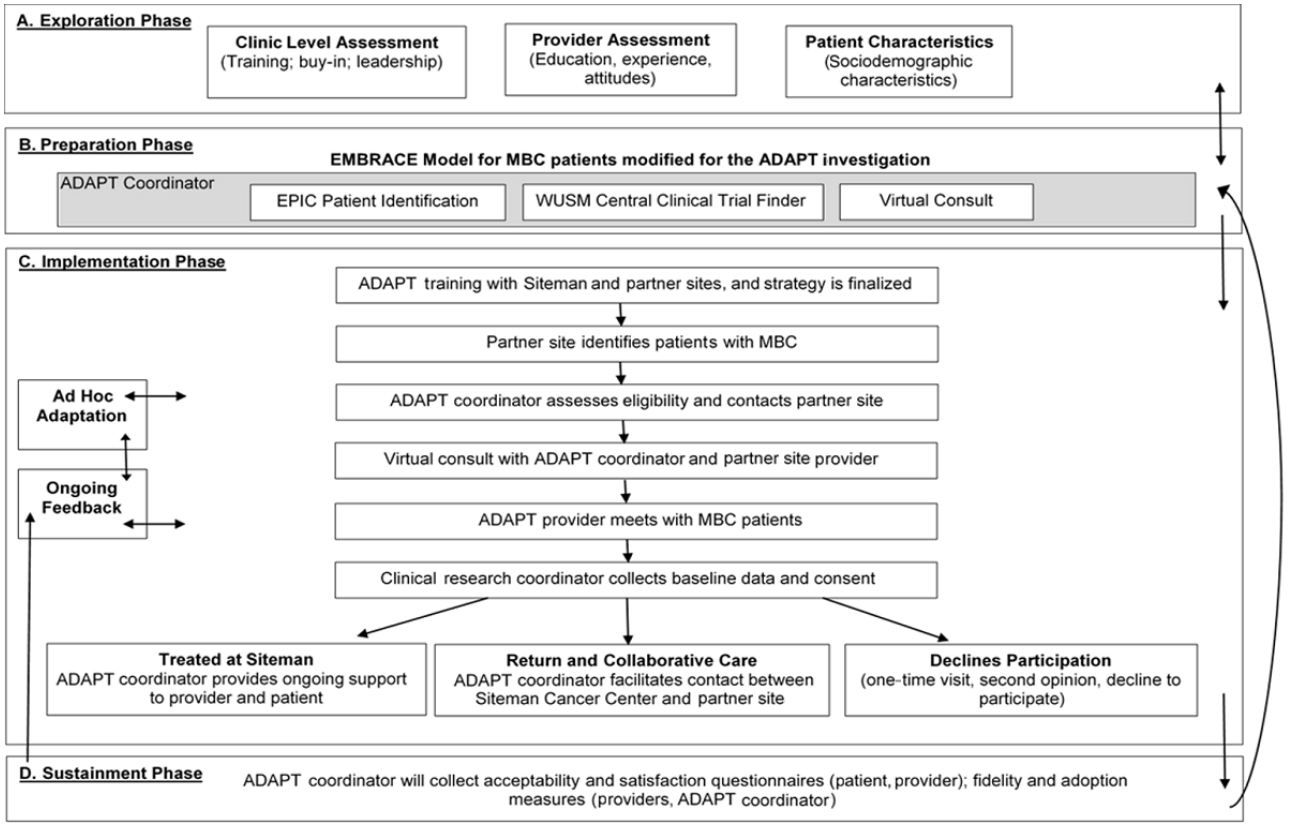
multilevel strategy by incorporating ongoing feedback to make modifications during the investigation, thereby enhancing our ability to intervene by identifying and testing real-time developments as needed to advance the pace of translating evidence into practice. Figure 1 shows the theoretical pathway of *Project ADAPT* using the DAP and EPIS implementation science framework [27,28].

Figure 1. Research strategy. Figure adapted from the Dynamic Adaptation Process and Exploration, Preparation, Implementation, Sustainment framework. EMBRACE: Ending Metastatic Breast Cancer for Everyone; Project ADAPT: project for adapting and developing an academic and community practice collaborative care model for metastatic breast cancer care; MBC: metastatic breast cancer; WUSM: Washington University School of Medicine.



Ethics Approval

WUSM/SCC received single IRB approval in May 2021 from the Washington University Institutional Review Board (Protocol #202104173-1001). Due to the various characteristics of our 3 partner sites, these sites are in different stages in the administrative and registration processes to obtain single IRB approval through the WUSM IRB. Utilizing the single IRB approval process strengthens the existing executive partnerships to create a sustainable research collaboration [26].

Study Settings

Washington University in St. Louis School of Medicine (WUSM) is partnering with the following 3 community hospitals within the St. Louis region to establish this care model: Missouri Baptist Medical Center (MBMC) in St. Louis County, Missouri; Southern Illinois Healthcare (SIH) in Carbondale, Illinois; and Phelps Health Delbert Day Cancer Institute (DDCI) in Rolla, Missouri. These hospitals are affiliated with broader regional health care organizations that offer the potential to expand and scale-up *Project ADAPT*. An existing informal referral relationship exists between each of these partner sites and SCC. Therefore, we are building off this foundational relationship to coordinate care for patients with MBC. Specifically, MBMC and SIH are affiliated with The BJC Collaborative, LLC, an organization inclusive of 7 health systems in Missouri and Illinois working together to enhance the quality of care, increase access to health services through meaningful population health benefits, and reduce the total cost of care within the Midwest region. Phelps Health is a county hospital serving South Central Missouri, whose Delbert Day Cancer Institute is affiliated with the Siteman Cancer Network, an affiliation led by SCC committed to improving the health and well-being of people and communities through research, treatment, and prevention. WUSM is the project's lead/coordinating site.

The lead site, WUSM, has an extensive history of research, education, and patient care, as one of the preeminent medical research institutions in the United States. SCC is the only NCI-designated cancer center in Missouri and is part of the main Washington University Medical Center campus with multiple satellite locations throughout the St. Louis region. SCC brings together over 450 physicians and researchers from WUSM, Barnes-Jewish Hospital, and St. Louis Children's Hospital (both part of BJC Healthcare). Thus, SCC provides several vital resources for cancer research in the St. Louis area, with extension throughout the SCC catchment area.

MBMC's Cancer Center is a regional leader in providing care and support to patients throughout their cancer care. This cancer center aims to deliver treatment, comprehensive care, and

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advanced research to patients receiving care in the surrounding areas. The hospital has over 1700 new cancer cases each year, and the cancer center is staffed with 8 medical oncologists. MBMC has outreach sites in more rural areas in Missouri and Illinois, for example, MoBap Sullivan in Sullivan, Missouri, and is an active partner in this effort to share best practices and recruit women with MBC. In 2019, prior to the COVID-19 pandemic (as this has caused significant disruptions in cancer care), MBMC's Cancer Center referred 3 out of 41 patients with MBC to SCC.

SIH is a leading health care system serving the people of southern Illinois. SIH offers services in rural clinics in addition to a regional referral center for the 16-county region. SIH aims to provide expertise and advanced treatments tailored for the needs of the rural setting. As the region's first dedicated cancer treatment center, the SIH Cancer Institute provides surgical and treatment options using evidence-based approaches to advance the care of patients with MBC. There are 5 medical oncologists, 2 radiation oncologists, and 1 breast surgical oncologist in the cancer program serving an estimated 200 breast cancer patients yearly. From 2016 to early 2019, out of the 26 patients with MBC seen at SIH, there were no referrals to SCC.

The DDCI provides cancer care services and continuity of care for patients in a rural 7-county region across South Central Missouri. The DDCI offers radiotherapy, medical oncology, laboratory, clinical research, and imaging services. All cancer treatment and support services are at a single location to ensure the best possible patient experience and to ease the burden of traveling to multiple locations for treatment. In addition, it offers ancillary services, such as patient education and customized counseling services, to achieve the mission to improve the health and wellness of people in the region. The Phelps Health DDCI had 10 patients with MBC, with only 1 referral made to SCC, in 2019.

Study Population

In the exploration phase, participants must meet the following inclusion criteria: (1) diagnosis of MBC (stage IV); (2) referral to SCC for MBC treatment; and (3) referral before the implementation phase of *Project ADAPT*. For the implementation phase, the inclusion criteria are (1) histologically or cytologically confirmed MBC (this includes newly diagnosed [de novo] or recurrent metastatic disease); (2) age ≥18 years; (3) self-reported ability to speak and understand English; and (4) willingness to provide written informed consent. There are no participant limitations based on sex.

For this protocol paper, providers recruited for this study are oncologists who primarily manage MBC cases and are involved in the referral process of patients with MBC. We have used the term "provider" throughout the protocol to make it inclusive for other sites that may replicate this study and have clinical buy-in from a variety of health care providers. The inclusion criteria for oncologists are as follows: (1) academic oncologists from SCC and oncologists from participating partner community sites, and (2) willingness to provide written informed consent. Table 1 shows the distribution of participants throughout the study phases.

Table 1. Participants involved in the study phases.

Phase	Patients	Providers
Exploration	A subset of patients with metastatic breast cancer referred to Siteman Cancer Center (SCC) before the implementation phase (n=10)	Oncologists from 3 community hospitals and oncologists at SCC (n=32)
Preparation	None recruited (patient advocate included as part of the research team)	Same group as in the exploration phase (including research team)
Implementation	Newly diagnosed (de novo) patients or patients with recurrent disease referred to SCC after the exploration phase (n=34)	Same group as in the exploration phase
Sustainment	Patients recruited in the implementation phase	Same group as in the exploration phase

Study Components

Project ADAPT has 5 intervention components designed to enhance communication between providers, continue engagement between research and clinical teams, and provide optimal patient care regardless of geographic location. These components are as follows: (1) ADAPT coordinator; (2) Epic communication between providers and research teams; (3) Powerful partnerships with collaborating sites; (4) WUSM clinical trial finder; and (5) Virtual consult/telemedicine.

ADAPT Coordinator

The ADAPT coordinator is the facilitator and intermediary between the NCI-designated SCC and our 3 community hospitals within the NCORP. The ADAPT coordinator handles all operations for the study to run smoothly. The ADAPT coordinator disseminates information to all sites and handles recruitment procedures, survey distribution, and data collection. The ADAPT coordinator also leads the strategy and standardizes the coordination for Epic patient identification and utilization of the clinical trial finder, as well as virtual consults between providers/telemedicine for patients. Specific training, including On Core training, Epic training, and research training, and a background in medicine, public health, or a health-related field to review clinical trial eligibility information may be beneficial for this role.

Epic Communication Between Providers and Research Teams

Hospitals in the United States are required to use an electronic medical record (EMR) system to manage patient health information [29,30]. Epic is a type of EMR system that enables

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customization and versatility across various hospital settings. The secure chat feature within Epic is the potential communication tool intended for study team communication. The use of streamlined Epic communication processes between community and academic center physicians and research staff is designed to improve patient and provider satisfaction, enable efficient consultation, and enhance clinical outcomes. In this adaptation, we aim to leverage existing technology to facilitate communication between the referring sites and SCC. Thus, we identified an electronic communication option, such as Epic, since oncologists were currently using this software to manage patients. When considering reproducing this method for sites using different EMR software or when scaling up to other sites with differing EMR software in the future, leveraging existing electronic communication channels, like secure group email or Microsoft Teams, may be worth exploring through acceptability and feasibility measures prior to selecting a communication channel.

This study relies on a uniform strategy for providers to obtain consults on patients with MBC via a previsit virtual consult that is tracked and readily available in the EMR (ie, Epic), significantly improving patient care and coordinating communication between providers. Thus, we have identified community sites that use Epic to facilitate communication. This process simplifies referrals and enhances information security, as this communication does not occur over email or phone calls, but instead through Epic.

Powerful Partnerships With Collaborating Sites

Partnerships with our 3 community hospitals offer access to a care network with an electronic health record (Epic) and diverse provider systems to study wide-ranging management of patients with MBC. This care model is designed as a bidirectional partnership since the community sites have access to NCORP resources. We aim to connect patients from SCC to these resources to enhance admission and enrollment in clinical trials at both community sites and SCC. Also noteworthy is that these 3 partner sites serve rural patient populations with MBC and are located across the St. Louis region, representing the breadth of care settings within the area.

WUSM Clinical Trial Finder

The WUSM clinical trial finder is a website that displays available clinical trials at WUSM and SCC. The WUSM clinical trial finder allows the ADAPT coordinator to identify clinical trials for which patients at partner sites may be eligible. The ADAPT coordinator facilitates coordination and communication with the treating oncologists and clinical team members to develop a detailed treatment plan for the patient. In addition, the ADAPT coordinator conducts virtual demonstrations and training to teach community sites the best approaches to navigate the website and clinical trial tree.

Virtual Consult/Telemedicine

The virtual health care feature of *Project ADAPT* consists of virtual consults between providers and telemedicine for patients. Virtual consults between providers at partner sites are designed to discuss potential referrals and clinical cases through secure Epic communication. These virtual meetings allow for discussion of patient matters and determination of clinical trial availability and eligibility for patients between oncologists at SCC and community partner sites. This digital strategy will enhance care delivery and reduce patient burden by preventing potentially unneeded in-person screening as traditionally carried out.

The second virtual feature is telemedicine. While there are multiple definitions of telemedicine, telemedicine generally applies digital media/platforms to aid the clinical decision of providers in the management of patients [31,32]. This strategy is designed for patients to receive care remotely through various virtual communication tools [33]. The emergence of COVID-19 has caused a large increase in telemedicine use throughout the US health sector in cancer care and primary health services [34,35]. *Project ADAPT's* telemedicine component affords a patient access to specialist care from SCC without the need for an in-person visit. This approach covers patients who need care but cannot travel to SCC. It can also reduce patient time and financial burden if consultation can be provided virtually rather than as traditional in-person visits, preventing unnecessary in-person consultations.

Study Measures

Several surveys employed within this study explore patients' and providers' satisfaction with the referral process and are grouped into patient and provider surveys. Surveys designed for the patient population are as follows: (1) ADAPT patient survey; (2) ADAPT patient sociodemographic survey; (3) Epic data extraction form; and (4) Decision Regret Scale [36] (Multimedia Appendices 1-5).

The ADAPT patient survey (Multimedia Appendix 1) captures patients' satisfaction and acceptability of the current referral process. There are open-ended and free-response options that offer participants the opportunity to provide insights and experiences valuable to the study. The ADAPT patient sociodemographic survey (Multimedia Appendices 2 and 3) includes baseline characteristics of patients with MBC referred from outside institutions to SCC to gain insights into the backgrounds of our patient sample population. The Epic data extraction form (Multimedia Appendix 4) gathers information on tumor characteristics, treatment history, and receptor status from Epic. The Decision Regret Scale [36] (Multimedia Appendix 5) evaluates patients' feelings of regret (if any) regarding transferring cancer care from partner sites to SCC.

Surveys for the providers recruited into *Project ADAPT* are as follows: (1) ADAPT provider survey and (2) Implementation Climate Scale [37] (Multimedia Appendices 6-8). The ADAPT provider survey (Multimedia Appendices 6 and 7) emphasizes providers' satisfaction and acceptability of the current referral process, and the Implementation Climate Scale [37] (Multimedia Appendix 8) captures the level of application of evidence-based health practices at the partner sites. These surveys also include free-response options that delve deeper into providers' encounters with the referral system.

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Study Phases/Procedures

Exploration Phase: Gathering Information and Recruitment

In the exploration phase, the ADAPT coordinator identifies approximately 10 patients through Epic who have been previously referred to SCC from external institutions (to the breast oncologists at SCC involved in this study). These patients are contacted via phone to inquire if they are willing to participate in this phase of the study. If they agree to participate, they consent during the phone call and complete the ADAPT patient survey and sociodemographic questions through the Research Electronic Data Capture (REDCap) link [38,39] sent to their email addresses or over the telephone.

Oncologists at SCC and the partner sites are involved during this study phase. The research team discusses the proposed ADAPT process through virtual meetings and refines the recruitment process from feedback during these meetings. These virtual meetings facilitate continued buy-in and leadership from referring providers to champion the intervention at their sites. In addition, providers at partner sites and SCC are recruited by email, provide consent, and then can complete the ADAPT provider survey through REDCap links sent to their email addresses.

The following privacy protections are enacted for all email communications involving protected health information: (1) emails are sent securely (ie, [secure] in the subject line); (2) the body of the email instructs the participant to send all information as a response to this thread and to not remove "[secure]" from the subject line; and (3) the participant's agreement to provide information over email is documented in our research records. Multimedia Appendix 9 outlines the recruitment processes of the exploration phase in a flow diagram.

Preparation Phase: Procedures

Research subjects are not recruited during this phase. Data collected during the exploration phase guide the preparation phase strategies, including how the ADAPT coordinator leads the process for facilitating the following: (1) patient identification for the implementation phase; (2) WUSM central clinical trial finder; and (3) virtual consult/telemedicine. There is ongoing engagement with oncologists and the research team at both SCC and community sites to incorporate modifications as needed at this study phase, as illustrated in Figure 1.

Implementation Phase: Recruitment and Procedures

The recruitment process can be done in 2 ways. The partner site clinical/research team members identify patients with MBC, and they contact the ADAPT coordinator who screens the patients with MBC for eligibility or the ADAPT coordinator identifies an eligible patient at a partner site through granted access to the Epic database through the following processes. The partner site provides a list of participating providers' clinic schedules and hospital names on Epic. According to the oncologists' schedules, the ADAPT coordinator maps out weekdays to screen providers' lists of scheduled patients before their appointment day in Epic. The ADAPT coordinator then contacts the partner site provider (or the provider's clinical team) scheduled to see the patient, alerting the provider of the patient's eligibility status and available ADAPT resources (eg, ADAPT coordinator, clinical trial finder, and virtual consultation/telemedicine). The clinical/research team members at the partner site discuss the options with the patient. If interested, the patient can provide consent to either the research team at the partner site or a SCC site research coordinator (including the ADAPT coordinator). The patient is treated at SCC or declines (eg, declines participation or decides to be treated at the referring facility). Patients can refuse to participate and continue treatment at their preferred location.

These recruitment strategies are designed to accommodate our partner sites' different human and material resources to provide a seamless recruitment process. Partner sites can either have the ADAPT coordinator lead the recruitment process of screening and identifying eligible participants through the detailed process outlined above while the research team obtains consent from the patients at the clinic through REDCap, or decide to oversee the recruitment process as the best fit for their respective centers and obtain consent from the patients at the clinic through REDCap. There must be regular communication between the ADAPT coordinator and the delegated recruitment research staff at these centers to evaluate or modify these processes if needed.

For those patients who provide consent, the ADAPT coordinator collects acceptability and satisfaction surveys at enrollment and at 3 and 6 months. During the implementation phase, providers complete the ADAPT provider survey and the Implementation Climate Scale [37] at baseline and at 3 and 6 months through REDCap. The providers recruited from the 3 community hospitals and at SCC in the exploration phase are the same providers involved at this stage, so they would not need to provide consent again. Multimedia Appendix 10 outlines the flow of the recruitment process.

Sustainment Phase: Recruitment and Procedures

The acceptability and satisfaction surveys collected at enrollment and at 3 and 6 months provide the feedback needed to adapt the implementation strategy (Figure 1). Our conceptual framework is a dynamic implementation approach to incorporate ongoing feedback to inform ad hoc adaptation. Therefore, we can modify the implementation strategy during our data collection process. During the sustainment phase, the ADAPT coordinator will complete adoption and fidelity observation measures to ensure the sustainment of the intervention. In addition, modified satisfaction and acceptability measures will be administered to patients and providers to continue evaluating and adjusting the program as needed.

Statistical Analysis

Quantitative Analysis

Only a subset of patients previously referred to SCC (n=10) who complete surveys in the exploration phase will require descriptive statistics for the measures completed.

The Epic data extraction form measures are collected at T0 and T2 in the implementation phase. Specifically, clinical or pathologic stage and the date of diagnosis of metastatic disease

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are collected at T0 only. Receptor status is collected at T0 for all the enrolled patients and at T2 for patients with a subsequent biopsy. The number of prior and current lines of therapy are collected at T0 and T2 for all the enrolled patients. The measures at T0 and T2 are shown in Table 2.

Table 2. Patient assessment tools/schedule.

Measures	Exploration (0-3 months)[a]	Preparation	Implementation phase[b]		
			T0	T1 (3 months)	T2 (6 months)
Epic data extraction form	Yes	No	Yes	No	Yes
Sociodemographic survey	Yes	No	Yes	Yes[c]	Yes[c]
ADAPT[d] patient survey	Yes	No	Yes	Yes	Yes
Decision Regret Scale [36]	No	No	No	Yes	Yes

[a]Only a subset of patients previously referred to SCC (n=10) is consented to complete surveys before the implementation phase begins.

[b]Patients enrolled in the implementation phase represent new patients referred from our partner sites to SCC for treatment.

[c]We are capturing changes to already provided sociodemographic information from enrolled participants, such as changes in insurance provider status.

[d]ADAPT: adapting and developing an academic and community practice collaborative care model for metastatic breast cancer care.

For other measures collected at multiple time points (eg, sociodemographic questions), a generalized estimating equation (GEE) model with appropriate link function is used to analyze the longitudinal data. The correlation among the repeated measures from the same participant needs to be considered. We are using an autoregressive of the first order as a working correlation structure, and patients with missing values at any time points are excluded from the GEE analysis. The GEE model includes time points. The GEE model's *P* values from type 3 analysis are used to assess whether the outcomes across all time points are different. The least-square means for each outcome at each time point are then estimated. The standard errors are calculated using the GEE sandwich method when accounting for within-patient correlation. All analyses are conducted using SAS (SAS Institute) at the 2-sided 5% significance level. To prioritize improving satisfaction and acceptability across educational groups, racial/ethnic groups, or diagnosis stage, a subgroup analysis by race/ethnicity to identify any potential similarities or differences in responses is conducted.

Qualitative Analysis

A minimum of 2 research team members will use conventional content analysis to analyze responses from the open-ended and free-response questions [40]. This approach is partially rooted in naturalistic inquiry to explicate patient experiences and perspectives [41]. Any discrepancies in the analysis will be resolved through consensus coding. If the 2 coders cannot reach a consensus, a third research team member will act as a tiebreaker. Topics derived from the content analysis are used to adapt and modify the implementation strategy. This mixed-methods approach allows for a more in-depth and rich description of patient acceptability and satisfaction to provide context to the quantitative data.

Sample Size Calculation

As this is a feasibility investigation, there is no pilot data. One purpose of this study is to obtain measures of central tendency and variability to inform power calculations for our future randomized controlled trial. Sample size estimates are dependent on the effect size, defined as the difference of T2 (6 months) and T0 (enrollment) divided by the standard deviation. Using a 2-tailed paired *t* test, 44 patients (including 10 patients from the exploration phase) and 32 oncologists are required to detect an effect size of 0.5 with 80% power at a level of significance of .05.

Results

The lead site WUSM received single IRB approval in June 2021, and data collection commenced immediately. As of August 2021, the research team has completed participant recruitment for the exploration phase with 10 patients and 11 providers from SCC, who completed surveys for the exploration phase, as shown in Tables 2 and 3. The participating sites are still at various stages of the single IRB approval process, which involves a signed reliance agreement between institutions, site registration, and a *Project ADAPT* application process. Once approvals are granted, oncologists at these partner sites are to complete surveys for the exploration and preparation phases to be finalized, as outlined in Table 1. We have incorporated a patient advocate into the study to understand patient cancer care pathways for reaching and engaging with more patients at the community level.

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Table 3. Provider assessment tools/schedule.

Measure	Providers involved	Exploration	Preparation[a]	T0[b]	T1 (3 months)	T2 (6 months)
ADAPT[c] provider survey	Siteman and community/partner site providers	Yes	No	Yes	Yes	Yes
Implementation Climate Scale [37]	Siteman and community/partner site providers	No	No	Yes	Yes	Yes

[a]No survey is administered during the preparation phase.

[b]The implementation phase starts at T0, marking the enrollment of patient participants to the study, and ends at T2.

[c]ADAPT: adapting and developing an academic and community practice collaborative care model for metastatic breast cancer care.

Discussion

Overview

Our adapted coordinated care model can enhance relationships among academic and community cancer centers. This model has the potential to improve patient and provider satisfaction and acceptability of the cancer care referral process. We anticipate that patients and providers can help identify limitations with the current MBC referral process to help identify opportunities to improve satisfaction and acceptability. Through *Project ADAPT*, we aim to positively impact clinical trial enrollment for patients with MBC, improve case discussion among providers, and provide a feasible and sustainable solution for improving care among patients with MBC. Moreover, as the number of women living with MBC continues to grow, our research extends beyond existing advancements in treatment [20,42] to evaluate interventions that have the potential to improve quality of life. We plan to disseminate our findings through academic platforms (eg, conferences and peer-reviewed journal articles), and we plan to make our data publicly available while adhering to IRB protocols. In addition, we will disseminate our findings to our community partner sites in a consumer-friendly plain language format.

There are few studies on the impact of collaborations among different hospitals to improve MBC care coordination. Only the EMBRACE program, to our knowledge, has conducted a multilevel systemic care coordination model for patients with metastatic breast cancer. WUSM received IRB approval in June 2021 and has completed participant recruitment for the exploration phase. WUSM has recruited 21 participants, including patients and providers. The latest community hospital, DDCI, joined the project in March 2021, while MBMC and SIH onboarded in late 2020. All partner sites are going through the single IRB registration in accordance with the current single IRB policy of the National Institutes of Health for multisite nonexempt human research carried out in the United States. The aim is to enhance and standardize the IRB review process among multiple research centers, avoiding duplication of review efforts to allow research to begin promptly [43]. This single IRB infrastructure has the potential to enhance the sustainability of these research partnerships and collaborations.

All communication requires reaching out to key stakeholders at these partner hospitals, presenting our research idea, and requesting collaboration virtually via Zoom meetings. Continued partnership and engagement have remained this way with a digital media platform by scheduling regular monthly meetings with all team members via Zoom to discuss updates on the study, recruitment and planning strategies, and IRB approval status. The research team meets at a time when most, if not all, can attend, and the ADAPT coordinator later sends out meeting minutes to all members of the group via email. During the research team meetings, study process modifications include creating study materials, such as the ADAPT patient flier for distribution to eligible patients at clinics and a page summary of *Project ADAPT* for providers.

We are approved to conduct virtual consultation for providers to share resources and knowledge among SCC, an NCI-designated cancer center, and our partner sites with NCORP clinical trial resources, creating a bidirectional relationship that improves patient care. This virtual consultation runs concurrently with telemedicine for patients. This platform of providing care to patients with MBC has become even more critical with the current COVID-19 pandemic [35]. This virtual experience also captures patients who would not be able to travel to SCC for whatever reason, but could still receive quality specialist care through this medium.

Patient recruitment for the exploration phase is via telephone calls, and surveys are distributed electronically through REDCap links. Utilizing e-consent for *Project ADAPT* has made recruitment manageable, especially during the COVID-19 pandemic. It resonates with studies showing that this approach can enhance access to participation among rural cancer patients in clinical trials, which is usually difficult due to geographic location [19,44]. Moreover, through virtual demonstrations via Zoom, the ADAPT coordinator has shown partner sites how to navigate the clinical trial tree finder.

Use of the digital EMR Epic messaging tool for communication among providers streamlines the referral process and allows providers access to real-time information regarding available clinical trials at SCC. Finally, as we prepare for the implementation phase, we strive to improve this design model with input from experts in different fields participating in the study and lessons learned from each stage of this study.

Limitations

We have buy-in and support from the leadership, oncology teams, and staff at the community partner sites. A minimum commitment of monthly scheduled communication throughout the duration of the project is expected, and continued engagement in the adaptation process will be needed from all sites. It is possible that the initial support and enthusiasm for this project will diminish, but we are using an

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implementation-science framework to enhance continued engagement. In addition, we are working with sites that use the Epic EMR system. The feasibility data collected in this investigation will give us a sense of the timeline, personnel, and community setting infrastructure, including the EMR system, needed for scaling up this type of study.

Opportunities for Future Research

WUSM research team members have launched a single IRB Support Network to develop a shared repository of resources and information to help guide partner sites through the single IRB process. We are in the process of creating a toolkit of resources to illustrate, in plain language, the single IRB application process. This toolkit will create a shared database with information about existing single IRB relationships with external partners (eg, key characteristics about the site and the research infrastructure, existing IRB agreements with WUSM, and past/current studies collaborated on with WUSM) and help to determine outreach strategies that best support partner sites throughout the single IRB process. For example, the study team has found that smaller community sites often lack third-party accreditations for their clinical research programs that may be more commonplace for larger academic health centers. In this way, the single IRB application process for studies that include a wide variety of recruitment sites would benefit from a streamlined approach to ensure the protection of human research subjects while accommodating the unique capabilities of each site.

In preparation for a larger trial, our team will complete provider-focused Pragmatic Explanatory Continuum Indicator Summary-2 (PRECIS-2) [45]. Evaluating our approach using the 9 PRECIS-2 domains (ie, eligibility, recruitment, setting, implementation resources, provider strategy flexibility, intervention flexibility, data collection, primary outcome, and primary analysis) will facilitate engagement from our care coordination stakeholders to match our research approach with the overall study aims of a future trial. The implementation science methods used throughout *Project ADAPT* will establish a robust methodological foundation for future trials investigating care coordination across multiple sites.

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Conflicts of Interest

NUL has received institutional research support from Genentech, Pfizer, Merck, Seattle Genetics, Zion Pharmaceuticals, Olema Pharmaceuticals, and AstraZeneca; consulting honoraria from Puma, Seattle Genetics, Daichii-Sankyo, AstraZeneca, Denali Therapeutics, Prelude Therapeutics, Olema Pharmaceuticals, Aleta BioPharma, Affinia Therapeutics, and Voyager Therapeutics; and has stock and other ownership interests in Artera Inc.

Multimedia Appendix 1
Adapting and developing an academic and community practice collaborative care model for metastatic breast cancer care (ADAPT) patient survey.
[DOC File , 93 KB - resprot_v11i7e35736_app1.doc]

Multimedia Appendix 2
Adapting and developing an academic and community practice collaborative care model for metastatic breast cancer care (ADAPT) patient sociodemographic survey (exploration and T0).
[DOC File , 108 KB - resprot_v11i7e35736_app2.doc]

Multimedia Appendix 3
Adapting and developing an academic and community practice collaborative care model for metastatic breast cancer care (ADAPT) patient sociodemographic survey (revised for patients at T1 and T2).
[DOC File , 98 KB - resprot_v11i7e35736_app3.doc]

Multimedia Appendix 4
Epic data extraction form.
[DOC File , 62 KB - resprot_v11i7e35736_app4.doc]

Multimedia Appendix 5
Patient Decision Regret Scale.
[DOC File , 27 KB - resprot_v11i7e35736_app5.doc]

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Multimedia Appendix 6
Adapting and developing an academic and community practice collaborative care model for metastatic breast cancer care (ADAPT) Siteman provider survey.
[DOC File , 62 KB - resprot_v11i7e35736_app6.doc]

Multimedia Appendix 7
Adapting and developing an academic and community practice collaborative care model for metastatic breast cancer care (ADAPT) referring provider survey.
[DOC File , 78 KB - resprot_v11i7e35736_app7.doc]

Multimedia Appendix 8
Provider Implementation Climate Scale.
[DOC File , 27 KB - resprot_v11i7e35736_app8.doc]

Multimedia Appendix 9
Recruitment procedures at the exploration phase.
[DOCX File , 28 KB - resprot_v11i7e35736_app9.docx]

Multimedia Appendix 10
Recruitment procedures at the implementation phase.
[DOCX File , 38 KB - resprot_v11i7e35736_app10.docx]

References

1. Miller KD, Nogueira L, Mariotto AB, Rowland JH, Yabroff KR, Alfano CM, et al. Cancer treatment and survivorship statistics, 2019. CA Cancer J Clin 2019 Sep 11;69(5):363-385 [FREE Full text] [doi: 10.3322/caac.21565] [Medline: 31184787]
2. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2016. CA Cancer J Clin 2016 Jan 07;66(1):7-30 [FREE Full text] [doi: 10.3322/caac.21332] [Medline: 26742998]
3. Siegel RL, Miller KD, Fuchs HE, Jemal A. Cancer Statistics, 2021. CA Cancer J Clin 2021 Jan 12;71(1):7-33 [FREE Full text] [doi: 10.3322/caac.21654] [Medline: 33433946]
4. Caswell-Jin J, Plevritis S, Tian L, Cadham C, Xu C, Stout N, et al. Change in survival in metastatic breast cancer with treatment advances: meta-analysis and systematic review. JNCI Cancer Spectr 2018 Nov;2(4):pky062 [FREE Full text] [doi: 10.1093/jncics/pky062] [Medline: 30627694]
5. Blake KD, Moss JL, Gaysynsky A, Srinivasan S, Croyle RT. Making the case for investment in rural cancer control: an analysis of rural cancer incidence, mortality, and funding trends. Cancer Epidemiol Biomarkers Prev 2017 Jun 09;26(7):992-997. [doi: 10.1158/1055-9965.epi-17-0092]
6. Belasco EJ, Gong G, Pence B, Wilkes E. The impact of rural health care accessibility on cancer-related behaviors and outcomes. Appl Health Econ Health Policy 2014 Aug 3;12(4):461-470. [doi: 10.1007/s40258-014-0099-4] [Medline: 24889860]
7. Moss JL, Liu B, Feuer EJ. Urban/rural differences in breast and cervical cancer incidence: the mediating roles of socioeconomic status and provider density. Womens Health Issues 2017 Nov;27(6):683-691 [FREE Full text] [doi: 10.1016/j.whi.2017.09.008] [Medline: 29108988]
8. Nguyen-Pham S, Leung J, McLaughlin D. Disparities in breast cancer stage at diagnosis in urban and rural adult women: a systematic review and meta-analysis. Ann Epidemiol 2014 Mar;24(3):228-235. [doi: 10.1016/j.annepidem.2013.12.002] [Medline: 24462273]
9. Jones SE. Metastatic breast cancer: the treatment challenge. Clinical Breast Cancer 2008 Jun;8(3):224-233. [doi: 10.3816/cbc.2008.n.025]
10. Li Y, Humphries B, Yang C, Wang Z. Nanoparticle-mediated therapeutic agent delivery for treating metastatic breast cancer-challenges and opportunities. Nanomaterials (Basel) 2018 May 24;8(6):361 [FREE Full text] [doi: 10.3390/nano8060361] [Medline: 29794968]
11. Peart O. Metastatic breast cancer. Radiol Technol 2017 May;88(5):519M-539M. [Medline: 28500107]
12. Kamaraju S, Fowler A, Weil E, Wisinski K, Truong T, Lehr M, et al. Leveraging antiprogestins in the treatment of metastatic breast cancer. Endocrinology 2021 Aug 01;162(8):2021. [doi: 10.1210/endocr/bqab060] [Medline: 33735382]
13. Walsh J, Harrison JD, Young JM, Butow PN, Solomon MJ, Masya L. What are the current barriers to effective cancer care coordination? A qualitative study. BMC Health Serv Res 2010 May 20;10(1):132 [FREE Full text] [doi: 10.1186/1472-6963-10-132] [Medline: 20482884]

XSL•FO
RenderX

14. Carlson RW, Allred DC, Anderson BO, Burstein HJ, Edge SB, Farrar WB, National Comprehensive Cancer Network. Metastatic breast cancer, version 1.2012: featured updates to the NCCN guidelines. J Natl Compr Canc Netw 2012 Jul 01;10(7):821-829 [FREE Full text] [doi: 10.6004/jnccn.2012.0086] [Medline: 22773798]
15. Gradishar WJ, Anderson BO, Abraham J, Aft R, Agnese D, Allison KH, et al. Breast Cancer, Version 3.2020, NCCN Clinical Practice Guidelines in Oncology. J Natl Compr Canc Netw 2020 Apr;18(4):452-478. [doi: 10.6004/jnccn.2020.0016] [Medline: 32259783]
16. Burstein H, Somerfield M, Barton D, Dorris A, Fallowfield L, Jain D, et al. Endocrine treatment and targeted therapy for hormone receptor-positive, human epidermal growth factor receptor 2-negative metastatic breast Cancer: ASCO Guideline Update. J Clin Oncol 2021 Dec 10;39(35):3959-3977. [doi: 10.1200/JCO.21.01392] [Medline: 34324367]
17. Charlton M, Schlichting J, Chioreso C, Ward M, Vikas P. Challenges of rural cancer care in the United States. Oncology (Williston Park) 2015 Sep;29(9):633-640 [FREE Full text] [Medline: 26384798]
18. Waterhouse DM, Harvey RD, Hurley P, Levit LA, Kim ES, Klepin HD, et al. Early impact of COVID-19 on the conduct of oncology clinical trials and long-term opportunities for transformation: findings from an American Society of Clinical Oncology survey. JCO Oncology Practice 2020 Jul;16(7):417-421. [doi: 10.1200/op.20.00275]
19. Levit LA, Byatt L, Lyss AP, Paskett ED, Levit K, Kirkwood K, et al. Closing the rural cancer care gap: three institutional approaches. JCO Oncology Practice 2020 Jul;16(7):422-430. [doi: 10.1200/op.20.00174]
20. Chung C, Carlson R. Goals and objectives in the management of metastatic breast cancer. Oncologist 2003;8(6):514-520 [FREE Full text] [doi: 10.1634/theoncologist.8-6-514] [Medline: 14657529]
21. Sprague BL, Ahern TP, Herschorn SD, Sowden M, Weaver DL, Wood ME. Identifying key barriers to effective breast cancer control in rural settings. Prev Med 2021 Nov;152(Pt 2):106741. [doi: 10.1016/j.ypmed.2021.106741] [Medline: 34302837]
22. Getz KA. Examining and enabling the role of health care providers as patient engagement facilitators in clinical trials. Clin Ther 2017 Nov;39(11):2203-2213. [doi: 10.1016/j.clinthera.2017.09.014] [Medline: 29079388]
23. Ramirez AG, Chalela P, Suarez L, Muñoz E, Pollock BH, Weitman S, et al. Early phase clinical trials: referral barriers and promoters among physicians. J Community Med Health Edu 2012;2:173. [doi: 10.4172/2161-0711.1000173]
24. Hughes M, Frank E, Merrill M, Santiago R, Kuhnly N, Crowley L, et al. Abstract P4-10-04: EMBRACE (Ending metastatic breast cancer for everyone): A comprehensive approach to improve the care of patients with metastatic breast cancer. Cancer Res 2018;78:P4-10-04. [doi: 10.1158/1538-7445.sabcs17-p4-10-04]
25. Fayanju OM, Jeffe DB, Tappenden JR, Beers CE, Drake BF, Gao F, et al. Breast cancer presentation in an urban health care Safety Net system. Mo Med 2012;109(5):405-411 [FREE Full text] [Medline: 23097949]
26. Salazar AS, Sekhon S, Rohatgi KW, Nuako A, Liu J, Harriss C, et al. A stepped-wedge randomized trial protocol of a community intervention for increasing lung screening through engaging primary care providers (I-STEP). Contemp Clin Trials 2020 Apr;91:105991. [doi: 10.1016/j.cct.2020.105991] [Medline: 32184197]
27. Aarons GA, Green AE, Palinkas LA, Self-Brown S, Whitaker DJ, Lutzker JR, et al. Dynamic adaptation process to implement an evidence-based child maltreatment intervention. Implement Sci 2012 Apr 18;7(1):32 [FREE Full text] [doi: 10.1186/1748-5908-7-32] [Medline: 22512914]
28. Aarons GA, Hurlburt M, Horwitz SM. Advancing a conceptual model of evidence-based practice implementation in public service sectors. Adm Policy Ment Health 2011 Jan 14;38(1):4-23 [FREE Full text] [doi: 10.1007/s10488-010-0327-7] [Medline: 21197565]
29. Defining Key Health Information Technology Terms. The National Alliance for Health Information Technology Report to the Office of the National Coordinator for Health Information Technology. 2008 Apr 28. URL: https://www.nachc.org/wp-content/uploads/2016/03/Key-HIT-Terms-Definitions-Final_April_2008.pdf [accessed 2022-05-04]
30. Davis Z, Khansa L. Evaluating the epic electronic medical record system: A dichotomy in perspectives and solution recommendations. Health Policy and Technology 2016 Mar;5(1):65-73. [doi: 10.1016/j.hlpt.2015.10.004]
31. Sood S, Mbarika V, Jugoo S, Dookhy R, Doarn CR, Prakash N, et al. What is telemedicine? A collection of 104 peer-reviewed perspectives and theoretical underpinnings. Telemed J E Health 2007 Oct;13(5):573-590. [doi: 10.1089/tmj.2006.0073] [Medline: 17999619]
32. Krishna MT, Knibb RC, Huissoon AP. Is there a role for telemedicine in adult allergy services? Clin Exp Allergy 2016 May 26;46(5):668-677. [doi: 10.1111/cea.12701] [Medline: 26742680]
33. Garattini L, Badinella Martini M, Zanetti M. More room for telemedicine after COVID-19: lessons for primary care? Eur J Health Econ 2021 Mar 24;22(2):183-186 [FREE Full text] [doi: 10.1007/s10198-020-01248-y] [Medline: 33231825]
34. Keesara S, Jonas A, Schulman K. Covid-19 and health care's digital revolution. N Engl J Med 2020 Jun 04;382(23):e82. [doi: 10.1056/nejmp2005835]
35. Gomez T, Anaya YB, Shih KJ, Tarn DM. A qualitative study of primary care physicians' experiences with telemedicine during COVID-19. J Am Board Fam Med 2021 Feb 23;34(Supplement):S61-S70. [doi: 10.3122/jabfm.2021.s1.200517]
36. Brehaut JC, O'Connor AM, Wood TJ, Hack TF, Siminoff L, Gordon E, et al. Validation of a decision regret scale. Med Decis Making 2003;23(4):281-292. [doi: 10.1177/0272989X03256005] [Medline: 12926578]

XSL•FO
RenderX

37. Ehrhart MG, Aarons GA, Farahnak LR. Assessing the organizational context for EBP implementation: the development and validity testing of the Implementation Climate Scale (ICS). Implement Sci 2014 Oct 23;9:157 [FREE Full text] [doi: 10.1186/s13012-014-0157-1] [Medline: 25338781]
38. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)--a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform 2009 Apr;42(2):377-381 [FREE Full text] [doi: 10.1016/j.jbi.2008.08.010] [Medline: 18929686]
39. Harris PA, Taylor R, Minor BL, Elliott V, Fernandez M, O'Neal L, REDCap Consortium. The REDCap consortium: Building an international community of software platform partners. J Biomed Inform 2019 Jul;95:103208 [FREE Full text] [doi: 10.1016/j.jbi.2019.103208] [Medline: 31078660]
40. Hsieh H, Shannon SE. Three approaches to qualitative content analysis. Qual Health Res 2005 Nov 01;15(9):1277-1288. [doi: 10.1177/1049732305276687] [Medline: 16204405]
41. Colorafi KJ, Evans B. Qualitative descriptive methods in health science research. HERD 2016 Jul 19;9(4):16-25 [FREE Full text] [doi: 10.1177/1937586715614171] [Medline: 26791375]
42. Chia SK, Speers CH, D'yachkova Y, Kang A, Malfair-Taylor S, Barnett J, et al. The impact of new chemotherapeutic and hormone agents on survival in a population-based cohort of women with metastatic breast cancer. Cancer 2007 Sep 01;110(5):973-979 [FREE Full text] [doi: 10.1002/cncr.22867] [Medline: 17647245]
43. Final NIH Policy on the Use of a Single Institutional Review Board for Multi-Site Research. National Institutes of Health. URL: https://grants.nih.gov/grants/guide/notice-files/NOT-OD-16-094.html [accessed 2021-11-11]
44. Doroshow J, Prindiville S, McCaskill-Stevens W, Mooney M, Loehrer P. COVID-19, social justice, and clinical cancer research. J Natl Cancer Inst 2021 Oct 01;113(10):1281-1284 [FREE Full text] [doi: 10.1093/jnci/djaa162] [Medline: 33057660]
45. Norton WE, Loudon K, Chambers DA, Zwarenstein M. Designing provider-focused implementation trials with purpose and intent: introducing the PRECIS-2-PS tool. Implement Sci 2021 Jan 07;16(1):7 [FREE Full text] [doi: 10.1186/s13012-020-01075-y] [Medline: 33413489]

Abbreviations

ADAPT: adapting and developing an academic and community practice collaborative care model for metastatic breast cancer care
DAP: dynamic adaptation process
DDCI: Phelps Health Delbert Day Cancer Institute
DFCI: Dana Farber Cancer Institute
EMBRACE: Ending Metastatic Breast Cancer for Everyone
EMR: electronic medical record
EPIS: Exploration, Preparation, Implementation, Sustainment
GEE: generalized estimating equation
IRB: institutional review board
MBC: metastatic breast cancer
MBMC: Missouri Baptist Medical Center
NCI: National Cancer Institute
NCORP: National Cancer Institute Community Oncology Research Program
PRECIS-2: Pragmatic Explanatory Continuum Indicator Summary-2
REDCap: Research Electronic Data Capture
SCC: Siteman Cancer Center
SIH: Southern Illinois Healthcare
WUSM: Washington University School of Medicine

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Protocol

Implementation of Evidence-Informed Behavioral Health Models to Improve HIV Health Outcomes for Black Men Who Have Sex With Men (Black MSM Initiative): Protocol for Program Evaluation

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Abstract

Background: The HIV epidemic in the United States disproportionately affects Black communities. Nearly half of Black men who have sex with men (MSM) will be diagnosed with HIV in their lifetime. There is a significant unmet need for behavioral health care services among Black MSM, and untreated behavioral health needs make it less likely the person is retained in HIV care.

Objective: This paper offers a description of the Implementation of Evidence-Informed Behavioral Health Models to Improve HIV Health Outcomes for Black Men who have Sex with Men (Black MSM) Initiative, a program to integrate clinical care and behavioral health/supportive services for Black MSM with HIV. The Black MSM Initiative is funded through the Health Resources & Services Administration HIV/AIDS Bureau Ryan White HIV/AIDS Program (RWHAP) Part F Special Projects of National Significance.

Methods: The components of the Black MSM Initiative include providing technical assistance to 8 Initiative demonstration sites; conducting a comprehensive and culturally responsive, mixed method, multisite evaluation; and disseminating evaluation findings and lessons learned to the RWHAP community.

Results: As of December 31, 2020, demonstration sites enrolled 809 clients in the multisite evaluation. The research team will continue evaluation data collection through December 2021 for analysis and dissemination starting in 2022. The Black MSM Initiative fully supports the US Department of Health and Human Services' Ending the HIV Epidemic in the United States Initiative.

Conclusions: In order to succeed, providers and programs will need to engage populations traditionally considered "hard to reach," like many people receiving RWHAP services. Findings and lessons learned from the Black MSM Initiative will expand the tool kit of solutions to support and retain Black MSM in HIV care, furthering the goals of the Ending the HIV Epidemic Initiative and the RWHAP.

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KEYWORDS

HIV infections; sexual and gender minorities; outcome assessment, health care; delivery of health care; African Americans; homosexuality, male; mental health services; HIV epidemic; minority population; epidemiology; peer support; health service; health outcomes; HIV; public health

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Introduction

Background

The HIV epidemic in the United States disproportionately impacts Black communities, and Black men who have sex with men (MSM) bear an unequal share of that burden. Black MSM account for less than one percent of the US population, but between 20%-25% of all new US HIV infections [1]. Furthermore, if current diagnosis rates persist, about half of Black MSM in the United States will be diagnosed with HIV in their lifetime, versus 1 in 11 white MSM [2]. In comparison, lifetime risk for all men in the United States is 1 in 68 [3]. In addition, Black MSM are less likely to achieve viral suppression than the national average for clients served by the Ryan White HIV/AIDS Program (RWHAP) [4]. This is in part because of the intersecting ways in which Black MSM are marginalized and experience disparities in access to health care [5].

Black MSM with HIV may have intersectional experiences with stigma or discrimination based on race, sexual orientation, gender expression or gender identity, and/or HIV status. Perceived stigma or discrimination, along with existing medical mistrust within the community, may influence Black MSM's ability to safely and comfortably access clinical or behavioral health care [6]. Cumulative experiences of discrimination or trauma negatively impact mental and physical health. Research indicates experiences of racism increase vulnerability to depression and other mental health conditions [7]. Unfortunately, there is significant unmet need for behavioral health care among Black MSM. Untreated behavioral health needs may also make it less likely a person is retained in HIV clinical care [8]. Further, compared to other MSM receiving outpatient HIV medical care, Black MSM face shortages of stable housing, nutritional support, substance use treatment, and mental health services [9].

Given these substantial inequities, the US Department of Health and Human Services Health Resources & Services Administration (HRSA) HIV/AIDS Bureau (HAB) RWHAP Part F Special Projects of National Significance (SPNS) funded an initiative to address the unique clinical, behavioral health, and social support needs of Black MSM with HIV. The purpose of the Implementation of Evidence-Informed Behavioral Health Models to Improve HIV Health Outcomes for Black Men who have Sex with Men ("the Black MSM Initiative") is to engage and retain Black MSM in HIV medical care and supportive services by addressing their behavioral health needs [10]. This aim of this paper is to describe the Black MSM Initiative's strategies to integrate clinical care, behavioral health care, and supportive services for the intended Black MSM audience; provide technical assistance to demonstration sites; design for the mixed method, culturally responsive evaluation (CRE) of the Initiative; and disseminate evaluation findings and lessons learned.

Overview of the Black MSM Initiative

Through the Black MSM Initiative, HRSA HAB funds 8 demonstration sites to adapt and implement one of 4 evidence-informed models of care (MOCs) expected to improve linkage to care, engagement, retention, and HIV health outcomes. Demonstration sites integrate clinical and behavioral health care to serve the comprehensive needs of Black MSM with HIV. The MOCs are a youth-focused case management intervention [11], Strength Through Youth Livin' Empowered (STYLE) [12], Brothers United/the Damien Center's Linkage to Care program [13], and Project Silk [14]. All models were originally developed to improve HIV care and treatment and/or HIV health outcomes for youth and/or adult men of color.

In addition, to support implementation and evaluation of the demonstration sites' interventions, HRSA HAB funds NORC at the University of Chicago (NORC) to serve as the Evaluation and Technical Assistance Provider (ETAP). The ETAP's four goals are to (1) provide technical assistance and capacity building assistance to the demonstration sites; (2) implement a comprehensive multisite evaluation; (3) develop and disseminate successful models, findings, best practices, and lessons learned to the RWHAP community; and (4) promote successful replication of effective evidence-informed interventions and/or MOCs through trainings, publications, and other dissemination products. Together, these activities facilitate engagement and retention of Black MSM in HIV care.

The demonstration sites represent a range of organizational types and experiences, including academic medical centers, federally qualified health centers, community-based organizations, and hospital/health systems. The nonclinical demonstration sites partner with other clinics to provide HIV clinical and behavioral health care to their clients. Sites are located across 7 states and operate in both urban and suburban settings. Seven of the sites are RWHAP Parts A, B, C, D, or F Dental recipients. Table 1 provides an overview of the 8 demonstration sites.

Table 2 provides an overview of the 4 MOCs and adaptations made to each MOC to better fit the site context or local population.

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Table 1. Overview of the demonstration sites.

Demonstration site	City, state	Selected model of care	Organizational type	Length of intervention	Target population
Christian Community Health Center	Chicago, IL	Youth-focused case management intervention	Community-based clinic (federally qualified health center)	12 months	Black MSM[a] LWH[b] aged ≥18 years
Parkland HIV Services Department, Dallas County Hospital District	Dallas, TX	Youth-focused case management intervention	Hospital system	9 months	Black MSM LWH aged 17-34 years
Duke University	Durham, NC	Strength Through Youth Livin' Empowered (STYLE)	Academic program, nonclinical	12 months	Black MSM LWH aged 18-35 years
Friends Research Institute, Inc.	Los Angeles, CA	Youth-focused case management intervention	Community research site	3 months	Black MSM LWH aged 18-65 years
GMHC Inc	New York, NY	Project Silk	Community-based organization	12 months	Black MSM LWH aged 18-45 years
CrescentCare	New Orleans, LA	Brothers United/The Damien Center's Linkage to Care program	Community-based clinic (AIDS service organization, federally qualified health center)	12 months	Black MSM and Black transgender men LWH aged ≥13 years
East Bay Advanced Care, Sutter Bay Hospitals	Oakland, CA	Youth-focused case management intervention	Hospital system	6-18 months, depending on enrollment date	Black MSM LWH (no age range)
Project ARK at Washington University	St. Louis, MO	Youth-focused case management intervention	Academic program, clinical	6 months	Black MSM LWH aged 18-29 years

[a]MSM: men who have sex with men.

[b]LWH: living with HIV.

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Table 2. Models of care and site adaptations.

Model of care	Number of sites	Model summary	Core components	Site adaptations
Youth-focused case management intervention	5	The goal of this intervention was to improve retention in HIV care for young Latino and African American MSM. Case managers provided supportive services to fill participants' identified needs for housing, nutrition support, substance abuse treatment, or mental health services.	• Two bachelor-level case managers • Clinic- and venue-based outreach • 24-month intervention • Psychosocial case management services	• Expanding eligible age range • Shortening intervention length (between 3 and 18 months) • Using peer case managers
Strength Through Youth Livin' Empowered (STYLE)	1	Strength Through Youth Livin' Empowered (STYLE) was designed to improve retention in HIV care through a social marketing campaign, outreach to youth and provision of HIV testing services, and a coordinated medical and social support network for recently diagnosed and lost-to-care youth with HIV.	• Medical case manager and peer outreach worker • Targeted venue-based and social marketing outreach • 24-month intervention • Case management and ancillary support services	• Combining case manager and outreach worker position • Adding a behavioral health provider • Shortening intervention length to 12 months • Using an app to engage clients virtually
Project Silk	1	Project Silk was a youth-led, adult-supported drop-in program for LGBTQ[a] individuals that offered recreation opportunities, food and snacks, health services like HIV/sexually transmitted infection testing, access to mental health counseling, and community resources.	• Engagement with House and Ball community • Recreation-based safe space focusing on artistic expression • Colocated supportive services	• Expanding the target population to include non–House and Ball clients
Brothers United/the Damien Center's Linkage to Care program	1	This program, run by an Indianapolis community-based organization, provided comprehensive wraparound and supportive services to the Black LGBTQ community. The program offered prevention and testing. Those who tested positive were referred to services that help them engage in care.	• Linkage to Care specialists • One-stop shop for comprehensive care and referral services • Support groups	Adding an on-site behavioral health therapist

[a]LGBTQ: lesbian, gay, bisexual, transgender, queer.

Target Population

The Black MSM Initiative target population is Black MSM with HIV. Specifically, to be eligible to participate, a client must be HIV positive; aged 13 and older; identify as a Black man who has sex with men (including cisgender men, transgender men, and gender nonconforming individuals assigned male at birth); and fit into one of the following categories: newly diagnosed/new to care, never entered into care, fallen out of care, at risk of falling out of care, or not virally suppressed. Risk factors for falling out of care are operationalized as ongoing behavioral health issues (eg, mental health and/or substance use disorders), a history of irregular engagement in care, housing and/or employment instability, a history of sexually transmitted infections, or a history of negative experiences in a health care setting. Demonstration sites could impose more restrictive eligibility criteria as needed for their intervention (eg, must have access to a smartphone).

The Black MSM Initiative uses several key definitions to describe project activities. As defined by HRSA, *HIV care services* include all HIV care and treatment services allowable through the RWHAP; *behavioral health* refers to mental or emotional well-being and/or actions that affect wellness; and *behavioral health care* includes screening and treatment for substance use disorders, alcohol and drug addiction, and serious psychological distress, suicide, and mental disorders [15]. *Evidence-informed interventions* are strategies, models, or approaches that have proven effective or shown promise as a methodology, practice, or means of improving the care and treatment of people with HIV.

Purpose

This paper describes the rationale for integrating clinical care, behavioral health care, and supportive services, and presents the Black MSM Initiative model, which includes providing technical assistance to demonstration sites, conducting a culturally responsive multisite evaluation, and disseminating evaluation findings and lessons learned.

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Methods

Strategies for Integrating Behavioral Health

The primary objective of the Black MSM Initiative is to integrate clinical and behavioral health care to improve health outcomes. Demonstration sites designed a variety of intervention activities to accomplish this goal, including peer support groups, individual counseling, motivational interviewing during case management sessions, and SMS text messaging services that screen for behavioral health concerns. To provide behavioral health care to enrolled clients, 6 demonstration sites offer in-house behavioral health services and all demonstration sites offer referrals to off-site behavioral health and supportive services, including substance use treatment.

To integrate clinical and behavioral health care, demonstration sites employ multiple strategies that include holding regular case conferences with case management staff, behavioral health staff, and HIV clinical providers to discuss clients and coordinate care; meeting regularly to identify and address client needs; improving cross-care team communication; and engaging behavioral health staff as members of the intervention team.

Additionally, to integrate care, demonstration sites follow clients through their receipt of behavioral health care and endeavor to eliminate barriers to care (eg, offering transportation to provider visits). Some demonstration sites provide warm handoffs from case managers/peer navigators to behavioral health providers and have providers introduce themselves during clinical or case management appointments. Case management/peer navigation staff aim to ensure clients understand behavioral health care and work to normalize this care. For example, some demonstration sites offer social support groups facilitated by peer staff, which discuss behavioral health needs, reframe mental or behavioral health as mental wellness, and focus on overall well-being. In addition to integrating behavioral health care, these techniques are valuable for sustaining client engagement.

Provision of Technical Assistance

The ETAP provides technical assistance (TA) and capacity building assistance (CBA) to the demonstration sites in intervention adaptation, implementation, and evaluation. The ETAP assesses the needs of the demonstration sites and coordinates trainings, provides resources, and develops tools. In addition to responding to specific requests from the demonstration sites, TA/CBA is provided proactively through regular teleconferences with each demonstration site, office hours, multisite meetings, site visits, teleconferences with frontline staff, and website resources. To leverage demonstration sites' expertise, the ETAP encourages and facilitates peer learning and development through these venues. Areas of TA/CBA include marketing and recruitment; retention; local evaluation; data collection and submission for the multisite evaluation; dissemination; sustainability; staff training, support, and self-care; and COVID-19 adaptations. To identify demonstration sites' needs and inform the provision of proactive TA, the ETAP conducted needs assessments, held calls with the sites, and developed a site typology.

The *needs assessments* gathered information on current capacity and anticipated needs for support around program adaptation, staffing, recruitment, implementation, retention, Institutional Review Board approval, local evaluation, and sustainability planning. The ETAP used findings from the needs assessments to identify gaps in site capacity and tailor TA provision. *Initial calls* with the sites facilitated in-depth learning about each sites' local context and MOC adaptations, implementation and local evaluation plans, and anticipated challenges and TA needs. Information from the calls was used to address the immediate needs of sites and identify topics for future cross-site discussions. These calls also informed the development of the multisite evaluation. The ETAP continues to meet with the demonstration sites monthly to monitor recruitment, enrollment, and evaluation progress and discuss TA needs. Following conduct of the first needs assessment and initial calls, the ETAP developed a *typology* to document and compare the demonstration sites, their selected MOCs, MOC adaptations, local evaluation design, and capacity for contribution to the multisite evaluation. As the ETAP learns more about each site, the ETAP updates the typology to facilitate meaningful provision of TA/CBA.

Multisite Evaluation Strategy

To assess the impact of the Black MSM Initiative on expected outcomes, the ETAP is conducting a culturally responsive, sequential, transformative, mixed method evaluation. The purpose of the multisite evaluation (MSE) is to (1) assess processes associated with implementing evidence-informed interventions, including barriers and facilitators to implementation (*process study*); (2) assess whether the evidence-informed interventions impact clinical and behavioral health outcomes (*outcomes study*); and (3) assess the costs of adapting and implementing the interventions by measuring labor and programmatic expenditures (*cost analysis*). The evaluation uses document review, demonstration site calls, site visits, key informant interviews, a pre-post client survey, demonstration site capture of implementation data, and client-level outcome data. Demonstration sites gather data at baseline and, at minimum, 6 and 12 months postbaseline. Table 3 summarizes the 3 evaluation components and how they align with MSE methods.

To design the evaluation, the ETAP first created an Initiative logic model that depicts the Black MSM Initiative's inputs, activities, outputs, and expected outcomes (Figure 1).

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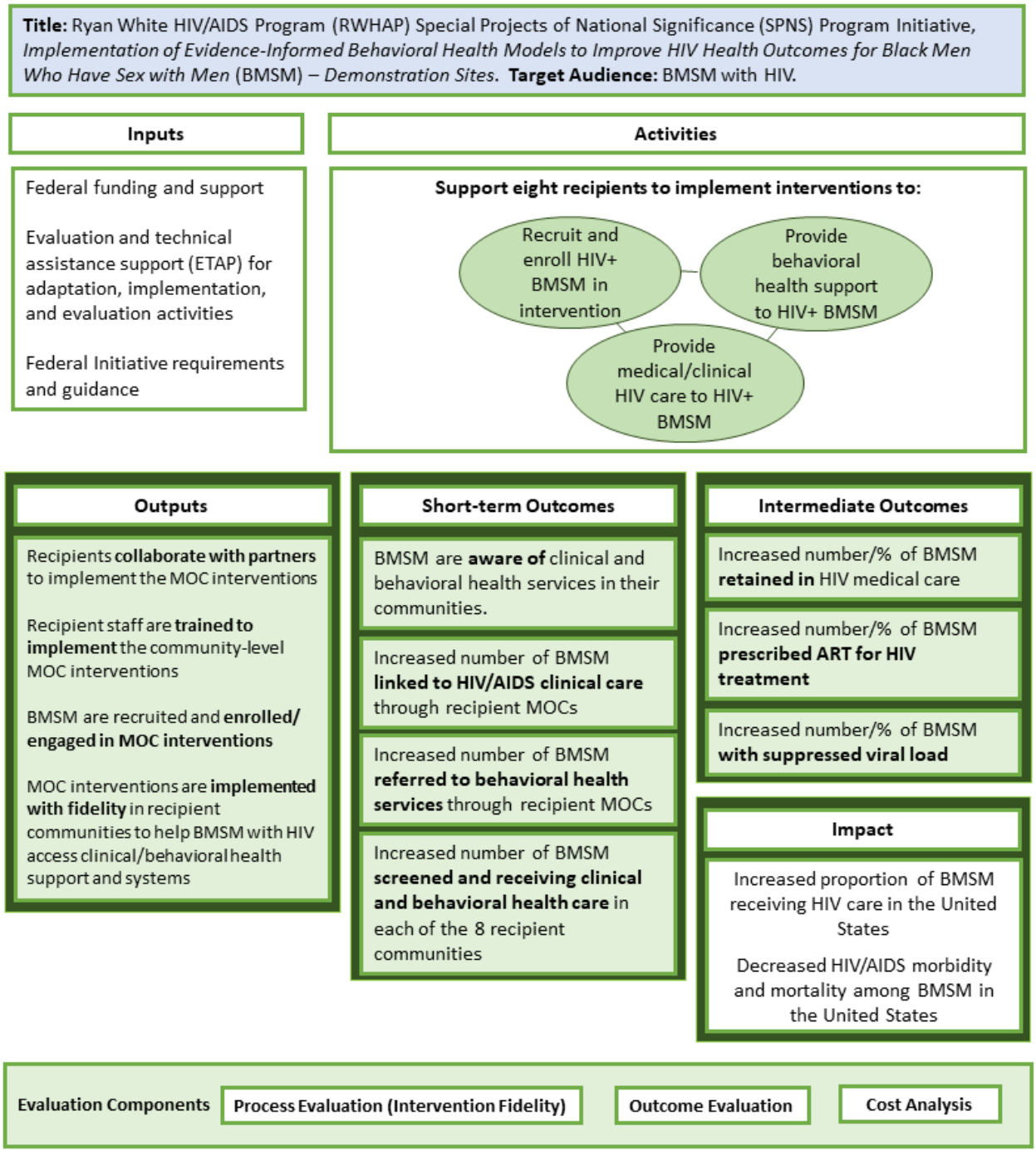
Table 3. Overview of the evaluation studies, aims, and methods.

Evaluation component	Study aim	Method type	Data collection frequency
Process study	Aim 1: Assess processes associated with implementing evidence-informed interventions, including barriers and facilitators to implementation.	Qualitative, quantitative	Baseline in year 1, twice in year 2, twice in year 3
Outcome study	Aim 2: Assess whether evidence-informed interventions impact clinical/behavioral health outcomes.	Quantitative	Baseline in year 1, twice in year 2, twice in year 3
Cost analysis	Aim 3: Assess the costs of adapting and implementing the interventions/MOCs by measuring labor and programmatic costs and expenditures incurred by each site.	Qualitative, quantitative	Once in year 1, once in year 2, once in year 3

Figure 1. Black MSM Initiative logic model. ART: antiretroviral treatment; BMSM: Black men who have sex with men; MOC: model of care; MSM: men who have sex with men.



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Following development of the logic model, the ETAP, in consultation with RWHAP SPNS Project Officers and demonstration site project teams, identified specific process study, outcome study, and cost analysis evaluation questions. The process study questions explore what factors influence adaptation and implementation of interventions; which intervention components are delivered with fidelity; and how clients are recruited to participate. Outcome study questions include whether the Initiative contributed to changed awareness of HIV care and behavioral health care/supportive services; linkage to care, screening, referral to care, receipt of care, retention, and engagement outcomes; and antiretroviral therapy (ART) prescription and HIV viral load outcomes. The cost analysis examines costs per client served and costs per key programmatic outcome. After determining the evaluation questions, the ETAP identified the appropriate evaluation framework and design.

The MSE uses a CRE approach [16,17]. The ETAP proposed CRE because it focuses on recognizing the centrality of culture, and invites and legitimizes the diverse perspectives of demonstration sites, stakeholders, and Black MSM with HIV. CRE seeks to enhance the social, political, and economic conditions of persons from traditionally underrepresented and underserved communities by executing valid evaluations [18]. In practice, this means the ETAP designed study questions and instruments to explore and account for the role of community context, demographics, socioeconomics, sexuality, gender, politics, and culture.

The ETAP uses a sequential, transformative strategy to collect and analyze relevant process and outcome measures [19]. Transformative research [20,21] focuses on studying the lives and experiences of diverse, often-marginalized groups; requires collaborative inquiry so as not to marginalize clients; and advances an agenda to improve clients' lives [22]. This evaluation design allows, at minimum, two distinct, sequential data collection phases (either qualitative or quantitative) and a theoretical perspective to guide the evaluation (Figure 2) [19,23].

Qualitative MSE data collection instruments include a document review extraction form to systematically extract relevant data from site-developed documents; protocols for annual site visits; and tailored, semistructured interview guides for annual key informant interviews. Quantitative instruments include a patient survey administered at baseline and 6 and 12 months postbaseline; a Demonstration Site Assessment Tool to track intervention service encounters; a Main Outcomes Instrument to collect individual-level clinical outcomes data also at baseline and 6 and 12 months postbaseline; and an Interview-Assisted Cost Worksheet to collect site-level cost information.

To analyze qualitative data, the ETAP uses applied thematic analysis to identify common themes, patterns, and interrelationships in the data relevant to expected outcomes and answer linked evaluation questions. To analyze quantitative data, the ETAP aggregates data across all demonstration sites to analyze and answer linked evaluation questions. Using generalized linear mixed effects models, the ETAP compares client outcomes between baseline and each of the follow-up time points (6 and 12 months) and assesses clustering effects within demonstration sites. The ETAP performs stratified analysis to determine whether changes in outcomes vary by subgroup. To complete the cost analysis, the ETAP uses micro-costing methodology to collect data on labor, supplies, facilities, and other cost inputs. The ETAP combines different cost inputs to create estimates of the aggregated costs of each intervention and total costs per client served, and will use bootstrapping if needed to estimate uncertainty. As the final step, the ETAP mixes the quantitative and qualitative data to ensure the findings are complementary and answer overarching MSE study questions.

Figure 2. Design of the multisite evaluation. QUAL: qualitative; QUANT: quantitative.

Ethics Approval

Ethical conduct of the study was overseen by the NORC Institutional Review Board, which determined the study to not be human subjects research because the ETAP did not receive any identifying information about participants. Identifiers were stored locally on secure servers; the ETAP audited data security during site visits. Several demonstration sites also obtained Certificates of Confidentiality to further protect participant privacy. All study procedures were conducted in accordance with the ethical standards set forth in the 1975 Declaration of Helsinki.

Dissemination Planning

The ETAP supports the dissemination of best practices and lessons learned from the Initiative and promotes replication of successful interventions. The ETAP facilitates timely dissemination of results and encourages cross-site collaboration through a Publications & Dissemination Committee, which includes representatives from HRSA, NORC, and each demonstration site. Complementary to dissemination, the ETAP collaborates with the RWHAP National Coordinating Resource Center, regional RWHAP AIDS Education and Training Centers, and other organizations to promote replication across the RWHAP community.

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The ETAP collaborates with the demonstration sites to develop a range of forthcoming dissemination and replication products, including implementation manuals, implementation toolkits, monographs, and spotlights. These products will provide background information, implementation guidance, and best practices for organizations interested in replicating efforts of the demonstration sites. Future publications will describe MSE methods and results, as well as notable adaptations, challenges/successes, and lessons learned, especially related to integrating behavioral health care and supporting clients amid COVID-19 and other 2020 social unrest. The demonstration sites will share their experiences with implementing the adapted MOCs and findings from local evaluations in future dissemination products.

Impact of the COVID-19 Public Health Emergency

In the United States, the COVID-19 Public Health Emergency (PHE) exacerbates persistent systemic inequities. According to the Centers for Disease Control and Prevention, interrelated social determinants of health like income, education, occupation, and access to health care put racial and ethnic minorities at increased risk of COVID-19–related morbidity and mortality [24]. Early evidence shows disparities in COVID-19 cases and deaths among people of color across the United States [25]; the rate of COVID-19 cases among Black or African American non-Hispanic persons is 2.6 times greater than the rate among White non-Hispanic persons [26]. In addition, the Centers for Disease Control and Prevention identifies immunocompromised individuals, including people with HIV, as being at increased risk for poor COVID-19 outcomes [27].

Following declaration of the COVID-19 PHE, stay-at-home orders, and social distancing guidelines, most demonstration sites closed their doors and ceased recruitment to mitigate viral spread. They continued to engage with existing clients via phone, text, or video meetings to the extent possible. In addition, demonstration sites reported an increase in basic needs among enrolled clients during the COVID-19 pandemic. Many clients continue to experience significant hardship due to the COVID-19 pandemic including job loss, housing instability, mental health concerns, and distress due to being sick or having friends and/or family members who are sick. By July 2020, all demonstration sites resumed some intervention activities and reopened for in-person or virtual engagement, depending on state, local, and institutional guidelines. However, most client interactions remain virtual, including evaluation data collection. Virtual engagement has required many demonstration sites to design new case management protocols and obtain Institutional Review Board or institutional approvals for the use of tools like Zoom videoconferencing software.

Results

The Black MSM Initiative continues to collect and synthesize robust evidence to examine proposed solutions to engage and retain Black MSM in HIV care. In response to the needs assessment, the ETAP offered TA and CBA on intervention adaptation, implementation, and evaluation. These efforts included developing guidance and definitions for the target audience and sample size; providing recommendations for recruiting eligible clients; developing and identifying measures for local evaluations; and supporting online platforms for sites with limited data collection infrastructure. Ongoing opportunities for TA include supporting retention and project engagement, boosting data and survey completion rates, and facilitating development of dissemination products that are cohesive, visually appealing, and accessible to a variety of audiences.

Sites continue to integrate behavioral health services through group, peer, and one-on-one support; facilitate relationships between behavioral health and clinical care teams; and reduce identified barriers to care. Teams have also contended with challenges related to the COVID-19 PHE as services moved into virtual spaces and clients experienced significant hardships related to job loss and housing instability. In particular, the COVID-19 PHE has made it difficult for some clients to sustain engagement in care when other survival needs took precedence. In response, sites have seen an uptick in social services needs and continue to work with community partners and clients to ensure those needs are met.

As of December 31, 2020, demonstration sites enrolled 809 clients in the MSE. Data collection will continue through December 2021.

Discussion

The study team began sharing early results from the MSE in December 2019 and expects to submit final results for publication in Spring 2022. In order to facilitate future replication by RWHAP providers and other organizations, the demonstration sites will create publicly available Implementation Manuals and Toolkits. NORC will also disseminate evaluation findings via future publications. As the Black MSM Initiative continues, the ETAP will increasingly support the sites with dissemination, replication, and sustainability activities.

The Black MSM Initiative fully supports the US Department of Health and Human Services' Ending the HIV Epidemic in the United States Initiative, which aims to reduce the number of new HIV infections by at least 90% in the next 10 years. In order to succeed, providers and programs will need to engage populations traditionally considered "hard to reach," like many people receiving RWHAP services. Findings and lessons learned from the Black MSM Initiative will expand the toolkit of solutions to support and retain Black MSM in HIV care, furthering the goals of the Ending the HIV Epidemic Initiative and the RWHAP.

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Conflicts of Interest

None declared.

References

1. HIV and African American Gay and Bisexual Men. Centers for Disease Control and Prevention. 2021 Sep 23. URL: https://www.cdc.gov/hiv/group/msm/bmsm.html [accessed 2021-12-28]
2. Lifetime risk of HIV diagnosis among MSM by race/ethnicity. Centers for Disease Control and Prevention. URL: https://www.cdc.gov/nchhstp/newsroom/2016/croi-2016.html#Graphics2 [accessed 2021-12-28]
3. Hess KL, Hu X, Lansky A, Mermin J, Hall HI. Lifetime risk of a diagnosis of HIV infection in the United States. Ann Epidemiol 2017 Apr;27(4):238-243 [FREE Full text] [doi: 10.1016/j.annepidem.2017.02.003] [Medline: 28325538]
4. Ryan White HIV/AIDS Program. Black/African American clients: HRSA's Ryan White HIV/AIDS Program, 2019. Health Resources & Services Administration. 2021. URL: https://ryanwhite.hrsa.gov/sites/default/files/ryanwhite/resources/population-factsheet-baa.pdf [accessed 2021-12-28]
5. Malebranche DJ, Peterson JL, Fullilove RE, Stackhouse RW. Race and sexual identity: perceptions about medical culture and healthcare among Black men who have sex with men. J Natl Med Assoc 2004 Jan;96(1):97-107. [Medline: 14746359]
6. Yang C, Krishnan N, Painter JE, Latkin C. The Association Between Disclosure of Same Sex Behavior to Healthcare Providers and PrEP Awareness Among BMSM in Baltimore. AIDS Behav 2019 Jul 21;23(7):1888-1892 [FREE Full text] [doi: 10.1007/s10461-019-02401-2] [Medline: 30666521]
7. Jones KT, Wilton L, Millett G, Johnson WD. Formulating the Stress and Severity Model of Minority Social Stress for Black Men Who Have Sex with Men. In: McCree DH, Jones KT, O'Leary A, editors. African Americans and HIV/AIDS. New York, NY: Springer; 2010:223-238.
8. Rooks-Peck CR, Adegbite AH, Wichser ME, Ramshaw R, Mullins MM, Higa D, Prevention Research Synthesis Project. Mental health and retention in HIV care: A systematic review and meta-analysis. Health Psychol 2018 Jun;37(6):574-585 [FREE Full text] [doi: 10.1037/hea0000606] [Medline: 29781655]
9. DeGroote NP, Korhonen LC, Shouse RL, Valleroy LA, Bradley H. Unmet Needs for Ancillary Services Among Men Who Have Sex with Men and Who Are Receiving HIV Medical Care - United States, 2013-2014. MMWR Morb Mortal Wkly Rep 2016 Sep 23;65(37):1004-1007 [FREE Full text] [doi: 10.15585/mmwr.mm6537a4] [Medline: 27657489]
10. Part F: Special Projects of National Significance (SPNS) Program. Health Resources & Services Administration. 2021 Oct. URL: https://hab.hrsa.gov/about-ryan-white-hivaids-program/part-f-special-projects-national-significance-spns-program [accessed 2021-12-28]
11. Wohl AR, Garland WH, Wu J, Au C, Boger A, Dierst-Davies R, et al. A youth-focused case management intervention to engage and retain young gay men of color in HIV care. AIDS Care 2011 Aug 09;23(8):988-997. [doi: 10.1080/09540121.2010.542125] [Medline: 21390879]
12. Hightow-Weidman LB, Smith JC, Valera E, Matthews DD, Lyons P. Keeping them in "STYLE": finding, linking, and retaining young HIV-positive Black and Latino men who have sex with men in care. AIDS Patient Care STDS 2011 Jan;25(1):37-45 [FREE Full text] [doi: 10.1089/apc.2010.0192] [Medline: 21162690]
13. Brothers United/The Damien Center. His Health. URL: https://www.hishealth.org/models-of-care/brothers-united-damien-center [accessed 2021-12-28]
14. Project Silk. His Health. URL: https://www.hishealth.org/models-of-care/project-silk [accessed 2021-12-28]

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15. National Framework for Quality Improvement in Behavioral Health Care. Substance Abuse and Mental Health Services Administration. 2012. URL: https://www.nasmhpd.org/sites/default/files/SAMHSA%20Quality%20Improvement%20Initiative.pdf [accessed 2021-12-28]
16. Hopson RK. Reclaiming Knowledge at the Margins: Culturally Responsive Evaluation in the Current Evaluation Moment. In: Ryan KE, Cousins JB, editors. The SAGE International Handbook of Educational Evaluation. Newbury Park, CA: Sage Publications; 2009:429-446.
17. Askew K, Beverly MG, Jay ML. Aligning collaborative and culturally responsive evaluation approaches. Eval Program Plann 2012 Nov;35(4):552-557. [doi: 10.1016/j.evalprogplan.2011.12.011] [Medline: 22284941]
18. Nelson-Barber S, LaFrance J, Trumbull E, Aburto A. Promoting culturally reliable and valid evaluation practice. In: Hood S, Hopson R, Frierson H, editors. The role of culture and cultural context: A mandate for inclusion, the discovery of truth, and understanding in evaluative theory and practice. Charlotte, NC: Information Age Publishing; 2005.
19. Creswell J. Research Design: Qualitative, Quantitative and Mixed Methods Approaches (3rd ed). Newbury Park, CA: Sage Publications; 2009.
20. Mertens D, Zimmerman HG. A transformative framework for culturally responsive evaluation. In: Hood S, Hopson R, Frierson H, editors. Continuing the journey to reposition culture and cultural context in evaluation theory and practice. Charlotte, NC: Information Age Publishing; 2014:275-287.
21. Hood S, Hopson RK, Kirkhart KE. Culturally Responsive Evaluation. In: Newcomer KE, Hatry HP, Wholey JS, editors. Handbook of Practical Program Evaluation. Hoboken, NJ: John Wiley & Sons; 2015.
22. Mertens DM. Transformative Mixed Methods. American Behavioral Scientist 2012 Feb 02;56(6):802-813. [doi: 10.1177/0002764211433797]
23. Creswell JW, Clark VLP. Designing and Conducting Mixed Methods Research (2nd ed). Newbury Park, CA: Sage Publications; 2011.
24. Health Equity Considerations and Racial and Ethnic Minority Groups. Centers for Disease Control and Prevention. 2020 Jul 24. URL: https://www.cdc.gov/coronavirus/2019-ncov/community/health-equity/race-ethnicity.html [accessed 2021-12-28]
25. Racial Data Dashboard. The COVID Tracking Project. 2021. URL: https://covidtracking.com/race/dashboard [accessed 2021-12-28]
26. COVID-19 cases, hospitalization, and death by race/ethnicity [Fact sheet]. Centers for Disease Control and Prevention. 2020 Aug 08. URL: https://www.cdc.gov/coronavirus/2019-ncov/covid-data/investigations-discovery/hospitalization-death-by-race-ethnicity.html [accessed 2021-12-28]
27. People with Certain Medical Conditions. Centers for Disease Control and Prevention. 2020 Oct 16. URL: https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html [accessed 2021-12-28]

Abbreviations

ART: antiretroviral treatment
CBA: capacity building assistance
CRE: culturally responsive evaluation
ETAP: Evaluation and Technical Assistance Provider
HAB: HIV/AIDS Bureau
HRSA: Health Resources & Services Administration
MOC: model of care
MSE: multisite evaluation
MSM: men who have sex with men
NORC: NORC at the University of Chicago
PHE: public health emergency
RWHAP: Ryan White HIV/AIDS Program
SPNS: Special Projects of National Significance
STYLE: Strength Through Youth Livin' Empowered
TA: technical assistance

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Protocol

A Self-management App for People Living With Mild Dementia (PRIDE): Protocol for a Pre-Post Feasibility Study

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Abstract

Background: With the rapid increase in the prevalence of dementia in the United Kingdom and beyond, the emotional, social, and economic burden on individuals, families, and health care services continues to rise. Currently, interventions that enable people living with dementia to better manage their condition and achieve a good quality of life are needed.

Objective: This study aimed to explore how the Promoting Independence in Dementia (PRIDE) app can promote and support the self-management of people living with mild dementia.

Methods: Feasibility of a pre-post study design incorporating the Reach, Effectiveness, Adoption, Implementation, and Maintenance framework will be studied. We will use up to 6 National Health Service Trusts as research sites and the Join Dementia Research website and accept self-referrals to recruit 60 to 90 people living with mild dementia. Participants will complete the PRIDE app intervention over 8 weeks with support from a dementia adviser facilitator. Measures exploring mood, physical well-being, and quality of life will be collected at baseline and at follow-ups at 3 and 6 months. Facilitators and National Health Service staff will be invited to complete interviews shortly after the intervention phase.

Results: Data collection began in June 2021 and is predicted to cease by the end of August 2022. Analysis of the quantitative measures will explore the impact of the PRIDE app on participants' independence, mood, and quality of life. Interview data will discuss participant experiences, how the use of the app affected them, and if it has the potential to be successfully implemented and maintained in dementia services.

Conclusions: This study will show the potential reach, effectiveness, and adoption of the PRIDE app intervention in the lives of people with mild dementia. The findings from this study will inform future research on the PRIDE app and any further developments to improve its effectiveness.

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KEYWORDS

dementia; protocol; self-management; quality of life; web-based; psychology; social; intervention; app

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Introduction

Background

Dementia currently affects an estimated 885,000 people in the United Kingdom [1]. Common symptoms include impaired ability and performance across multiple cognitive domains, such as memory, cognitive ability, and communication, which appear even in the early stages of the condition and can disrupt day-to-day activities [2-4].

Enabling people with dementia to achieve a high quality of life and live well independently has been highlighted as a priority in the United Kingdom [5]. With the increasing prevalence of dementia, providing people with the skills and understanding to manage their condition more effectively is now more important than ever. Given the progressive nature of dementia, self-management can support people with dementia and their families and optimize the level of autonomy and independence they are capable of and reduce excess disability [5]. Effective self-management of dementia requires individuals to understand their diagnosis and learn strategies to cope with the challenges that dementia brings [6]. This approach can help people retain independence and engage in daily activities and social relationships [6]. Self-management has the potential to benefit both the population with dementia and the health and social care sectors, as it supports individuals in maintaining their independence, increasing their overall well-being, and reducing the financial and social costs of paid and unpaid care [7]. Systematic reviews have suggested that psychosocial interventions have the potential to positively impact cognitive function, activities of daily living, and reduce disability [4].

Promoting Independence in Dementia (PRIDE), created by a team at University College London, is a psychosocial intervention for people living with mild dementia [8]. Delivered through a handbook and 3 facilitated sessions, PRIDE aims to improve the independence and quality of life of people with mild dementia and the friends and family that support them by enhancing decision-making, reducing stigma, and encouraging participation in mental, physical, and social activities. Elements of self-management were incorporated into PRIDE to encourage a person with dementia to take an active role in managing their condition [9]. For PRIDE, the selective optimization and compensation model was identified as a suitable approach, as it encourages giving the individual as much control as possible [9]. The selective optimization and compensation model proposes that people can manage their lives independently and successfully through these 3 regulations [10]. Selection focuses on identifying strengths and goals, optimization makes the best use of resources to maintain a person's independence, and compensation finds alternative ways or external aids to adapt and promote engagement [9,10]. As part of the PRIDE feasibility study, the research team transformed the information from the paper handbook into a web-based platform, the PRIDE app [8]. During this phase, patient and public consultations were conducted on the initial prototype app to support the adaptation from paper to a web-based format. For this study, researchers at the University of Nottingham (UoN) have worked closely with the app development company to further enhance this PRIDE app prototype, which is now ready to be piloted by participants. Feedback from this study will contribute to future developments in the app to increase its usability. In this context, the term *app* refers to the intervention being web-based, rather than a downloadable app, and accessible on computers, tablets, and mobile phones

This study will incorporate the Reach, Effectiveness, Adoption, Implementation, and Maintenance (RE-AIM) framework [11] to explore the effectiveness and impact of the PRIDE app on people living with mild dementia. The RE-AIM framework was designed to assess and evaluate health behavior interventions, better understand their impact, and improve the translation of research into broader health services [11]. It has been successfully incorporated into the design, reporting, and reviewing of other self-management–focused studies, trialing web- or app-based interventions [12,13]. One example was demonstrated by Yoshida et al [13] who incorporated RE-AIM to review app- and text messaging–based self-management interventions in diabetes. The reporting of factors varied between the dimensions within the 20 included studies. Factors of reach (inclusion and exclusion criteria, sample size, and participation rate), effectiveness (results of follow-ups), adoption (description of intervention location), and implementation (intervention duration and frequency) were reported in the included papers [13]. However, there was a lack of reporting on some factors, including representativeness (reach), attrition rates (effectiveness), description of staff who delivered interventions and the method used to identify and recruit them (adoption), cost of implementation measures (implementation), and cost of maintenance measures (maintenance). Overall, many gaps were identified in the reporting of RE-AIM criteria in mobile-based intervention studies, which need to be resolved through further research to improve the quality of reporting [13]. The RE-AIM framework is constructed using five dimensions:

1. Reach—whether an intervention found the target population
2. Effectiveness (or Efficacy)—the short- and long-term impacts of an intervention
3. Adoption—whether the target staff, settings, and individuals use the intervention
4. Implementation—whether the intervention has been delivered and implemented as intended
5. Maintenance—the degree to which an intervention is sustained over time and in the most cost-effective manner

Objectives

This protocol is written in accordance with the SPIRIT (Standard Protocol Items: Recommendations for Interventional Trials) checklist for reporting protocols [14]. The overall aim of the study is to explore how the PRIDE app can support the self-management of people living with mild dementia, using the RE-AIM framework: (1) the extent to which the PRIDE app has the capacity to reach people with mild dementia, (2) the effectiveness of the intervention, and (3) the adoptability of the intervention. The findings will contribute to future developments of the PRIDE app and inform a larger trial of its effectiveness.

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Methods

Ethics Approval

This study has been reviewed and approved by the Oxford Research Ethics Committee (21/SC/0066). All minor and substantial amendments will be reviewed by the UoN and Oxford Research Ethics Committee. All participants, supporters, and interviewees will provide written informed consent.

Study Design

We plan to conduct a pre-post feasibility study of the PRIDE app in people living with mild dementia. The RE-AIM framework [11] will enable us to identify key components for effective adoption, successful implementation, and sustained use of the PRIDE app, and identify potential barriers to the wider use of web-based psychosocial interventions for dementia.

The expected data collection period will be up to 12 months from the enrollment of the first participant. Participant recruitment will be carried out for up to 6 months, and follow-up will continue for a maximum of 6 months following the end of recruitment. All 5 RE-AIM framework dimensions will be explored in this study. However, as the intervention is not being implemented in normal routine care, the implementation and maintenance dimensions will not be assessed in depth and will instead be explored as secondary objectives.

Study Setting

Research activities, including participant recruitment and intervention delivery, will be carried out within secondary care National Health Service (NHS) Trusts. The study will start as a single NHS Trust site, using relevant services within their region, and then proceed to recruit up to 5 additional research sites through the National Institute for Health and Care Research's Clinical Research Network portfolio. To give sites more flexibility, the services they use are within their discretion. Any service with the capacity and where service users meet the inclusion criteria is eligible, and sites can use as many services as they have the capacity to. All intervention delivery and data collection activities will be conducted remotely, either on the web or via telephone or video calls.

Recruitment

There will be 3 possible pathways through which potential participants will be identified for recruitment in the study.

NHS Pathway

Participants will be recruited from NHS Services for people with dementia within participatory care trusts by their research and delivery team. The initial approach will be from a member of the patient's usual care team, who will obtain patients' consent to pass their details onto the research and delivery teams, who will then complete a prescreening telephone interview and the case report forms.

Recruitment from this pathway will be divided into group targets, such as age and ethnicity, to increase the diversity and representativeness of the end participant sample. For example, recruiting participants will be divided into the following age groups: >65 years, 65 to 74 years, 75 to 84 years, and >85 years. The initial target will be to recruit 15 participants from each age group. Similarly, with ethnicity, the initial target will be to recruit a minimum of 1 Black, Asian, or Minority Ethnic individual for every 3 White participants. It is hoped that by using group targets, the recruited participants will represent the full spectrum of people living with mild dementia in England. If the ethnicity of participants is not as diverse as possible, then sites will be asked to oversample BAME to maximize their representativeness in the final participant group.

Join Dementia Research

Join Dementia is a web-based self-registration service that enables volunteers with memory problems or dementia, carers of those with memory problems or dementia, and healthy volunteers to register their interest in participating in research. We will register the study at the site and set inclusion and exclusion criteria. Volunteers who register their interest in the study will be contacted by the UoN team, who will then conduct the prescreening telephone interview and complete the case report forms.

Self-referral

Participants will also be able to self-refer directly to the UoN team. Potential participants may become aware of the study through relevant local and national charities, patient organizations, and through the general promotion of the study through relevant organizations' newsletters, social media, mailing lists, and websites.

Participants

The minimum recruitment aim for the entire study is 60 participants living with dementia and a maximum of 90 participants. The recruitment target for individual NHS Trusts will be 10 to 15 people living with dementia. Each participant will have the option to participate with a supporter (a relative or close friend); however, this is not a criterion for inclusion. All participants will be assigned to the PRIDE app, and they will continue to receive their usual care outside of the study. The ability to provide informed consent is vital. As we are unable to collect this in person owing to the impact of the COVID-19 restrictions, informed consent forms and information sheets were provided to interested participants. Members of the research or NHS site teams will go through the documents over telephone or video calls with everyone to ensure that they understand these documents before signing up for the study.

Inclusion and Exclusion Criteria

The inclusion and exclusion criteria are presented in Textbox 1.

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Textbox 1. Inclusion and exclusion criteria.

Inclusion criteria

- Aged ≥18 years
- Self-report a medically confirmed diagnosis of mild dementia
- Able to provide informed consent and engage with the intervention
- Have access to Wi-Fi, a computer or tablet computer, telephone number, and email address.

Exclusion criteria

- Living in a care home or other institutionalized setting

Intervention

Overview

The PRIDE app is a web-based handbook that provides information, case stories, and support for self-management across a range of topics often affected by a dementia diagnosis. The topics covered within the app are Keeping Mentally Active, Keeping Physically Active, Keeping Socially Active, Making Decisions, Getting Your Message Across, Receiving a Diagnosis, and Keeping Healthy.

This study will be delivered by facilitators called dementia advisers and PhD students managing the study. The advisers will usually be NHS workers, ideally with some prior experience in dementia services, who volunteer to complete 2 mandatory training sessions and can commit to delivering the intervention to at least one participant. Training sessions, delivered by the PhD student, will last 20 to 45 minutes and introduce facilitators to the PRIDE program and the key sections of the PRIDE app. Following training, dementia advisers will be paired with the participants and will begin the PRIDE app intervention. There will be 3 one-to-one sessions, delivered remotely via video or telephone calls, which will last between 30 and 90 minutes each and will be spaced 2 to 4 weeks apart.

Session 1: Introduction

Lasting approximately 60 to 90 minutes, this session will provide participants with a brief overview of the aims of PRIDE, complete the core introductory session pages, encourage them to reflect on their daily activities, and introduce the PRIDE app.

The general content of the Introduction session is presented in Textbox 2.

Advisers will encourage participants to identify important aspects of their daily lives, discuss how to maintain or enhance the activities or routines they value, and identify new activities they might benefit from. Participants will choose 3 topics and plan at least one activity they want to work on, which will be reviewed in later sessions.

Textbox 2. General content of the introduction session.

1. Aim of Promoting Independence in Dementia (PRIDE)
2. Complete PRIDE profile
3. Core topics
   - Finding a balance
   - People and connections
   - Keep going
4. Personalize topics—participants will choose 3 main topics to focus on
5. Familiarization with the PRIDE app
   - Log-in process
   - Adding social contacts
   - Activity plans

Session 2: Review

The PRIDE app has a built-in review page for participants to complete alongside their advisers, and all key discussion points and progress will be recorded. Advisers will encourage participants to reflect on their progress and create or amend specific plans for activities or actions that will promote their independence. Choices and activities may be refined according to the participants' and supporters' experience of implementation and any needs that may have arisen since the first session. Barriers that may have prevented progress will be discussed, and the solutions will be explored. New activity options may also be set within the lifestyle domain topics. Emphasis will be

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placed on encouraging participants to continue implementing their plans between their sessions.

Session discussions will include the following:

1. Progress since the last session and providing positive feedback
2. What worked or helped them achieve goals and what hindered
3. Overcoming barriers
4. Satisfaction with current plans and if any changes are wanted

Session 3: Final

In the final session, participant progress will be reviewed again, and a maintenance plan exploring how PRIDE could continue to support them after the study will be developed to encourage long-term change.

Session discussion will include the following:

1. Progress since the last session
2. How PRIDE could continue to help them in the future—PRIDE's "Plan, do, review" steps are a practical approach to help them continue their everyday activities
3. Encouragement to maintain a normal routine and social contact and use the steps when planning new activities

Plan, Do, Review

A principal technique of the PRIDE program is plan, do, review, and advisers will incorporate the technique to support participants in creating specific plans for activities or actions that will promote their independence. The participant and supporter will put their plans into practice between sessions and record their progress on the PRIDE app. To encourage participants, advisers will do the following:

1. Help them think about the action they would like to take or the activity they would like to do that would promote their independence
2. Support them in planning activities they would like to work on based on their topic choices, such as where their activity will take place, when they can begin their action plan or start making changes, and how they can do things in different ways
3. Explain how to record activities between sessions

Evaluation Outcomes

This study will record quantitative and qualitative data to collect all aspects of the RE-AIM framework that we will explore. Table 1 outlines how each RE-AIM concept will be explored through analyses of quantitative and qualitative data.

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Table 1. How Reach, Effectiveness, Adoption, Implementation, and Maintenance (RE-AIM) dimensions will be addressed in the study.

RE-AIM dimension	Definition	How addressed in the study
Reach	The absolute number, proportion, and representativeness of individuals contacted and those who are willing to participate in the intervention and reasons given as to why or why not choose to participate in the study.	Recruitment and characteristic figures (identification): eligibility rate, characteristics of eligible people approached (age, gender, and ethnicity), participation rate, and representativeness of participants; app use data, participant characteristics, and interviews (engagement): Did participants engage regularly with the PRIDE[a] app? What were the characteristics of those who used the app and why? The baseline to 6-month participation figures.
Effectiveness	Does the PRIDE app positively impact important individual outcomes, such as mood and quality of life and whether there are any potential negative effects?	Change of pre- and postintervention scores: CASP-19[b], IADL[c], EQ-5D-5L, GDS[d], EID-Q[e], and global change measure.
Adoption	The absolute number, proportion, and representativeness of settings and the target patient group and intervention facilitators who are willing to initiate a program and why.	Postintervention qualitative interviews with participants: How did participants feel they benefited from using the app and why or why not? How did the app affect their lives; for example, impact on daily activities and independence? Did they need additional help to use it? app use: How much did participants use the app and for how long? Which elements were most useful? participant retention rate: How many participants continued the study after baseline? How many completed the 3 intervention sessions? interviews with facilitators and clinical staff: How would the app fit into the existing services? How well was it delivered? Who is best to deliver it? How will the app be paid for?
Implementation	The extent to which an intervention may be delivered as intended and whether individuals would use the intervention.	Postintervention qualitative interviews with participants, facilitators, and clinical staff (information on delivery, barriers for delivery, and implementation): the ease of using the app, whether workarounds were needed, and if so, why? How would the app fit into the existing services? Who is best to deliver it? How will the app be paid for?
Maintenance	The long-term effects of a program on outcomes (usually 6 or more months) and the extent a program becomes part of routine practice.	Postintervention qualitative interviews with participants, facilitators, and clinical staff: How would the app fit into the existing services? Who is best to deliver it? How could the app be integrated into the existing care system?

[a]PRIDE: Promoting Independence in Dementia.

[b]CASP-19: Control, Autonomy, Self-realization, and Pleasure Scale-19.

[c]IADL: Lawton Instrumental Activities of Daily Living Scale.

[d]GDS: Geriatric Depression Scale.

[e]EID-Q: Engagement and Independence in Dementia Questionnaire.

Sample Size

For a pre-post comparison, 62 participants will be needed to detect a moderate effect size (Cohen *d*=0.4 and correlation=0.4) using 80% power at a 2-tailed .05 significance level. We will approach up to 200 people with mild dementia and aim to recruit a minimum of 60 and a maximum of 90 participants for the study, depending on the resources available, each with an optional supporter. These figures represent the total number of participants with dementia across all recruitment sites.

Quantitative Outcomes

Overview

Quantitative measures will be collected at baseline, 3 months, and 6 months from participants and supporters. For participants, the outcomes collected will help to evaluate the effectiveness of the PRIDE app and its impact on their quality of life. Measures completed by supporters will explore the impact of the PRIDE app on their mood, quality of life, and perceived change in their relatives or friends with dementia. Measures will be completed either on the web or on paper, with the final decision left to the participant or the supporter. All participants and supporters will have the option to complete their questionnaires with the help of a researcher, who will be either a PhD student or a member of their local research team, and this will be done remotely over telephone or video calls. As measures will be completed remotely, the researchers will be reliant on the participants or supporters to communicate any difficulties encountered when completing them.

People Living With Dementia

Control, Autonomy, Self-realization, and Pleasure Scale-19: Baseline and 3 Months and 6 Months After the Intervention

The Control, Autonomy, Self-realization, and Pleasure Scale [15] has 19 items, each measured on a 4-point Likert scale (0=never, 1=not often, 2=sometimes, and 3=often). Items will include “I feel left out of things” and “I enjoy the things that I do.” Scores range from 0 to 57, with higher scores indicating higher levels of well-being [16]. The total and individual item scores will be recorded and used for the analysis.

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EuroQoL Quality of Life Questionnaire-5 Domains, 5 Levels: Baseline and 3 Months and 6 Months After the Intervention

The EuroQoL Quality of Life Questionnaire-5 Domains, 5 Levels [17] measures 5 domains of quality of life: mobility, self-care, usual activities, pain or discomfort, and anxiety or depression. Each domain has 5 levels: no problems, slight problems, moderate problems, severe problems, and extreme problems. The levels are scored from 1 to 5 to indicate increasing severity. The participant indicates which level is most appropriate for their situation and provides a self-rated health score on the vertical visual scale, which ranges from 0 to 100 (where 100 is the best health). Individual item and health scores will be recorded and used in the analysis.

Lawton Instrumental Activities of Daily Living Scale: Baseline and 3 Months and 6 Months After the Intervention

The Lawton Instrumental Activities of Daily Living Scale [18] contains 8 domains that assess an individual's ability to complete tasks necessary for independent living, such as preparing meals and maintaining a clean house. Each domain will be scored either 0 or 1, and a summary score of 0 (low functioning) to 8 (high functioning) will be used in the analysis. The measure is particularly good at identifying how a person is functioning at present and for identifying improvement or deterioration over time.

Geriatric Depression Scale: Baseline and 3 Months and 6 Months After the Intervention

The Geriatric Depression Scale (short form) is a 15-item measure that can be self-reported or read out to the participants if required. Each item has a "yes" or "no" answer, and the response indicating depression is scored as a point. A score of 0 to 5 is normal, a score >5 suggests depression, and a score of ≥10 indicates depression [19]. The total score will be used in the analysis.

Engagement and Independence in Dementia Questionnaire: Baseline and 3 Months and 6 Months After the Intervention

The Engagement and Independence in Dementia Questionnaire has 26 items that assess the degree to which a person with dementia feels independent and engages socially with those around them. It reflects the multifaceted nature of independence in dementia and includes items related to remaining active, decision-making, reciprocity, and connectedness to others. Each item is measured on a 5-point Likert scale (0=not true at all, 4=true nearly all the time) and was developed for a sample of older adults with dementia [20]. The total and individual item scores will be recorded and used for the analysis.

Global Change (Self-rated): 3 Months and 6 Months After the Intervention

The global change measure will ask participants about any change in their well-being and sense of independence since the baseline. The questions will be "Compared with 3/6 months ago when you started in the PRIDE study, how would you rate your general well-being now?" and "Compared with 3/6 months ago when you started in the PRIDE study, how independent do you feel now?" A 5-point ordinal scale (1=much better, 3=no change, and 5=much worse) and (1=much more independent, 3=no change, and 5=a bit less independent) will be used to measure change.

Supporters (Informal Carers)

General Health Questionnaire: Baseline and 3 Months and 6 Months After the Intervention

The General Health Questionnaire [21] has 12 items that assess an individual's current state and asks whether it differs from their usual state. Each item is rated on a 4-point scale (less than usual, no more than usual, rather more than usual, or much more than usual). Two popular scoring methods are used: General Health Questionnaire (0-0-1-1) and Likert (0-1-2-3), each providing a total score for analysis. The total and individual item scores will be recorded for the analysis. For both methods, the wording of the items means that reverse scoring is not required. The severity level is indicated by how high the score is.

EuroQoL Quality of Life Questionnaire-5 Domains, 5 Levels: Baseline and 3 Months and 6 Months After the Intervention

As with the participants, individual item and health scores will be used in the analysis.

Global Change (Proxy-Rated): 3 Months and 6 Months After the Intervention

The global change measure asks supporters about their perceived change in participants' well-being and sense of independence since baseline. The questions will be "Compared with 3/6 months ago when you started in the PRIDE study, how would you rate the general well-being of your relative/friend now?" and "Compared with 3/6 months ago when you started in the PRIDE study, how independent do you feel your relative/friend is now?" A 5-point ordinal scale (1=much better, 3=no change, and 5=much worse) and (1=much more independent, 3=no change, and 5=a bit less independent) will be used to measure change.

Qualitative Outcomes

The experiences and perspectives of the study participants and facilitators will be explored through postintervention interviews. Up to 20 participants and dyads will be invited to discuss and reflect on their experience of using the PRIDE app. Additional interviews will be conducted with up to 10 facilitators and 5 senior NHS service staff to explore their experiences of delivering the intervention and how the PRIDE app could be implemented into existing services. Interviews and analysis will be conducted by a PhD student managing this study.

Participants and their supporters, if taking part, will be invited to attend an interview at 8 to 10 weeks, shortly after the completion of the intervention. The final number of interviewees will be determined based on the data saturation. Participants will be asked at the point of obtaining consent and again, when invited, whether they are comfortable with being contacted to complete the interviews. Because of the COVID-19 pandemic, interviews are likely to be conducted remotely, via telephone or video calls. They will be audio recorded and will last for a maximum of 45 minutes.

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Additional facilitator and service staff interviews will also be conducted remotely and audio recorded. An email to the research sites will ask volunteers to complete short interviews, which will discuss their facilitation experiences. Through snowball sampling, we aim to interview 5 additional service staff members who could provide feedback on the potential implementation and maintenance of the PRIDE app intervention. Both interviews will last for a maximum of 30 minutes.

The research team developed semistructured interview schedules. This approach will be adopted to ensure that topics relevant to the study's aims are discussed. Consideration will be given as to how the order of questioning could improve the interview content and whether prompts will be needed to further expand the answers provided. However, the interview schedule will be flexible enough to allow for the discussion of any additional topics mentioned by the participants, which may be beneficial to the research aims if explored.

For participant interviews, questions will explore their quality of life, experiences of using the intervention, and the impact of the lifestyle changes encouraged by the intervention. The themes covered will include the following:

1. Acceptability of the intervention and whether they enjoyed using the PRIDE app
2. Experience of using the intervention and its impact on daily life
3. Factors that may mediate or moderate the impact or effectiveness of the intervention
4. Likelihood of using the skills or behavior changes in the future
5. Barriers to and facilitators for continued use of the behavior changes encouraged through the intervention

For facilitator interviews, the themes covered will include the following:

1. Barriers to and facilitators for the delivery of the intervention
2. Skills and competencies required for delivery
3. Ease of delivery

For clinical staff, the themes covered will include the following:

1. How the PRIDE app intervention could fit into the existing care model
2. Would it be a financially viable intervention in the current health care system

Data Analysis

Quantitative and qualitative data will be analyzed to provide insight into whether participants have adopted the intervention in their daily lives, whether they would be willing to continue to use the intervention, and whether it has had a positive effect on their quality of life and dementia self-management. Data will be analyzed anonymously using Stata 17 (StataCorp). As patients will be recruited from various study sites and measured at baseline and follow-up, all measures will be summarized by site and across the measuring time. Outcome data will first be explored through descriptive analysis, with the mean (SD) for normally distributed variables, median (IQR) for skewed variables, and frequency (%) for each level of categorical variables.

To evaluate the efficacy of the PRIDE app, multilevel linear regression modeling will be conducted to quantify the change estimates (95% CI) from baseline to the first and second follow-ups for normally distributed outcomes. The skewed outcome, if any, will be transformed for multilevel modeling. To understand the reach of the PRIDE app, analyses will be conducted on eligibility percentage—the number of potentially eligible participants approached, participation rate, and demographics—to understand who was approached and how representative the final participant sample is. Participant retention rate figures will show how well the intervention was adopted by participants and whether the PRIDE app could be a suitable long-term intervention for people with dementia. Analyses of pre- and postintervention outcome measures will reveal whether the PRIDE app was effective in improving the respective dimensions measured.

From the PRIDE app use data, we will be able to analyze the number of times participants accessed the app, which topics were most popular, and the duration of app use (using log-in and log-off times). These figures will help us understand whether participants actively engaged with the PRIDE app and how well the app was adopted in their daily lives. Missing outcome information will be examined, and its influence on each change score estimate will be checked using data with missingness imputed using multiple imputations with an analytic model used to impute missingness, assuming the missingness mechanism is Missing-At-Random.

Qualitative interview data will be pseudonymized and transcribed verbatim by an NHS-approved transcription service. Participants' comments will be anonymized to maintain confidentiality. The data will be analyzed through thematic analysis by a PhD student. Thematic analysis has been chosen because of its flexible application; appropriateness for the study's methodology and research aims; and ability to identify, examine, and report recurring and unexpected themes found within the interviews [22].

A deductive approach to thematic analysis will be incorporated, thereby enabling more focused analysis, with the themes identified driven by the research aims and topics that need to be explored. The following analytical process will be applied [22]:

- Stage I—familiarization of data: the audio recordings will be transcribed and read multiple times to ensure familiarization. Initial ideas for codes are noted in the margin of the transcript.
- Stage II—generating initial codes: initial ideas will be coded and data extracts relevant to these codes collated.
- Stage III—searching for themes: ideas for themes will be developed in the initial coding and extraction stages. Additional data relevant to these themes will be collected. The study's research aims will be kept in mind during the development of the themes.
- Stage IV—reviewing themes: a diagram will be created and reviewed, showing the relationship among themes, data extracts, and data as a whole.

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- Stage V—defining and naming themes: a further thorough analysis of themes will be conducted, with clear definitions and names developed for each theme.
- Stage VI—producing the report: appropriate codes, themes, and data extracts will be finalized for analysis, with these suited to the research aims.

Monitoring

The occurrence of an adverse event as a result of participation in this study is not expected and therefore will not be routinely recorded by the UoN team. However, individual sites will be able to follow local procedures to monitor and record any events. The UoN team will be informed of any adverse events affecting the study participants.

Results

The analysis of measures will explore the impact of the PRIDE app on participants' independence, mood, and quality of life. Pre- and postscores on outcome measures will show any statistical result of the potential effect of participation on individuals. Overall mean scores will help provide insight into the impact of app use across all participants and supporters, providing an indication of whether the PRIDE app could benefit people living with mild dementia and their supporters. With regard to the RE-AIM elements, reach will be understood through the participation rate and demographics, which will show the characteristics of the participants recruited and how well they have been retained. Pre- and postoutcome scores will support potential effectiveness. Adoption will be explored using the participant retention rate and use data gathered from the PRIDE app. This will help us understand whether the participants actively engaged with the app and how well it was adopted in their daily lives.

Interview data will discuss participants' experiences of taking part in the study, whether they enjoyed using the PRIDE app, and if they felt it had had a positive effect on their well-being and independence. The questions for the facilitator and service staff will focus on the ease of session delivery, barriers to successful delivery, and whether the PRIDE app could be implemented and maintained within the existing health care system. Themes that are generated through the thematic analysis process [22] will complement the quantitative data in terms of the RE-AIM elements, in particular, the adoption, implementation, and maintenance of the PRIDE app by participants and dementia services. Data collection began in June 2021 and is predicted to cease by the end of August 2022. As of January 2022, the study has recruited 4 NHS sites and 23 participants and supporters. Data analysis is yet to begin, and the study findings are anticipated to be published in Spring 2023. All data will be analyzed anonymously.

Discussion

Overview

This RE-AIM study will explore the PRIDE app psychosocial intervention to support self-management in people living with mild dementia. Through quantitative and qualitative data, we will evaluate its reach, effectiveness, and adoptability in the independence and quality of life of the participants and their supporters before and after the intervention. Additional data collected from intervention facilitators and clinical staff will help us to better understand how the PRIDE app could be successfully implemented and maintained in existing dementia services.

In some cases, the process of seeking a diagnosis can be prolonged due to service delivery, diagnosis stigma, and more recently, the impact of the COVID-19 pandemic. Regarding the PRIDE app study, this might mean that by the time of diagnosis, some individuals would be ineligible to participate. Therefore, the inclusion criteria ask for mild dementia but place no exact assessment figures. All potential participants will complete a prescreening interview where the relevant researcher will access their suitability and complete a case report form. We recognize that completing measures remotely may result in feelings of embarrassment or reluctance if participants experience issues and do not feel confident about asking for support. However, steps will be taken to provide as much support as possible to the participants throughout their involvement in the study. This will include follow-up contact if measures have not been completed within the timeframe to ensure that participants are not experiencing any issues. Further research on self-management interventions may benefit from including those with mild cognitive impairment and determining whether they have an effect on individuals' self-management of the condition and any reduction in the risk of developing dementia.

Limitations

Our study is small scale, with no control group, which reduces the generalizability and reliability of the findings. A small sample size also means that we are not able to demonstrate the individual needs of different dementias. However, if the results indicate potential feasibility and effectiveness, it will be important to conduct a larger trial with a greater number of participants and a control group to validate any initial findings and explore any differences among dementia diagnoses. A patient and public consultations group will be established to provide ongoing input from people and families living with dementia. Members will provide feedback on interview schedules, dissemination materials, and how best to disseminate the findings to relevant people. A paper discussing the development process of the PRIDE app is in progress and will include the original development and more recent modifications.

Conclusions

Dementia affects every aspect of an individual's life. Equipping them with relevant knowledge and support facilitates greater self-management and enables people living with dementia and their families to have a better quality of life. This study will be the first to explore whether the PRIDE app intervention can have a positive impact on the self-management of people living with mild dementia through a pre- and postoutcome study design. The knowledge generated from this RE-AIM study will help with the continuing development of the PRIDE app and other similar interventions and in the design of future studies. The data will also help us understand the potential clinical implications of the PRIDE app and how it might be best integrated into existing services.

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Authors' Contributions

ARL wrote and prepared the manuscript for publication. BG provided knowledge and input for statistical measures and outcome analyses. JR contributed to explaining the Reach, Effectiveness, Adoption, Implementation, and Maintenance framework. OM and MO provided significant feedback on the manuscript and aided in the development of content.

Conflicts of Interest

None declared.

References

1. Wittenberg R, Hu B, Barraza-Araiza L, Rehill A. Projections of Older People with Dementia and Costs of Dementia Care in the United Kingdom 2019-2040. London: Care Policy and Evaluation Centre, London School of Economics and Political Sciences; 2019.
2. Dementia Guide. NHS England. URL: https://www.nhs.uk/conditions/dementia/ [accessed 2022-01-26]
3. Toms GR, Quinn C, Anderson DE, Clare L. Help yourself: perspectives on self-management from people with dementia and their caregivers. Qual Health Res 2015 Jan;25(1):87-98. [doi: 10.1177/1049732314549604] [Medline: 25192761]
4. McDermott O, Charlesworth G, Hogervorst E, Stoner C, Moniz-Cook E, Spector A, et al. Psychosocial interventions for people with dementia: a synthesis of systematic reviews. Aging Ment Health 2019 Apr;23(4):393-403. [doi: 10.1080/13607863.2017.1423031] [Medline: 29338323]
5. Prime Minister's challenge on dementia 2020. GOV.UK. URL: https://www.gov.uk/government/publications/prime-ministers-challenge-on-dementia-2020 [accessed 2022-07-15]
6. Mountain GA, Craig CL. What should be in a self-management programme for people with early dementia? Aging Ment Health 2012 Feb 24;16(5):576-583. [doi: 10.1080/13607863.2011.651430] [Medline: 22360274]
7. Whitlatch CJ, Orsulic-Jeras S. Meeting the informational, educational, and psychosocial support needs of persons living with dementia and their family caregivers. Gerontologist 2018 Jan 18;58(suppl_1):S58-S73. [doi: 10.1093/geront/gnx162] [Medline: 29361068]
8. Csipke E, Moniz-Cook E, Leung P, Yates L, Birt L, Walton H, et al. Feasibility and acceptability evaluation of the Promoting Independence in Dementia (PRIDE) intervention for living well with dementia. Int Psychogeriatr 2021 Jun;33(6):601-614. [doi: 10.1017/S1041610220001386] [Medline: 32847643]
9. Yates L, Csipke E, Moniz-Cook E, Leung P, Walton H, Charlesworth G, et al. The development of the Promoting Independence in Dementia (PRIDE) intervention to enhance independence in dementia. Clin Interv Aging 2019;14:1615-1630 [FREE Full text] [doi: 10.2147/CIA.S214367] [Medline: 31571842]
10. Freund AM, Baltes PB. Life-management strategies of selection, optimization and compensation: measurement by self-report and construct validity. J Personality Social Psychol 2002 Apr;82(4):642-662. [doi: 10.1037/0022-3514.82.4.642]
11. Glasgow RE, Vogt TM, Boles SM. Evaluating the public health impact of health promotion interventions: the RE-AIM framework. Am J Public Health 1999 Sep;89(9):1322-1327. [doi: 10.2105/ajph.89.9.1322] [Medline: 10474547]
12. Palermo TM, de la Vega R, Dudeney J, Murray C, Law E. Mobile health intervention for self-management of adolescent chronic pain (WebMAP mobile): protocol for a hybrid effectiveness-implementation cluster randomized controlled trial. Contemporary Clin Trials 2018 Nov;74:55-60 [FREE Full text] [doi: 10.1016/j.cct.2018.10.003] [Medline: 30290276]
13. Yoshida Y, Patil SJ, Brownson RC, Boren SA, Kim M, Dobson R, et al. Using the RE-AIM framework to evaluate internal and external validity of mobile phone-based interventions in diabetes self-management education and support. J Am Med Inform Assoc 2020 Jun 01;27(6):946-956 [FREE Full text] [doi: 10.1093/jamia/ocaa041] [Medline: 32377676]
14. Chan A, Tetzlaff J, Altman D, Laupacis A, Gøtzsche PC, Krleža-Jerić K, et al. SPIRIT 2013 statement: defining standard protocol items for clinical trials. Ann Intern Med 2013 Feb 05;158(3):200-207 [FREE Full text] [doi: 10.7326/0003-4819-158-3-201302050-00583] [Medline: 23295957]
15. Hyde M, Wiggins RD, Higgs P, Blane DB. A measure of quality of life in early old age: the theory, development and properties of a needs satisfaction model (CASP-19). Aging Ment Health 2003 May;7(3):186-194. [doi: 10.1080/1360786031000101157] [Medline: 12775399]
16. Stoner CR, Orrell M, Spector A. The psychometric properties of the control, autonomy, self-realisation and pleasure scale (CASP-19) for older adults with dementia. Aging Ment Health 2019 May 22;23(5):643-649. [doi: 10.1080/13607863.2018.1428940] [Medline: 29356567]
17. EQ-5D-5L. EuroQol. URL: https://euroqol.org [accessed 2020-05-14]

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18. Lawton MP, Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living. Gerontologist 1969 Sep 01;9(3 Part 1):179-186. [doi: 10.1093/geront/9.3_part_1.179]
19. Yesavage JA, Sheikh JI. Geriatric Depression Scale (GDS). Clin Gerontologist 2008 Oct 25;5(1-2):165-173. [doi: 10.1300/J018v05n01_09]
20. Stoner C, Orrell M, Spector A. Psychometric properties and factor analysis of the engagement and independence in dementia questionnaire (EID-Q). Dement Geriatr Cogn Disord 2018 Sep 4;46(3-4):119-127. [doi: 10.1159/000488484] [Medline: 30179862]
21. Goldberg DP, Gater R, Sartorius N, Ustun TB, Piccinelli M, Gureje O, et al. The validity of two versions of the GHQ in the WHO study of mental illness in general health care. Psychol Med 1997 Jan 01;27(1):191-197. [doi: 10.1017/s0033291796004242] [Medline: 9122299]
22. Braun V, Clarke V. Using thematic analysis in psychology. Qual Res Psychol 2006 Jan;3(2):77-101. [doi: 10.1191/1478088706qp063oa]

Abbreviations

NHS: National Health Service
PRIDE: Promoting Independence in Dementia
RE-AIM: Reach, Effectiveness, Adoption, Implementation, and Maintenance
SPIRIT: Standard Protocol Items: Recommendations for Interventional Trials
UoN: University of Nottingham

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Protocol

Lessons From the COVID-19 Pandemic to Improve the Health, Social Care, and Well-being of Minoritized Ethnic Groups With Chronic Conditions or Impairments: Protocol for a Mixed Methods Study

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Abstract

Background: The COVID-19 pandemic has inequitably impacted the experiences of people living with ill health/impairments or from minoritized ethnic groups across all areas of life. Given possible parallels in inequities for disabled people and people from minoritized ethnic backgrounds, their existence before the pandemic and increase since, and the discriminations that each group faces, our interest is in understanding the interplay between being disabled AND being from a minoritized ethnic group.

Objective: The overarching aim of the Coronavirus Chronic Conditions and Disabilities Awareness (CICADA) project, building on this understanding, is to improve pandemic and longer-term support networks, and access to and experiences of care, services, and resources for these underserved groups, both during the pandemic and longer term, thereby reducing inequities and enhancing social, health, and well-being outcomes.

Methods: This mixed methods study involves three "sweeps" of a new UK survey; secondary analyses of existing cohort and panel surveys; a rapid scoping review; a more granular review; and qualitative insights from over 200 semistructured interviews, including social network/map/photo elicitation methods and two subsequent sets of remote participatory research workshops. Separate stakeholder cocreation meetings, running throughout the study, will develop analyses and outputs. Our longitudinal study design enables the exploration of significant relationships between variables in the survey data collected and to the assessment of changes in variables over time, including consideration of varying pandemic contexts. The qualitative data will provide more granular detail. We will take a strengths and assets–based approach, underpinned by the social model of disability and by intersectional considerations to challenge discrimination. Our exploration of the social determinants of health and well-being is framed by the social ecological model.

Results: The CICADA project was funded by the Health and Social Care Delivery Research (HSDR) Programme of the United Kingdom (UK) National Institute for Health and Care Research (NIHR) in March 2021 and began in May 2021. Further work within the project (84 interviews) was commissioned in March 2022, a substudy focusing on mental health, specifically in

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Northeast England, Greater Manchester, and the Northwest Coast of the United Kingdom. Data collection began in August 2021, with the last participants due to be recruited in September 2022. As of January 2022, 5792 survey respondents and 227 interviewees had provided data. From April 2022, the time of article submission, we will recruit participants for the substudy and wave 2 of the surveys and qualitative work. We expect results to be published by winter 2022.

Conclusions: In studying the experiences of disabled people with impairments and those living with chronic conditions who come from certain minoritized ethnic groups, we are aiming for transformative research to improve their health and well-being.

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KEYWORDS

racism; minoritized ethnic group; disabled; social care; intersectional; pandemic; social networks; public health; migrant; COVID-19

Introduction

Background and Rationale

The particular challenges faced by vulnerable groups during the COVID-19 pandemic, including people from minoritized ethnic backgrounds and people with underlying health conditions/impairments [1-7], are now well recognized. In the United Kingdom, 17.2% of the population were recorded as disabled in 2020, but represented 59.5% of all UK COVID-19 deaths up to November 2020 [8]. Similarly, although 13% of the UK population are from minoritized ethnic backgrounds, they represented 33% of critically ill COVID-19 patients between February and August 2020 [5,6]. This was partly because chronic conditions such as diabetes and cardiovascular disease are disproportionately prevalent in some minoritized ethnic groups [9] as well as being risk factors for serious illness or death from COVID-19 [10]. Moreover, perceived discrimination and perceived lower socioeconomic status are also associated with a greater COVID-19 health risk [11]. These findings show the importance of considering different intersecting factors that compromise good health outcomes. As shown in Textbox 1, the pandemic has inequitably impacted the experiences of people living with ill health/impairments or from minoritized ethnic groups across all areas of life and not only in relation to COVID-19 illness [1,2,11].

Textbox 1. Inequities for minoritized ethnic groups, and those with chronic conditions/impairments, increasing their risk of poor pandemic health and well-being outcomes.

1. Increased risk of isolation, abuse, or neglect, **and poor access to informal emotional and well-being support** due to national pandemic responses, stigma, changed activities, priorities, attitudes of others, a state of "normalized absence, pathologized presence," among other factors [12].

2. Inequitable formal treatment, support, and care from attitudinal, structural, policy, cultural, linguistic, communication, and economic barriers, leading for example to difficulties implementing recommended COVID-19 avoidance strategies, vaccine mistrust, and risk of severe illness.

3. Psychosocial factors raising COVID-19 risks, reducing the capacity to cope with social, economic, and psychological pandemic impacts, including worries about people "back home."

4. Unemployment/reduced income (eg, zero-hour contracts, overrepresentation in the unskilled service sector, "no recourse" to welfare).

Given parallels in the inequities for disabled people and people from minoritized ethnic backgrounds, the increase in these inequities since the pandemic, and the discrimination that each group faces, we were interested in understanding the interplay between being disabled AND being from a minoritized ethnic group. This has been a neglected area in research and policy. Certainly before COVID-19 vaccination programs were rolled out, there was more focus on the COVID-19 mortality rates of discriminated-against groups than on their general health and well-being during the pandemic. Moreover, international concern about pandemic-induced mental health issues has tended to take a population-wide focus, sidelining the especially poor pandemic-related mental health experienced by some people from different minoritized ethnic groups [13] (for an example, see [14]).

Most peer-reviewed published articles on chronic conditions/impairments and the pandemic have been survey- or audit-based considerations of reduced patient footfall for, or access to, consultations. In a global COVID-19 survey, 17% of 548 respondent rheumatologists estimated that 25% of their patients had no access to telehealth [15] and therefore little clinical support. It is increasingly recognized worldwide that the rapid move to remote health care has accentuated inequities for some. Problems with pandemic telehealth services are currently under scrutiny in the United Kingdom and have been experienced by Coronavirus Chronic Conditions and Disabilities Awareness (CICADA) study clinical team members [16], although remote consultations also have recognized benefits.

Interviews in Italy with representatives from seven voluntary organizations that specialized in disability highlighted bureaucratic challenges, and shortfalls in advice, coordinated care plans, and interagency coordination to compensate for reduced services in the pandemic [17]. Similar issues have been reported in the grey literature. Systemic prepandemic failures were perceived by respondents to a European Federation of Neurological Associations global survey to have led to the collapse of normal neurology care pathways during the pandemic [18]. Health care services for people with rare and complex conditions have fared especially badly according to the European H-CARE Survey [19]. In the United Kingdom, the organization National Voices collated 2020 data from a range of third-sector pandemic surveys specializing in disability

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and health conditions, reporting issues with mental health; managing symptoms and/or deteriorating health and finances; access to medication, food, health, and social care; impacts on carers; and problems with accessing or understanding information [20].

There are several examples in peer-reviewed journals of small surveys internationally that have shown how reduced access to treatment negatively impacts patients' symptomatic control, including cases of Parkinson disease [21], migraine [22], rheumatology [23], and chronic refractory neuropathic pain [24], leading to an increased reliance on support networks [25].

Even within these studies, there is very little recognition of the way the particular challenges faced as a result of belonging to a minoritized ethnic group might intersect with, or be compounded by, the challenges faced by having underlying health conditions/impairments. Minoritized ethnic groups with a chronic condition or impairment are more likely to die from COVID-19 [3-8,10,25] in the historical context of poorer health outcomes more generally [4,7,26-28]. The unifying explanation is ingrained racism. Twenty-five percent of doctors responding in a US survey reported that preexisting socioeconomic issues caused by structural racism, combined with institutional racism, when added to pandemic constraints on care, made it even more challenging to care for Black patients with asthma than others in the pandemic [29]. Another US survey showed that pandemic telehealth was used by Black patients more than by White patients. This was attributed to the need of Black patients to compensate for prior health and health care disparities caused by systemic racism [30].

Aim and Research Questions

Given the current evidence gaps and the pressing need for these to be filled, the broad questions underlying this research project are therefore: (1) Are the pandemic-related issues faced in different aspects of daily living summative, additive, or broadly similar in people from minoritized ethnic groups who also have chronic conditions/impairments as compared to people belonging to either one of these two categories? (2) What can we learn about how different people successfully draw on different assets, coping strategies, and other strengths or developed solutions to deal with these issues in different pandemic contexts? (3) Which intersecting social categories are the most significant in shaping these answers? (4) How can a systematic, living map of existing evidence contribute to understanding the pandemic-relevant experiences of having an impairment/chronic condition and belonging to a minoritized ethnic group?

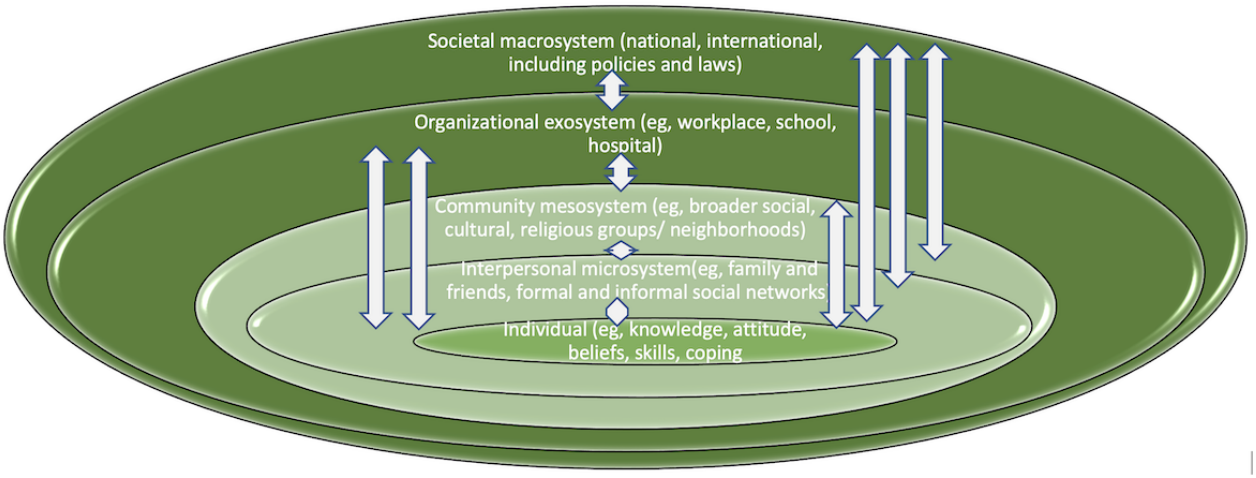
In aiming to answer these questions, we will undertake primary and secondary research to improve our understanding of the pandemic-related issues faced by minoritized ethnic groups with chronic conditions/impairments in different aspects of daily living, and the different assets, strengths, and solutions they have drawn on. To better understand their particular experiences, we compare their perspectives with those of people self-identifying as being of White British ancestry, with and without chronic conditions/impairments, and people from minoritized ethnic groups with no chronic conditions/impairments. We will use our findings to help to mitigate inequities, and improve their experiences; support networks; and access to and experiences of care, services, and resources. We plan to achieve this by developing and informing evidence-based formal and informal strategies, guidelines, recommendations, and interventions for health and social care policy and practice. These outputs are intended to improve social, health, and well-being outcomes for underserved groups, both during the COVID-19 pandemic and in the longer term.

Theoretical Underpinnings

Theoretical Framework

We will take a strengths and assets–based approach, underpinned by the social model of disability and by intersectional considerations to challenge discrimination [31,32]. Our exploration of the social determinants of health and well-being is framed by the social ecological model [33,34] (Figure 1).

Figure 1. The social ecological model (adapted from Bronfenbrenner [35]); arrows show the bidirectional flows of interactions between levels as a complex system.



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Disability Models

Medical or biopsychosocial models of disability have led to the continued disenfranchisement and marginalization of people with physiological impairments, through the conflation of pathoanatomical diagnostic criteria with disability itself [35,36]. In other words, the two are inseparable and the person with the diagnosis is only seen as dysfunctional. This leads to ableism (discrimination in favor of nondisabled people) [37] and disablism, defined as "discriminatory, oppressive, or abusive behaviors arising from the belief that disabled people are inferior to others" [38] (page 9).

The CICADA study resists the use of these deficit-focused disability models, instead taking as its starting point the social model of disability because of its currency, usefulness in driving transformative outputs, and relevance to much-needed revisions in continuing discriminatory statute and law [39]. This continued discrimination persists despite the United Nations Convention on the Rights of Persons with Disabilities [40]. In the social model, impairments, as physiological problems of the body, are decoupled from disability, which results from exclusionary social oppression and prejudices [37]. Society, by accommodating impairments through the removal of iniquitous barriers to inclusion, can enable the full participation of all, across every area of life.

While important, the social model has limitations that are the topic of much discussion [41,42]. For example, Siebers [41] argues for: (1) more complex understandings of embodied variation and (2) more dynamic problematization of the liminal spaces occupied by lived reality than afforded by the social model. Arendt's [42] criticism of the social model is that more account needs to be taken of the ways people with impairments internalize and make meaning of their lived experiences. We will therefore also draw on alternative nondeficit models in our analyses. Our overall interest is in how individuals with chronic conditions or impairments experience and make meaning of the world through their embodiment within it at the intersection with various other simultaneously and variably interacting social factors.

Intersectionality

Rather than separately considering the multiple social categories of "identity, difference, and disadvantage" [43] (p.171) such as gender, racial/ethnic minoritization, disability, and occupation, we consider them as coexisting interacting systems of oppression. In other words, they work together (are mutually constitutive) under discriminatory institutional and structural conditions to create [44-47] lower levels of physical and mental health, poor access to quality health care, and poorer health outcomes [48-51]. Citizenship status adds an infrequently considered further important layer of complexity that we explore in the CICADA study [50]. There is a particular lack of research on the ways that health outcomes are shaped for undocumented migrants through their structural construction as "illegal" [51] within a hostile environment [52] with "no recourse" to welfare and housing support.

We consider both individual experiences of day-to-day discrimination and the wider context. We use the term "minoritized ethnic groups" to emphasize the stigmatization and oppression that a racialized society bestows on particular ethnic groups as racialized "others" [53], rather than to necessarily ascribe to them a "minority" status. An alternative term, "racialized communities," is also used in some study documents to indicate the nature of this oppression.

Shifting identities among people who have recently migrated, in the face of racism, can include the racialization process of "becoming White." This process tends to be neglected in the health literature [54] and is one that we also consider. We hypothesize negative consequences for recent immigrants of Arab or Central and East European ancestry, who may experience the tensions of being symbolically included in a White ethnic category but are excluded from many of its benefits [54], in a manner that is often invisible because of the lack of its exploration.

Through considerations such as these, built into the study design, intersectionality theory will allow us to develop complex nuanced insights into differences, while minimizing the risks of essentializing some combinations as inherently problematic or considering the minoritized experience as homogenous.

Social Ecological Approach

Intersectionality conceptualizes the ways an individual's social interactions are shaped by their multiple subject positions (eg, as a female, recent migrant, disabled person). The social ecological model [33,34] highlights the ways this individual is positioned at the center of a system of mutually influencing sets of social determinants, incorporating their personal, community, regional, and national (policy and society) ecosystems of norms and practices. Embodied experiences of migration, citizenship, chronic conditions, and impairments are necessarily intersectional with areas of potential discrimination and oppression across the different levels of the social ecological model. Hence, there is a need for a range of comparisons and involvement of multiple stakeholders in our study to ensure that any potential strategies and recommendations we develop will apply both within and across the different levels [55]. This also fits with the new UK National Health Service (NHS) tiered Integrated Care Plan [56], which is relevant as the CICADA study is set in the United Kingdom.

Intersectional interactions across the levels of the social ecological model are in constant flux, which Bronfenbrenner [57] represented by the chronosystem in development of his original model. Recognizing the importance of these changes over time, our study is longitudinal. Our work is also underpinned by the Consolidated Framework for Implementation Research (CFIR) [58]. This is an amalgamation of various implementation theories that target different levels of the social ecological model, and we use it to comprehensively explore the feasibility of implementation of our recommendations and other outputs. The CFIR is easy to operationalize, flexible (the user selects relevant themes from a pool of 39), and facilitates actionable findings across multilevel implementation contexts.

Assets-Based Approach

Our intersectional and critical disabilities approaches facilitate the interrogation of our data for participant assets and strengths

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as well as the barriers they face. For example, small cross-sectional analyses suggest that some chronic conditions and impairments may confer resilience to mental health or well-being effects of the pandemic [59,60]. In a UK analysis of chronic fatigue during the pandemic, Reddit reported more severe symptoms in some people but also more accessible opportunities to interact (through online video calls) [61]. Strengths/assets-based approaches involve a holistic focus on both personal strengths (internal factors such as resilience and external factors such as material assets) and social and community networks. This opens up spaces for individuals who experience disadvantage to be viewed as important partners in the development of change processes rather than problems to be acted upon. Our approach falls under a branch of assets-based work sometimes termed "positive deviance." This looks for positive outcomes in the face of adversity, as well as behavior and community development needs, where further support could develop or add to assets and strengths. We are mindful to ensure this does not reduce the need for state intervention (we will take pains not to deproblematize contexts or suggest that improvements should be a community, rather than a policy, responsibility). A strengths-based approach does not try to take the focus away from the structural causes of inequities [62] but rather aims to empower communities and individuals [62] in meaningful and sustainable ways. It is based on salutogenic theory [63], which positions people as coproducers of health, rather than consumers of health services [64], and recognizes the need to consider that individuals have intersectional identities. This approach has greater transformative potential than deficit-focused approaches [65].

Methods

Ethics Approval

The study has Institute of Education, University College London, Research Ethics Approval (UCL IoE REC 1372, and amendment 1450 Covid-19; Data protection registration number: Z6364106/2020/06/24) and will follow FAIR Open Science principles of accountability and transparency [66]. We also have NHS ethics approval to recruit participants at NHS sites (IRAS: 310741, CPMS ID: 51755–CICADA recruitment).

Overall Design

We will use a longitudinal mixed methods approach to develop a rich understanding of study participants' mental and physical health, coping strategies, access to resources, and informal and formal social and health care support experiences. We will explore relevant assets and strengths for well-being enhancement, and examine variations through the lens of intersectionality. Analyses, outputs, dissemination, and implementation plans will be cocreated with key stakeholders.

Our design (Figure 2) includes three "sweeps" (ie, repetitions) of a new UK survey, secondary analyses of existing cohort and panel surveys, a rapid scoping review, and a more granular review. We will incorporate qualitative insights from 210 semistructured interviews, including network/map/photo elicitation methods, and two subsequent sets of remote participatory research workshops that roughly coincide with survey sweeps two and three, designed instead of second and third sweep interviews to minimize participant burden. Stakeholder cocreation meetings will run throughout the study and are key to implementation of outputs. Policymakers such as those within Public Health England (now the UK Health Security Agency), and practitioners such as clinicians and social support workers specify an urgent need for participatory work with minoritized ethnic groups [67]. Our embedded social network analysis will provide important insights on how to improve information channels, routes into health/social care and support, resilience to stress, and postdisaster recovery [13,65]. We will include consideration of new service delivery models, some of which are already planned to continue beyond the pandemic (eg, telemedicine [68,69]). Our longitudinal study design enables us to explore significant relationships between variables in the survey data we collect and the changes in these variables over time. We will include consideration of varying pandemic contexts such as lockdowns, restrictions, and their relaxation. The qualitative data will provide more granular detail.

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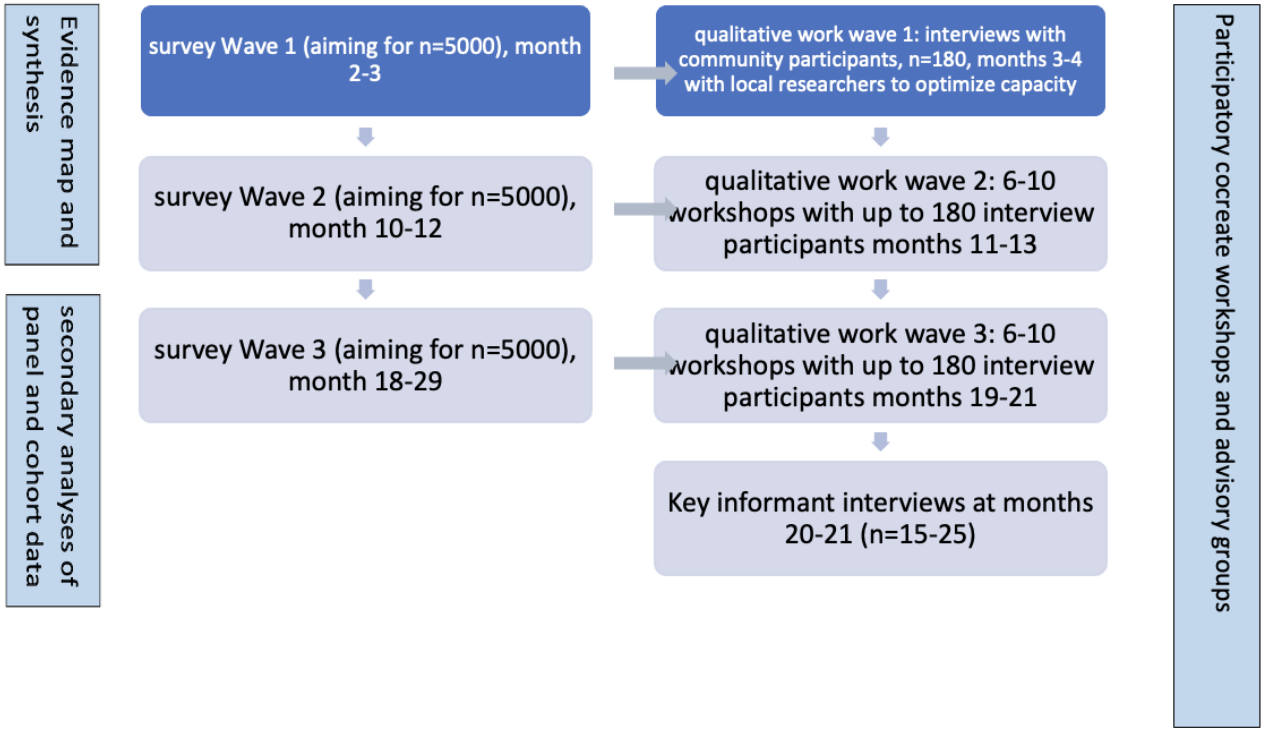
Figure 2. Flowchart for the design of the CICADA study.



Primary Data Collection

Topic Guides for the Survey, Interviews, and Research Workshops

The lefthand column of Table 1 shows the eight topics that run throughout the study. These topics have informed the reviews, topic guides, research workshops, and surveys. Instruments included within our surveys are shown in the righthand column of Table 1 as an example; they are mostly validated by their developers in different newly migrated populations, and thus are particularly appropriate for use in this study.

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Table 1. Eight topics that run through all parts of the study, with the corresponding survey instruments/items.

Topics across all study stages that structure the reviews, topic guides, and surveys	Survey instruments/items
Intersectionalities	A range of demographic variables [70,71]
Behavioral responses to COVID-19 risk-reduction measures, including vaccination	"Control of life" (including COVID-19–related aspects)
Access to resources, support, care, vaccines, including digital transformation, service innovations	QOCS-ID[a] [72], Vulnerability Assessment Framework [73] for care needs, UK government SAGE group–recommended questions
Social networks	Developed from the Close Persons questionnaire [74] to contextualize other topics
Mental and physical well-being/quality of life as primary outcomes	WHOQOL-BREF-ID[b] [72].
Coping	Including tolerance to uncertainty, positive appraisal style, attitudes to being ill (WHO[c] ADS[d] [72]), pandemic health and mental health consequences (Global Mental Health Assessment Tool [75]), why they arose, and how issues can be mitigated
Local and regional differences in responses linked to policies/ interventions and associated impacts	Apart from within-survey analysis, we will match respondents' area code of postcode with area-level (1) ONS[e]-registered COVID-19 cases, hospitalizations, and deaths; and (2) Google data on social distancing adherence
Vaccines, future policies	Free-text comment boxes

[a]QOCS-ID: World Health Organization Quality of Life-Disability.

[b]WHOQOL-BREF-ID: World Health Organization Quality of Life.

[c]WHO: World Health Organization.

[d]ADS: Anxiety and Depression Scale.

[e]ONS: Office for National Statistics.

Primary Outcomes

The primary online survey outcomes are: (1) formal/informal care measured using de novo questions and the World Health Organization (WHO) Quality of Care and Support-Disability questionnaire (QOCS-ID) at 4, 10, and 16 months; (2) quality of life measured using the World Health Organization Quality of Life tool (WHOQOL-BREF-ID) at 4, 10, and 16 months; (3) control of life measured using the "control of life" validated questionnaire at 4, 10, and 16 months; (4) physical and mental health measured using the WHO Anxiety and Depression Scale (ADS) at 4, 10, and 16 months; the Vulnerability Assessment Framework at 10 and 16 months; and the Global Mental Health Assessment Tool at 10 and 16 months; and (5) social networks measured using an adapted Close Persons questionnaire (for online work) at 4, 10, and 16 months in the online survey and as part of the semistructured interview (using closed questions, open questions, photographs taken by participants to represent their networks without any personal identifying information, and maps drawn of networks).

Secondary Outcomes

Secondary outcomes include fear of death measured using the Templer Death Anxiety Scale [76] at 10 and 16 months by online survey. Thematic qualitative data from survey free text, interviews, and workshops will be analyzed, including (1) patient experiences of health and social care, and other forms of formal and informal support during the pandemic, and their perspectives on the impacts on their health; (2) consideration of the impacts of their identity (eg, disabled, from a specific ethnicity, from a low-income background) on these experiences; (3) consideration of their beliefs (health beliefs, COVID-19–related beliefs, vaccination beliefs) and how these affect other themes; and (4) consideration of coping mechanisms, and strategies and assets used in relation to their access to and use of resources, services, and support as this affects their health and well-being.

Surveys will vary by sweep. Key outcome and exposure variables that we expect to change over time will be measured in all three sweeps to study trajectories. Theoretically stable concepts (eg, tolerance to uncertainty, demographic characteristics) will be measured only in one sweep. Key topics may be added to sweeps 2 and 3 that have been identified through our other work.

Review

Aims and Process

Our two-stage review work will: (1) create a systematic (living) map to summarize the pandemic-relevant experiences of living with impairments/chronic conditions and/or being from a minoritized ethnic group across the topics listed in Table 1, and (2) undertake an in-depth analysis and synthesis on specific aspects determined according to the map.

This review will ground the research in current evidence and generate themes that can be incorporated in the primary data collection design.

In both stages, two reviewers will independently screen titles, abstracts, and full texts against inclusion criteria, and extract data. They will compare a subset of this work to check for consistency as quality control, with any disagreements to be resolved by a third reviewer. We will assess risk of bias using Cochrane-recommended checklists, also noting the provenance

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and publication status of sources. Data extraction will be managed in EPPI-Reviewer software and will reflect the inclusion criteria and the designated aims of the review.

Inclusion Criteria

The review inclusion criteria, using a modified SPIDER (Sample, Phenomenon of Interest, Design, Evaluation topics, Research source, Setting) [77] framework are summarized in Textbox 2.

The outcomes and the focus of the granular review will depend on the evidence available, and gaps in the evidence will be highlighted for future study. Reporting will follow PRISMA (Preferred Reporting Items of Systematic Reviews and Meta-analyses) guidelines. The review is registered with Prospero (CRD42021262590).

Textbox 2. Inclusion criteria according to the SPIDER framework.

***S**ample:* People with any chronic condition/impairment and/or from a minoritized ethnic group within their country of residence (see "Setting" below).

***P**henomenon of **I**nterest:* Lived experience during the pandemic, social networks, and relationships between intersectional variables and health and social care outcomes. Testimony from informal and formal carers may be included where it: (1) directly relates to the topics, and (2) considers the perspective of people with a chronic condition/impairment and/or from a minoritized ethnic group.

***D**esign:* All study designs.

***E**valuation topics:* The topics listed in Table 1.

***R**esearch source:* All sources of research evidence, both peer-reviewed and preprint/grey literature, augmented by data from tweets (given a fast-moving pandemic-responsive field) and websites of relevant public bodies/agencies.

Setting: International studies (although the setting of our study is the United Kingdom, it is important to develop a broader knowledge that may be transferable to the United Kingdom, or may provide context, useful models, or lessons to be learned).

Filter restrictions are:

Date: Peer-reviewed articles published since 2000, grey literature since January 2019, and other sources since 2020 to balance currency of the data with the identification of a broad view of developing issues.

Language: English.

Data Analysis

Reporting of the data will depend on the types of included studies (eg, descriptive statistics, narrative synthesis, and diagrams). We will perform subgroup analyses where appropriate.

Use of Existing Data Sets

We will undertake secondary analysis of data relevant to the topics in Table 1 from several existing data collections for triangulation and complementary insights. This includes the ActEarly City Collaboratory Consortium's [78] pandemic surveys of families in Bradford and East London, and pandemic surveys within nationally representative cohort studies curated at the Centre for Longitudinal Research (CLS), University College London. None of these data sets has our overall focus but they do include some relevant questions. The overlapping variables between the ActEarly, CLS data, and our own survey will enable us to compare and assess data quality across surveys.

To place our primary survey data within existing and prior national contexts, we will perform our secondary quantitative analyses for three periods: before the pandemic (up to January 1, 2020), prior to relaxation of the winter-spring 2021 lockdown in the United Kingdom (up to May 12, 2021), and thereafter (up to autumn 2022). Should the data enable, we will also subdivide the third period to match the dates of the three sweeps of our primary survey. Since these are secondary analyses, we will be mindful of and discuss relevant biases, and will contextualize the results according to the evolution of the pandemic.

Three-Sweep Primary Survey

Survey Sampling and Recruitment

The primary survey is online and will collect quantitative and qualitative (free text) data. Survey sampling across the four nations of the United Kingdom will be open to any adult living in the United Kingdom, but purposively targeted via selected sites and networks to encompass all conditions/impairments and organizations supporting minoritized ethnic groups, including recently arrived and undocumented migrants. Sampling will not depend on individual patient data such as those that could be obtained via electronic health records to ensure we include people who are self-diagnosed or who perceive themselves to have a different diagnosis to the one held in the electronic record, as well as participants not registered with primary care. We will be mindful of the different biases this may cause, and will collect data on whether or not a diagnosis exists and whether the person agrees with this diagnosis for in-depth understanding.

The three survey sweeps will be evenly spaced over 15 months, with each sweep open for 1 month. Recruitment will predominantly involve distribution of a survey link via social media, and specialist and national networks (such as academic, health service, third sector), as well as mailing lists and large databases of adults interested in health research across the United Kingdom. We recognize that this strategy, being nonrandomized, will be biased such as toward those already interested in research participation or who are active users of third-sector sites and have online access. We will make available print copies for community groups involving participants lacking internet access. We will compare respondent demographics to

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whole population estimates where possible to explore representativeness (although formal data are limited).

Survey Numbers and Power

Our new longitudinal survey will enable a description of the trajectories of key variables and outcomes and the links between them. Free-text data will also be analyzed for patient experience. The survey will not be used to test a particular treatment or focus on a single effect.

In our basic structural equation modeling (SEM), we have six core latent variables (factors) per sweep: (1) quality of life, (2) control of life, (3)access to care, (4) coping mechanisms, (5)mental health, and (6)social networks.

Considering statistical power in SEM [79], the required sample size increases with the number of latent variables, but at a decreasing rate (ie, the required sample size difference between a model with one vs two latent variables is larger than that between a model with three vs two latent variables). The required sample size also decreases strongly as the loadings on latent variables increase (ie, the magnitude of the association between latent and observed variables, where values below 0.9 are generally taken to show a confounding effect). Moreover, the power increases as the number of items (questions) used to measure each latent variable increases.

In terms of our study, each latent variable will be measured by several items (the average number being more than 8). In a worst-case scenario with average loadings of around 0.5 and an item missingness of 20% (as suggested from ActEarly work), a sample size of 800 per subgroup per sweep will yield useful analyses. We have four main subgroups (ie, self-identifying as minoritized ethnicities with a chronic condition/impairment, minoritized ethnicities without a chronic condition/impairment, of White British ancestry with a chronic condition/impairment, and of White British ancestry without a chronic condition/impairment). Using these four comparator groups enables us to fully understand the nature of relationships between different variables and the influence of chronic condition/impairment and minoritized ethnic group categories on each, both separately and combined. Thus, the required sample size is calculated at 800×4=3200, although we aim for 5000 for a more robust sample [79].

Survey Analysis

A descriptive statistical summary will be updated with each sweep. More in-depth analysis, using SPSS, R, Stata, or Python, will exploit all three sweeps of the data, with the following research questions:

1. How do outcomes (resource access, formal/informal care, quality of life, control of life, physical and mental health, social networks) and outcome trajectories differ by sample subgroups (minoritized group, condition/impairment, citizenship status) and intersectional combinations? This cuts across all three of our overarching research questions.
2. To what extent can COVID-19 prevalence and pandemic adherence to social distancing at the area level explain differences in outcomes and outcome trajectories across subgroups and in terms of intersectionalities (as a proxy for pandemic contextual factors)? This relates to our third overarching research question.
3. How do the outcomes interrelate within and across survey sweeps, and how does this differ across groups of the sample and in terms of intersectionalities? This cuts across all three of our overarching research questions.

For research questions 1 and 2, we will exploit the longitudinal nature of the data using latent growth modeling (LGM), with multiple group analysis, varying different combinations to consider the effect of intersectionalities on outcomes. Depending on geographical coverage and the numbers recruited, the LGM estimation for research question 2 could be carried out at the within-area level to examine the causal impact of the change in COVID-19 prevalence and pandemic social distancing across the sweeps on each key outcome, under the assumption that this is exogenous. We will examine the plausibility of this assumption and detail possible sources of endogeneity. This will be important for policy given our unique subgroups focus. For example, our data could help clarify why specific groups may find it unfeasible to adhere to recommended behavioral responses. For research question 3, we will estimate a developmental cascade model, including all three data sweeps and key variables, to explore how the key variables are associated with one another, both within survey sweeps and over time. We will fit the LGM models using SEM; this offers useful tools for dealing with missing data due to nonresponse and attrition.

The *social network support module* of our model will consider how respondents are connected to others who provide support to the respondent (eg, through relations such as friendship, kinship, exchanges, activities) [80,81]. Characteristics such as the participant network's size, composition, and resources available will result in a latent "network capital" variable created through measurement analysis within the SEM as a novel contribution. These network metrics will be used to provide a descriptive presentation of the network(s) and any changes over time.

Missing Data

We will require completion of almost every question on every page for participants to proceed so that we can undertake the association analyses required. This means that there should generally be no *missing* items in any measures. However, this requirement may lead to *completion attrition*, with respondents giving up and logging off. We will try to mitigate this possibility in the design, which will allow participants to save responses and return to the survey later, and the survey will be developed and piloted with 30 people from our advisory group and patient advisory group (PAG). There is also the risk of attrition *between* sweeps. Participants will be asked to provide an email address upon enrolling online. The RedCap online secure system that we will use will automatically recontact them for sweep 2/3 follow-up questionnaires (with reminders). This automatic process makes for efficient and secure second and third sweep recruitment to reduce the risk of missing respondents. Lotteries appear effective in some online surveys [82] and we are including a £50 (~US $63) Amazon voucher as an incentive given at random.

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To handle missing data, and address panel attrition and item nonresponse, we will use modern methods, including full information maximum likelihood; multiple imputation with chained equations that produce unbiased estimates under assumptions of missing at random (ie, missingness dependent on observable data only) and multivariate normality; and pattern mixture models that address missing not at random (ie, missingness dependent on unobserved data), assuming correct model specification [83]. These techniques, under certain assumptions, ameliorate loss of statistical power due to missing data and possible biases due to systematic missingness.

Interviews

Interview Sampling Frame

Our interview sampling frame follows an intersectional approach that allows us to consider and compare assumed homogeneity: (1) across chronic conditions/impairments irrespective of heritage, and (2) across ancestries irrespective of chronic condition/impairment. The aim of this is to tease out intersectional factors and heterogeneity. To achieve this, we will use a purposive quota sampling approach. At analysis, the focus may switch to other commonalities such as shared barriers or enablers in accessing health and social care resources.

Possible attrition between sweeps (up to 20% based on ActEarly experience) may require further recruitment if theme/pattern saturation is not reached, or early saturation may lead us to more theoretical sampling. The main interview inclusion criteria are summarized in Textbox 3.

We recognize the heterogeneity within these groups, and the way these categories are laden with assumptions such as with regard to multimorbidities, the concept of being British, the ancestry of people who are born in particular countries, and the apparent essentialization of specific groups. However, to ensure in-depth data while keeping sample numbers to a feasible level, we decided to use these problematic categorizations as tools to better organize our research so that we can then unpack and critique them [84]. The groups have been chosen to reflect recent migration waves to the United Kingdom (albeit that some people from these groups may have lived in the United Kingdom for decades) and to capture those groups most at risk of hospitalization or death from COVID-19.

The main interview exclusion criteria are: (1) student migrants, as they are likely to have structured educational institution support; and (2) residents of detention centers/closed facilities linked to national migration policies (eg, new asylum-seekers/refugees, displaced or trafficked persons), as these are deemed complex cases with specific considerations.

Textbox 3. Inclusion criteria for the interview.

- Any condition/impairment, including self-diagnosis, that chronically affects daily activities; the condition should have lasted for at least 12 weeks and have no defined endpoint. These will be categorized in an adaptation of the UK Government Statistical Service harmonized data recommendations as: mental, mobility, stamina/breathing/fatigue (including heart problems), hearing/vision loss, developmental/intellectual, and food-related. These categorizations will then be analyzed.
- People living in the United Kingdom who were born in, or whose parents were born in, Arabic, Central and Eastern European, South Asian, or sub-Saharan African countries, with people of self-defined White British ancestry as comparators.
- Aged 18+ years
- Self-identification of migrant status (with recruitment aiming to cover the range of people whose status is categorized as: undocumented, on temporary visas, with indefinite leave to remain, or British citizens).

Interview Sites

We sample from five interview sites within England for maximal sampling diversity in migrant population density, proportion of EU to non-EU migrants, and reasons for migration to enhance transferability, which we will explore against our four-nations survey findings. This is important as we only sample in England for qualitative work due to differences in the devolved nations' responses to the pandemic and their health and social care systems. Sites for our qualitative research are London, Southeast England, Northeast England, West Midlands, and Yorkshire. While this means that some of our findings may be more relevant to England, we expect the principles to be similar across the four nations, and we will consider this in our reporting and outputs.

Recruitment to Interviews

We will recruit interview participants from advertisements/links distributed through a range of platforms and networks, as well as through local lay coresearchers. We will rely on participant self-identification of citizenship status and condition/impairment. Posters, advertisements, and snowball sampling will target those who lack resources or technology to be recruited via online messages; they can contact us by telephone or email. Collaborators will provide recruitment and data collection support through organizations such as Born in Bradford (BiB) in Yorkshire, a long COVID center [85] in Gateshead, the Bromley-by-Bow community center in East London, and migrant charities in London and Canterbury.

Interview Process

Respondents can choose to have their interviews by phone, remote video methods, or face to face, depending on extant pandemic restrictions. Our PAG leads will help train lay community members to undertake some interviews locally at our five sites, supported by the core team. Interviews will be recorded. Attention will be given to making the interviews fully accessible and inclusive, and all researchers will be vigilant to the participant needs such as requiring frequent breaks.

All potential participants will be informed about the study in plain English (read to them if needed) and told that interviews will be in English by default. Where a participant feels more

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comfortable being interviewed in another language, if a researcher fluent in that language is available, this will be arranged. Translated and accessible study documents will be provided if required to ensure that participants are able to give fully informed consent.

We will probe in interviews for the same topics as covered in the survey (Table 1). For social networks, we will discuss the data from the following participant preinterview tasks: (1) a brief questionnaire, data from which we will translate into network "maps" using Network Canvas software; and (2) photographs and sketch-maps of the local area where people live, and the places significant to their health care and social interactions, using their smartphones or disposable cameras that we will provide. These data will also be thematically analyzed. This ethnographic approach facilitates a safe social space to communicate difficult issues and has been used to explore migrant resettlement [86].

Research Workshops and Cocreation Meetings

Design

The two research workshops and four cocreation meetings will all be participatory and designed for participants to work in equitable partnership. They will be led by a core team member and a PAG member. They will aim for outputs relevant to the "real world" that will maintain participant voices and will ensure the research outputs can be implemented. Each session will last approximately 4 hours (2 hours if held remotely).

Research Workshop Recruitment, Sampling, and Process

The make-up/number of research workshop groups per sweep (2 and 3) will be determined by considering any typologies (patterns in intersectionalities and outcomes) from sweep 1 data. Participants will be recruited from sweep 1 interviews.

Sweep 2 workshops will discuss scenarios, or structured vignettes, shown as short videos recorded by community members reading scripts. Content will be developed from sweep 1 data into a pandemic-relevant story, with accessible transcripts provided in advance. Discussion will consider changes from previous findings. Sweep 3 workshops will follow a similar pattern with updated vignettes. We will also use participatory scenario planning [87], a policy tool whereby participants are encouraged to explore alternative futures, their impacts, and relevant action plans. To ensure inclusivity, we will work with our PAG group on workshop accessibility and will offer repeat interviews as an alternative.

Cocreation Meeting Recruitment, Sampling, and Process

Cocreation meeting participants will include patients and carers (our aim is that they will be representative of our interview participants), as well as key stakeholders in their support and care. They will be recruited via professional or dedicated community networks such as government and policy, welfare, social and health care staff migrant, settlement, and racialization-specific services; third-sector organizations; and community leaders. We will aim for two representatives from each of these groups per workshop, thus with approximately 20 people in each meeting. We will be assisted in this process by our PAG.

The cocreation meetings will involve discussion of findings from each data sweep and their cocreated translation into outputs to feed into the next stages or final study outputs, depending on what is appropriate at the time each workshop is held. To enable inclusion and stimulate discussion and outputs, we will use arts-based and participatory approaches such as miro.com, Collaborative Poetics materials [88], and other cocreation tools [89,90].

Key Informant Interviews

To explore how outputs can be implemented in policy and practice, 15-25 interviews (up to 5 per site) will be conducted with key informants. These will be identified from earlier phases of the study. These are likely to be drawn from the same categories as our cocreation meetings.

Recruitment plans and topic guides will be informed by our other findings and cocreated in our cocreation meetings, and with members of our advisory groups.

Analysis of Interviews and Workshops

Deductive framework analysis of the workshop, interview, photo, and key informant data will be used for general dissemination and policy-relevant themes that can be mapped to the survey for added insight. We will also remain open to adding inductive themes throughout the analysis. Data collection and analysis will be concurrent for quick outputs and to test emerging and discordant themes.

Interview data will also undergo Keyword in Context (word frequency–based) analysis to compare specific constructs. We will undertake discourse and narrative analyses on a data subset, produced from participant pairs, matched on features identified as important in earlier analysis. Coding, using NVivo, will be undertaken by the core team, with feedback from the advisory groups and cocreation meetings. We will follow good practice for transparency, quality, and rigor. Anonymized data will be archived for secondary analyses.

PAG Involvement

We have an active PAG; its members will take part in the cocreation meetings, as well as advising on all stages of the study. They will be supported to be coauthors in any publications we coproduce. We have two PAG coapplicant coleads. We will adhere to the seven principles of patient engagement [91], namely: shared purpose, respect and accessibility, representativeness, roles and responsibilities, capacity and capability for engagement, transparency in communication and documentation, and continuity and sustainability.

Overall Data Synthesis and Dissemination

We will use cascaded dissemination at each data sweep, tailored to our key audiences, that emphasize practical solutions and implementation. The dissemination plan will be determined with our PAG and through our cocreation meetings.

Overall synthesis will provide an executive overview for easy assimilation by policymakers and practitioners. This will indicate where changes to health/social care policy and practice are likely to be most effective. Synthesis will be results-based; that is, tabulation will be derived from data analyses, with table

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columns for themes/topics and rows for each distinct set of quantitative and qualitative data. Some data will need to be transformed (quantified or qualitized) for tabulation, such as network graphs. We will interrogate the tabulated data using anchor questions based on the PerSPectif (Perspective, Setting, Phenomenon of interest/problem, Environment, [optional Comparison], Time/timing, Findings) framework [92] (eg, informed by patterns of data convergence/divergence).

An overview of findings and ideas for outputs will be presented to participating communities more widely via collaborator platforms, to give them the opportunity to reflect upon and interrogate researchers' interpretations and analysis of the data. Findings and ideas for outputs will also be distributed through trusted community channels such as places of worship, trusted religious leaders, community champions—possibly tapping into the infrastructure developed from COVID-19 vaccine rollout—and community groups, including collaborators such as Bromley-by-Bow. This will enable broader community input into the final project outputs. All findings will be publicly available via our website in accessible forms for lay consumption with assistance from our PAG.

Results

The CICADA project was funded by the Health and Social Care Delivery Research (HSDR) program of the National Institute for Health and Care Research (NIHR) in March 2021 and began in May 2021. Further work within the project was commissioned in March 2022. This will provide a subset of data focused on mental health specifically in Northeast England and will add Greater Manchester and the Northwest Coast to our sites, where the NIHR has identified a particular need. Data collection began in August 2021, with the last participants due to be recruited in September 2022. As of January 2022, at the close of wave 1, we had 5792 survey respondents with usable data from 4300 respondents, and had completed 227 interviews. We plan to collect 84 further interviews for the newly funded substudy. At the time of submission, beginning April 2022, we are recruiting participants for the substudy and wave 2 of the surveys and qualitative work. We expect all results to be submitted for publication by winter of 2022.

Discussion

Anticipated Findings and Potential Impact

In undertaking this study, we will fill a gap in the evidence about the pandemic experiences of disabled people and people living with chronic conditions, particularly those from minoritized ethnic groups. We expect to contribute considerable new knowledge through our mixed methods approach. We consider issues such as those relating to access to health and social care and resources, formal and informal networks of support, and discrimination and marginalization. However, we are particularly interested in the strengths and assets that have improved our participants' capacity to cope with the pandemic.

We believe this is important, as many iniquitous pandemic health and well-being challenges, such as those faced by minoritized ethnic groups at the intersection with chronic conditions/impairments and insecure citizenship status, can be mitigated by small adjustments to health and social care service policy and delivery, formal networks such as community health services, and informal networks such as family and friends [25]. We expect to provide recommendations for these adjustments and for potential interventions through our longitudinal mixed methods analyses. We may also produce some simple interventions ourselves. To attempt to tease out the impact of the pandemic, we will: (1) model relationships between mediating variables (including social network features) and health and social outcomes; and (2) explore participant current and recent experiences, and recall of prepandemic experiences and inequities.

Building on Prior Research

We are undertaking both primary research and secondary data analyses. While the design and focus of our study are unique, the pandemic has fostered the development of a number of contemporary studies looking at particular disabilities, particular "stakeholders" in disability experiences (eg, disabled people, health and social care services staff, carers, young people), and particular racial and ethnic groups. Our scoping review, which began in 2021 and includes grey literature, will be updated in autumn 2022 to ensure our findings are reported in the context of these other studies. We will publish our reviews. Our secondary analyses of other panel data will help to contextualize our own findings; for example, we are analyzing data from a survey that began before but overlapped with our own, which also includes some relevant data.

Strengths and Limitations

We will provide rich quantitative and qualitative data, with a large sample size for qualitative interviews, providing in-depth information through quota sampling. Our creative participatory and equitable approach will be key to cocreating our outputs with relevant stakeholders. This will include members of the populations we hope will benefit, third-sector organizations, clinicians, social care staff, and policy staff. This will ensure outputs that have real credibility, real-world relevance and value, can be implemented, and are sustainable.

Although the ideal study design would include an experimental evaluation of outputs, we cannot undertake full feasibility testing and trialing of any interventions we suggest, as this is an 18-month study. We may, however, explore implementation enablers and barriers and acceptability in small proof-of-concept evaluations; these are likely to require ethical review amendment.

We are not using randomized sampling in any part of the study, which is likely to introduce bias. However, rigorous synthesis of the multiple types of data we produce, our strong patient representation, our participatory approach across stakeholder groups, our overall rigor and adherence to principles of Open Science, and a reflexive approach to biases should help to contextualize findings within these limitations.

We focus on specific minoritized ethnic groups and specific sites within England in our qualitative work. This has benefits in terms of the depth of analysis for particular groups and settings, but could reduce transferability of findings to other

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groups and settings, which we will explore through our survey and other existing data sets. Categorizations are laden with assumptions that need to be explored.

The survey, being primarily digital, will exclude people with poor access to the digital world, although we do offer alternatives such as paper-based copies. There is also the potential for pandemic survey fatigue.

In studying the experiences of disabled people with impairments and those living with chronic conditions who come from certain minoritized ethnic groups, we are aiming for transformative research. We are sensitive to the social constructionist nature of terms that are used to categorize particular groups, which can result in tensions. However, we need to disseminate our findings using terms that have meaning to our key audiences. We intend to report on the issues and tensions as part of our wider push for change.

Conclusions

Current understandings and considerations are limited with regard to the health and social care and support received by disabled people or those living with chronic conditions who are from certain minoritized ethnic groups. Inequities existing before the pandemic have been made worse by it, and public and policy awareness of this exacerbation provides an opportunity for change. This study, using an intersectional assets-based approach and drawing on participatory and mixed methods, aims to fill a gap in the evidence to help inform changes that reduce inequities.

Acknowledgments

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Authors' Contributions

CR conceived the study idea, overall methodology, conceptualizations, and the initial study design, and wrote the first draft of the manuscript. She leads on the study overall. OA and BN contributed to the design of the quantitative methods, and VR, JC, and SK contributed to theoretical conceptualizations. OA, EB, JE, LG, RD, JC, and SK provided substantial revisions to the original draft. KA and AFWW are undertaking data collection. All authors read, edited, and approved the final manuscript.

Conflicts of Interest

None declared.

Multimedia Appendix 1
Peer-review report by the National Institute for Health Research.
[PDF File (Adobe PDF File), 4937 KB - resprot_v11i6e38361_app1.pdf]

References

1. Orcutt M, Spiegel P, Kumar B, Abubakar I, Clark J, Horton R, Lancet Migration. Lancet Migration: global collaboration to advance migration health. Lancet 2020 Feb 01;395(10221):317-319. [doi: 10.1016/S0140-6736(20)30107-0] [Medline: 32007150]
2. Kuper H, Banks LM, Bright T, Davey C, Shakespeare T. Disability-inclusive COVID-19 response: What it is, why it is important and what we can learn from the United Kingdom's response. Wellcome Open Res 2020;5:79 [FREE Full text] [doi: 10.12688/wellcomeopenres.15833.1] [Medline: 32500099]
3. Abuelgasim E, Saw LJ, Shirke M, Zeinah M, Harky A. COVID-19: Unique public health issues facing Black, Asian and minority ethnic communities. Curr Probl Cardiol 2020 Aug;45(8):100621 [FREE Full text] [doi: 10.1016/j.cpcardiol.2020.100621] [Medline: 32448759]
4. Spencer A, Watermeyer B, Rogers A. The importance of tackling the social determinants of health to address the unmet need within cancer services. Reflections from build back fairer: the COVID-19 Marmot Review. Clin Oncol (R Coll Radiol) 2022 Mar;34(3):145-147. [doi: 10.1016/j.clon.2021.11.003] [Medline: 34802845]
5. Mathur R, Rentsch CT, Morton CE, Hulme WJ, Schultze A, MacKenna B, OpenSAFELY Collaborative. Ethnic differences in SARS-CoV-2 infection and COVID-19-related hospitalisation, intensive care unit admission, and death in 17 million adults in England: an observational cohort study using the OpenSAFELY platform. Lancet 2021 May 08;397(10286):1711-1724 [FREE Full text] [doi: 10.1016/S0140-6736(21)00634-6] [Medline: 33939953]
6. Mirza M. New issues in refugee research. Unmet needs and diminished opportunities: disability, displacement and humanitarian healthcare, Research report 212. UNHCR United Nations Refugee Agency. 2011. URL: https://www.unhcr.org/

XSL•FO
RenderX

research/working/4e0dbdb29/unmet-needs-diminished-opportunities-disability-displacement-humanitarian.html [accessed 2022-05-31]
7. Clarke SK, Kumar GS, Sutton J, Atem J, Banerji A, Brindamour M, et al. Potential impact of COVID-19 on recently resettled refugee populations in the United States and Canada: perspectives of refugee healthcare providers. J Immigr Minor Health 2021 Mar;23(1):184-189 [FREE Full text] [doi: 10.1007/s10903-020-01104-4] [Medline: 33067740]
8. Putz C, Ainsl D. Coronavirus (COVID-19) related deaths by disability status, England, Wales March to 14 July 2020. Office for National Statistics. URL: https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/articles/coronaviruscovid19relateddeathsbydisabilitystatusenglandandwales/2marchto14july2020 [accessed 2022-05-31]
9. Harding S, Balarajan R. Limiting long-term illness among black Caribbeans, black Africans, Indians, Pakistanis, Bangladeshis and Chinese born in the UK. Ethn Health 2000 Mar;5(1):41-46. [doi: 10.1080/13557850050007338] [Medline: 10858938]
10. Razaq A. BAME COVID-19 deaths? What do we know? Rapid Data Evidence Review. Centre for Evidence-Based Medicine. URL: https://www.cebm.net/wp-content/uploads/2020/05/BAME-COVID-Rapid-Data-Evidence-Review-Final-Hidden-in-Plain-Sight-compressed.pdf [accessed 2022-05-31]
11. Thomason ME, Hendrix CL, Werchan D, Brito NH. Social determinants of health exacerbate disparities in COVID-19 illness severity and lasting symptom complaints. medRxiv. 2021 Jul 19. URL: https://www.medrxiv.org/content/10.1101/2021.07.16.21260638v1 [accessed 2022-05-31]
12. Fang ML, Sixsmith J, Lawthom R, Mountian I, Shahrin A. Experiencing 'pathologized presence and normalized absence'; understanding health related experiences and access to health care among Iraqi and Somali asylum seekers, refugees and persons without legal status. BMC Public Health 2015 Oct 19;15(1):923 [FREE Full text] [doi: 10.1186/s12889-015-2279-z] [Medline: 26386559]
13. Iob E, Frank P, Steptoe A, Fancourt D. Levels of severity of depressive symptoms among at-risk groups in the UK during the COVID-19 pandemic. JAMA Netw Open 2020 Oct 01;3(10):e2026064 [FREE Full text] [doi: 10.1001/jamanetworkopen.2020.26064] [Medline: 33104209]
14. Sheridan Rains L, Johnson S, Barnett P, Steare T, Needle JJ, Carr S, COVID-19 Mental Health Policy Research Unit Group. Early impacts of the COVID-19 pandemic on mental health care and on people with mental health conditions: framework synthesis of international experiences and responses. Soc Psychiatry Psychiatr Epidemiol 2021 Jan;56(1):13-24 [FREE Full text] [doi: 10.1007/s00127-020-01924-7] [Medline: 32804258]
15. Mehta B, Jannat-Khah D, Fontana MA, Moezinia CJ, Mancuso CA, Bass AR, et al. Impact of COVID-19 on vulnerable patients with rheumatic disease: results of a worldwide survey. RMD Open 2020 Oct 02;6(3):e001378 [FREE Full text] [doi: 10.1136/rmdopen-2020-001378] [Medline: 33011680]
16. CICADA: Coronavirus Chronic Conditions and Disabilities Awareness Study. URL: https://cicada-study.org.uk/ [accessed 2022-05-31]
17. Boldrini P, Garcea M, Brichetto G, Reale N, Tonolo S, Falabella V, et al. Living with a disability during the pandemic. "Instant paper from the field" on rehabilitation answers to the COVID-19 emergency. Eur J Phys Rehabil Med 2020 Jun;56(3):331-334. [doi: 10.23736/s1973-9087.20.06373-x]
18. Addressing the impact of COVID-19 on the lives of people living with neurological disorders. European Federation of Neurological Associations (EFNA). 2021 Jun. URL: https://www.efna.net/wp-content/uploads/2021/06/EFNA-Report_Final-.pdf [accessed 2022-05-31]
19. Le Cam Y. Results of the H-CARE Pilot Survey for the development of a validated scale and of a Common Feedback Mechanism to measure healthcare experience for rare diseases in Europe. EURORDIS-Rare Diseases Europe. 2017 May 08. URL: https://www.eurordis.org/results_hcaresurvey [accessed 2022-05-31]
20. Fiona Weir on behalf of the National Voices coalition. What we know now: What people with health and care needs experienced during the first wave of COVID-19 A rapid review of data from over 66,000 responses to National Voices members? surveys, September 2020, National Voices coalition. National Voices. URL: https://www.nationalvoices.org.uk/sites/default/files/public/news/download/what_we_know_now_1.pdf [accessed 2022-05-31]
21. Cheong J, Goh Z, Marras C, Tanner C, Kasten M, Noyce A, Movement Disorders Society Epidemiology Study Group. The Impact of COVID-19 on access to Parkinson's disease medication. Mov Disord 2020 Dec;35(12):2129-2133. [doi: 10.1002/mds.28293] [Medline: 32860226]
22. Al-Hashel J, Ismail I. Impact of coronavirus disease 2019 (COVID-19) pandemic on patients with migraine: a web-based survey study. J Headache Pain 2020 Oct 24;21(1):115 [FREE Full text] [doi: 10.1186/s10194-020-01183-6] [Medline: 32972360]
23. Ziadé N, el Kibbi L, Hmamouchi I, Abdulateef N, Halabi H, Hamdi W, et al. Impact of the COVID‐19 pandemic on patients with chronic rheumatic diseases: a study in 15 Arab countries. Int J Rheum Dis 2020 Sep 05;23(11):1550-1557. [doi: 10.1111/1756-185x.13960]
24. Baranidharan G, Bretherton B, Eldabe S, Mehta V, Thomson S, Sharma ML, et al. The impact of the COVID-19 pandemic on patients awaiting spinal cord stimulation surgery in the United Kingdom: a multi-centre patient survey. Br J Pain 2021 Aug;15(3):282-290 [FREE Full text] [doi: 10.1177/2049463720948092] [Medline: 34373788]

XSL•FO
RenderX

25. Loubaba M, Jones T. The impact of COVID-19 on black, Asian and minority ethnic communities, NIHR special report, 20/05/2020, UoB_COVID1. National Institute for Health Research. 2020 May 20. URL: https://arc-w.nihr.ac.uk/Wordpress/wp-content/uploads/2020/05/COVID-19-Partner-report-BAME-communities-BCC001.pdf [accessed 2022-05-31]
26. Anderson B. Citizenship: What is it and why does it matter? The Migration Observatory. URL: https://migrationobservatory.ox.ac.uk/resources/primers/citizenship-what-is-it-and-why-does-it-matter/ [accessed 2021-08-22]
27. Williams DR, Collins C. Racial residential segregation: A fundamental cause of racial disparities in health. Public Health Reports 2001 Sep;116(5):404-416. [doi: 10.1016/s0033-3549(04)50068-7]
28. Link BG, Phelan J. Social conditions as fundamental causes of disease. J Health Soc Behav 1995;35:80. [doi: 10.2307/2626958]
29. Baptist AP, Lowe D, Sarsour N, Jaffee H, Eftekhari S, Carpenter LM, et al. Asthma disparities during the COVID-19 pandemic: a survey of patients and physicians. J Allergy Clin Immunol Pract 2020 Nov;8(10):3371-3377 [FREE Full text] [doi: 10.1016/j.jaip.2020.09.015] [Medline: 32980585]
30. Campos-Castillo C, Anthony D. Racial and ethnic differences in self-reported telehealth use during the COVID-19 pandemic: a secondary analysis of a US survey of internet users from late March. J Am Med Inform Assoc 2021 Jan 15;28(1):119-125 [FREE Full text] [doi: 10.1093/jamia/ocaa221] [Medline: 32894772]
31. Miller P, Parker S, Gillinson S. Disablism: How to tackle the last prejudice. London: Demos; 2004.
32. Crenshaw K. Demarginalizing the intersection of race and sex: a Black feminist critique of antidiscrimination doctrine, feminist theory and antiracist politics. Univ Chic Leg Forum 1989;140:67 [FREE Full text] [doi: 10.4324/9780429500480-5]
33. Bronfenbrenner U. Ecology of the family as a context for human development: research perspectives. Dev Psychol 1986 Nov;22(6):723-742. [doi: 10.1037/0012-1649.22.6.723]
34. Heise LL. Violence against women: an integrated, ecological framework. Violence Against Women 1998 Jul 30;4(3):262-290. [doi: 10.1177/1077801298004003002] [Medline: 12296014]
35. Rivas C, Tomomatsu I, Gough D. The many faces of disability in evidence for policy and practice: embracing complexity. Evid policy 2021 May 01;17(2):191-208. [doi: 10.1332/174426421x16147909420727]
36. Casanova EL, Widman CJ. A sociological treatment exploring the medical model in relation to the neurodiversity movement with reference to policy and practice. Evid Policy 2021 May 01;17(2):363-381. [doi: 10.1332/174426421x16142770974065]
37. Oliver M. The social model of disability: thirty years on. Disabil Soc 2013 Oct;28(7):1024-1026. [doi: 10.1080/09687599.2013.818773]
38. Goodley D. The Dis/ability Complex. J Divers Gender Stud 2018;5(1):5. [doi: 10.11116/digest.5.1.1]
39. Bunbury S. Unconscious bias and the medical model: How the social model may hold the key to transformative thinking about disability discrimination. Int J Discrim Law 2019 Feb 28;19(1):26-47. [doi: 10.1177/1358229118820742]
40. Resolution adopted by the General Assembly on 13 December 2006. 61/106. Convention on the Rights of Persons with Disabilities. United Nations. URL: https://www.un.org/en/development/desa/population/migration/generalassembly/docs/globalcompact/A_RES_61_106.pdf [accessed 2021-09-05]
41. Siebers T. Disability theory. Ann Arbor, MI: University of Michigan Press; 2008.
42. Arendt H. Responsibility and judgement. New York: Schocken; 2003.
43. Cole ER. Intersectionality and research in psychology. Am Psychol 2009 May;64(3):170-180. [doi: 10.1037/a0014564] [Medline: 19348518]
44. Collins P. Black feminist thought: knowledge, consciousness, and the politics of empowerment. New York: Routledge; 1990.
45. Crenshaw K. Mapping the Margins: intersectionality, identity politics, and violence against women of color. Stanford Law Review 1991 Jul;43(6):1241. [doi: 10.2307/1229039]
46. Shulz AJ, Mullings L. Gender, race, class & health: intersectional approaches. San Francisco, CA: Jossey-Bass; Jun 29, 2016:297-298.
47. Bernstein KS, Park S, Shin J, Cho S, Park Y. Acculturation, discrimination and depressive symptoms among Korean immigrants in New York City. Community Ment Health J 2011 Mar 4;47(1):24-34 [FREE Full text] [doi: 10.1007/s10597-009-9261-0] [Medline: 19888652]
48. Frost DM. Hostile and harmful: Structural stigma and minority stress explain increased anxiety among migrants living in the United Kingdom after the Brexit referendum. J Consult Clin Psychol 2020 Jan;88(1):75-81. [doi: 10.1037/ccp0000458] [Medline: 31647276]
49. Martynowska K, Korulczyk T, Mamcarz PJ. Perceived stress and well-being of Polish migrants in the UK after Brexit vote. PLoS One 2020;15(7):e0236168 [FREE Full text] [doi: 10.1371/journal.pone.0236168] [Medline: 32702031]
50. Gee G, Ryan A, Laflamme DJ, Holt J. Self-reported discrimination and mental health status among African descendants, Mexican Americans, and other Latinos in the New Hampshire REACH 2010 Initiative: the added dimension of immigration. Am J Public Health 2006 Oct;96(10):1821-1828. [doi: 10.2105/ajph.2005.080085]
51. Sanchez GJ. Face the nation: race, immigration, and the rise of nativism in late twentieth century America. Int Migration Rev 2018 Jun 20;31(4):1009-1030. [doi: 10.1177/019791839703100409]

XSL•FO
RenderX

52. Kirkup J. Theresa May interview: 'We're going to give illegal migrants a really hostile reception'. The Telegraph. 2012 May 25. URL: https://www.telegraph.co.uk/news/0/theresa-may-interview-going-give-illegal-migrants-really-hostile/ [accessed 2021-08-17]
53. Viruell-Fuentes EA. “It's a lot of work”. Du Bois Rev 2011 Apr 15;8(1):37-52. [doi: 10.1017/s1742058x11000117]
54. Naber N. Ambiguous insiders: an investigation of Arab American invisibility. Ethnic Racial Stud 2010 Dec 07;23(1):37-61. [doi: 10.1080/014198700329123]
55. McLeroy KR, Bibeau D, Steckler A, Glanz K. An ecological perspective on health promotion programs. Health Educ Q 1988 Sep 04;15(4):351-377. [doi: 10.1177/109019818801500401] [Medline: 3068205]
56. Integrating care: Next steps to building strong and effective integrated care systems across England. NHS England. 2020. URL: https://www.england.nhs.uk/publication/integrating-care-next-steps-to-building-strong-and-effective-integrated-care-systems-across-england/ [accessed 2022-05-31]
57. Bronfenbrenner U, Ceci SJ. Nature-nurture reconceptualized in developmental perspective: a bioecological model. Psychol Rev 1994 Oct;101(4):568-586. [doi: 10.1037/0033-295x.101.4.568] [Medline: 7984707]
58. Keith R, Crosson J, O?Malley A. Using the Consolidated Framework for Implementation Research (CFIR) to produce actionable findings: a rapid-cycle evaluation approach to improving implementation. Implementation Sci 2017;12:15. [doi: 10.1186/s13012-017-0550-7]
59. Umucu E, Tansey T, Brooks J, Lee B. The protective role of character strengths in COVID-19 stress and well-being in individuals with chronic conditions and disabilities: an exploratory study. Rehab Counsel Bull 2020 Oct 26;64(2):67-74. [doi: 10.1177/0034355220967093]
60. Ciaffi J, Brusi V, Lisi L, Mancarella L, D'Onghia M, Quaranta E, et al. Living with arthritis: a "training camp" for coping with stressful events? A survey on resilience of arthritis patients following the COVID-19 pandemic. Clin Rheumatol 2020 Dec;39(11):3163-3170 [FREE Full text] [doi: 10.1007/s10067-020-05411-x] [Medline: 32979101]
61. Brewer G, Stratton K. Living with chronic fatigue syndrome during lockdown and a global pandemic. Fatigue: Biomed Health Behav 2020 Oct 01;8(3):144-155. [doi: 10.1080/21641846.2020.1827503]
62. Foley W, Schubert L. Applying strengths-based approaches to nutrition research and interventions in Indigenous Australian communities. J Critical Dietetics 2013;1(3):15-25.
63. Antonovsky A. The salutogenic model as a theory to guide health promotion. Health Promot Int 1996;11(1):11-18. [doi: 10.1093/heapro/11.1.11]
64. Morgan A, Ziglio E. Revitalising the evidence base for public health: an assets model. Promot Educ 2007;14(Suppl 2):17-22. [doi: 10.1177/10253823070140020701x] [Medline: 17685075]
65. Hombrados-Mendieta I, Millán-Franco M, Gómez-Jacinto L, Gonzalez-Castro F, Martos-Méndez MJ, García-Cid A. Positive influences of social support on sense of community, life satisfaction and the health of immigrants in Spain. Front Psychol 2019;10:2555. [doi: 10.3389/fpsyg.2019.02555] [Medline: 31803103]
66. Wilkinson M, Dumontier M, Aalbersberg IJJ, Appleton G, Axton M, Baak A, et al. The FAIR Guiding Principles for scientific data management and stewardship. Sci Data 2016 Mar 15;3:160018. [doi: 10.1038/sdata.2016.18] [Medline: 26978244]
67. After-care needs of inpatients recovering from COVID-19. NHS England. 2020. URL: https://www.cambscommunityservices.nhs.uk/docs/default-source/luton-adults-general/c0388_after_care_needs_of_inpatients_recovering_from_covid-19_5_june_2020.pdf [accessed 2022-05-31]
68. Iyengar K, Jain VVR, Vaishya R. Pitfalls in telemedicine consultations in the era of COVID 19 and how to avoid them. Diabetes Metab Syndr 2020;14(5):797-799 [FREE Full text] [doi: 10.1016/j.dsx.2020.06.007] [Medline: 32534432]
69. Cavagna L, Zanframundo G, Codullo V, Pisu MG, Caporali R, Montecucco C. Telemedicine in rheumatology: a reliable approach beyond the pandemic. Rheumatology 2021 Jan 05;60(1):366-370 [FREE Full text] [doi: 10.1093/rheumatology/keaa554] [Medline: 32893293]
70. Glover RE, van Schalkwyk MC, Akl EA, Kristjannson E, Lotfi T, Petkovic J, et al. A framework for identifying and mitigating the equity harms of COVID-19 policy interventions. J Clin Epidemiol 2020 Dec;128:35-48 [FREE Full text] [doi: 10.1016/j.jclinepi.2020.06.004] [Medline: 32526461]
71. Aksoy O, Bann D, Fluharty M, Nandi A. Religiosity and mental wellbeing among members of majority and minority religions: Findings from Understanding Society: the UK Household Longitudinal Study. Am J Epidemiol 2022 Jan 01;191(1):20-30 [FREE Full text] [doi: 10.1093/aje/kwab133] [Medline: 33977294]
72. WHOQOL Disabilities Group. WHO QOL Disabilities. Geneva: World Health Organization; 2011.
73. Vulnerability Assessment Framework Questionnaire Validation Workshop Summary. UNHCR. 2016. URL: https://bit.ly/2YQ1G4P%20 [accessed 2020-06-30]
74. Stansfeld S, Marmot M. Deriving a survey measure of social support: the reliability and validity of the close persons questionnaire. Soc Sci Med 1992 Oct;35(8):1027-1035. [doi: 10.1016/0277-9536(92)90242-i]
75. Sharma VK, Lepping P, Cummins AGP, Copeland JRM, Parhee R, Mottram P. The Global Mental Health Assessment Tool--Primary Care Version (GMHAT/PC). Development, reliability and validity. World Psychiatry 2004 Jul;3(2):115-119 [FREE Full text] [Medline: 16633473]

XSL•FO
RenderX

76. Templer DI. The construction and validation of a Death Anxiety Scale. J Gen Psychol 1970 May 06;82(2d Half):165-177. [doi: 10.1080/00221309.1970.9920634] [Medline: 4394812]
77. Cooke A, Smith D, Booth A. Beyond PICO: the SPIDER tool for qualitative evidence synthesis. Qual Health Res 2012 Oct 24;22(10):1435-1443. [doi: 10.1177/1049732312452938] [Medline: 22829486]
78. Wright J, Hayward A, West J, Pickett K, McEachan RM, Mon-Williams M, et al. ActEarly: a City Collaboratory approach to early promotion of good health and wellbeing. Wellcome Open Res 2019;4:156 [FREE Full text] [doi: 10.12688/wellcomeopenres.15443.1] [Medline: 31840089]
79. Wolf EJ, Harrington KM, Clark SL, Miller MW. Sample size requirements for structural equation models: an evaluation of power, bias, and solution propriety. Educ Psychol Meas 2013 Dec 09;76(6):913-934 [FREE Full text] [doi: 10.1177/0013164413495237] [Medline: 25705052]
80. Powell W, Smith-Doerr LNL. Networks and economic life. In: Smelser NJ, Swedberg R, editors. The Handbook of Economic Sociology. Princeton, NJ: Princeton University Press; 1994:379-402.
81. Valente TW. Social networks and health: models, methods, and applications. New York: Oxford University Press; 2010.
82. Calderwood L. Reducing non-response in longitudinal surveys by improving survey practice, PhD thesis. University College London. 2016 Jun 01. URL: https://discovery.ucl.ac.uk/id/eprint/1475673/ [accessed 2022-05-31]
83. Enders C. Applied missing data analysis. Surrey: Guilford Press; 2010.
84. Shim J, Darling K, Lappe M, Thomson L, Lee S, Hiatt R, et al. Homogeneity and heterogeneity as situational properties: producing--and moving beyond?--race in post-genomic science. Soc Stud Sci 2014 Aug;44(4):579-599 [FREE Full text] [doi: 10.1177/0306312714531522] [Medline: 25272613]
85. Decary S, Dugas M, Stefan T, Langlois L, Skidmore B, Bhe?reur A, et al. Care Models for Long COVID - A Rapid Systematic Review. SPOR Evidence Alliance, COVID-END Network. 2021. URL: https://sporevidencealliance.ca/wp-content/uploads/2021/06/Care-Models-for-Long-COVID_Full-Report_2021.06.18.pdf [accessed 2022-05-31]
86. Sutherland C, Cheng Y. Participatory-action research with (im)migrant women in two small Canadian cities: using photovoice in Kingston and Peterborough, Ontario. J Immigrant Refugee Stud 2009 Sep 08;7(3):290-307. [doi: 10.1080/15562940903150089]
87. Oteros-Rozas E, Martín-López B, Daw TM, Bohensky EL, Butler JR, Hill R, et al. Participatory scenario planning in place-based social-ecological research: insights and experiences from 23 case studies. Ecol Soc 2015;20(4):32. [doi: 10.5751/es-07985-200432]
88. The Collaborative Poetics Network. The Collaborative Poetics Network Resource Pack. 2018. URL: https://cpb-eu-w2.wpmucdn.com/blogs.brighton.ac.uk/dist/4/4113/files/2018/06/CP-Draft-Resource-Pack-FINAL-PILOT-V-2hmywt4.pdf [accessed 2022-05-31]
89. The Co-Creating Welfare Project partners. Co-creating Welfare: Training course material preparing professionals to co-create welfare solutions with citizens, 2019, Universidade do Minho. Instituto de Educação. 2019. URL: https://repositorium.sdum.uminho.pt/bitstream/1822/62580/1/CCW-Training-course%2Bmaterial.pdf [accessed 2021-09-05]
90. Thomson A, Rivas C, Giovannoni G. Multiple sclerosis outpatient future groups: improving the quality of participant interaction and ideation tools within service improvement activities. BMC Health Serv Res 2015 May 23;15:105 [FREE Full text] [doi: 10.1186/s12913-015-0773-8] [Medline: 25903748]
91. Patient Engagement Keystone Summit 2018 White Paper. KLAS research. 2018 Nov 06. URL: https://klasresearch.com/report/patient-engagement-keystone-summit-2018-white-paper/1494 [accessed 2021-09-05]
92. Booth A, Noyes J, Flemming K, Moore G, Tunçalp Ö, Shakibazadeh E. Formulating questions to explore complex interventions within qualitative evidence synthesis. BMJ Glob Health 2019;4(Suppl 1):e001107 [FREE Full text] [doi: 10.1136/bmjgh-2018-001107] [Medline: 30775019]

Abbreviations

ADS: Anxiety and Depression Scale
BiB: Born in Bradford
CFIR: Consolidated Framework for Implementation Research
CICADA: Coronavirus Chronic Conditions and Disabilities Awareness Study
CLS: Centre for Longitudinal Research (London)
HSDR: Health and Social Care Delivery Research
LGM: latent growth modeling
NHS: National Health Service
NIHR: National Institute for Health and Care Research
PAG: patient advisory group
PerSPectif: Perspective, Setting, Phenomenon of interest/problem, Environment, (optional Comparison), Time/timing, Findings
PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-analyses
QOSC-ID: World Health Organization Quality of Care and Support-Disability

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SEM: structural equation modeling
SPIDER: Sample, Phenomenon of Interest, Design, Evaluation topics, Research source, Setting
WHO: World Health Organization
WHOQOL-BREF-ID: World Health Organization Quality of Life

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Protocol

Valorization of Natural Cardio Trekking Trails Through Open Innovation for the Promotion of Sustainable Cross-generational Health-Oriented Tourism in the Connect2Move Project: Protocol for a Cross-sectional Study

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Abstract

Background: Hiking is one of the most popular forms of exercise in the alpine region. However, besides its health benefits, hiking is the alpine activity with the highest incidence of cardiac events. Most incidents occur due to overexertion or underestimation of the physiological strain of hiking.

Objective: This project will establish a standardized cardio trekking test trail to evaluate the exercise capacity of tourists within hiking areas and deliver a tool for the prevention of hiking-associated cardiac incidents. Further, individual exercise intensity for a hiking tour will be predicted and visualized in digital maps.

Methods: This cooperation study between Austria and Germany will first validate a 1-km outdoor cardio trekking test trail at 2 different study sites. Then, exercise intensity measures on 8-km hiking trails will be evaluated during hiking to estimate overall hiking intensity. A total of 144 healthy adults (aged >45 years) will perform a treadmill test in the laboratory and a 1-km hiking test outdoors. They will wear a portable spirometry device that measures gas exchange, as well as heart rate, walking speed, ventilation, GPS location, and altitude throughout the tests. Estimation models for exercise capacity based on measured parameters will be calculated.

Results: The project "Connect2Move" was funded in December 2019 by the European Regional Development Fund (INTERREG V-A Programme Austria-Bavaria – 2014-2020; Project Number AB296). "Connect2Move" started in January 2020 and runs until the end of June 2022. By the end of April 2022, 162 participants were tested in the laboratory, and of these, 144 were tested outdoors. The data analysis will be completed by the end of June 2022, and results are expected to be published by the end of 2022.

Conclusions: Individual prediction of exercise capacity in healthy individuals with interest in hiking aims at the prevention of hiking-associated cardiovascular events caused by overexertion. Integration of a mathematical equation into existing hiking apps will allow individual hiking route recommendations derived from individual performance on a standardized cardio trekking test trail.

Trial Registration: ClinicalTrails.gov NCT05226806; https://clinicaltrials.gov/ct2/show/NCT05226806

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International Registered Report Identifier (IRRID): DERR1-10.2196/39038

(JMIR Res Protoc 2022;11(7):e39038) doi:10.2196/39038

KEYWORDS

cardiorespiratory fitness; exercise; field test; hiking safety

Introduction

Regular physical activity improves exercise capacity [1,2] and reduces the risk of developing cardiovascular diseases [3]. Endurance and strength training have the highest levels of evidence in current national and international guidelines as therapeutic components for the prevention and rehabilitation of cardiovascular diseases [4]. Hiking is a popular mode of exercise in mountainous regions worldwide and is being performed by millions of people, including those with an increased cardiovascular risk [5]. Despite its well-known beneficial effects on the cardiovascular system, intensive and exhaustive physical activities can lead to cardiac events, especially in untrained individuals. As a result, hiking is the alpine activity with the highest incidence of cardiac events, including sudden cardiac death [6-8]. These critical incidents occur mostly due to overestimating personal fitness and choosing overly demanding hiking routes or neglecting weather conditions (temperature, wind, rainfall, snow, etc). In few cases, hikers know about their higher risk and prevent incidents during hikes through medical prevention check-ups beforehand. Such a check-up for heart health and an evaluation of the exercise capacity during standard conditions could ideally be done by a simple ergometry test. Based on its results, training and hiking recommendations could be given by an expert. To further enhance the safety of hiking as a means of preventing cardiovascular disease and helping prevent cardiac incidents, this study aims to develop and validate a standardized 1-km cardio trekking test trail (CTTT) that can be set up in mountainous areas to determine individual physical fitness levels and personalize categories of exercise intensities during walking and hiking. Additionally, we will perform scientific mapping of 2 cardio trekking trails based on several performance parameters, such as heart rate and gas exchange. The realization of those study aims should not substitute the medical prevention examination but rather provide an additional prevention method to predict cardiovascular demand in individual hikers.

This study is part of a larger project that aims to appreciate natural and evidence-based cardio trekking trails through open innovation methods for the sustainable promotion of cross-generational health-oriented tourism, called "Connect2Move." The project has been funded by the European Regional Development Fund (INTERREG V-A Programme Austria-Bavaria – 2014-2020; Project Number AB296). This project aims to redesign existing hiking routes into themed trails and digitally redesign those trails. Expected cardiovascular load based on individual cardiorespiratory fitness will be visualized in digital maps, in addition to the usual description of the length, altitude, path condition, and duration. For valorization and implementation in the participating communities, an open innovation approach is chosen, which involves regional stakeholders and the target population early in the development process, and is scientifically and medically supervised. Two cross-border, climate-friendly, biological concepts for physical activity promotion/cardio trekking in the Alps will be developed. The ideas can increase year-round gentle health tourism and promote individual health literacy for tourists and locals.

Methods

Study Design

This cross-sectional study to reduce the risk of cardiac events in hiking consists of 3 work packages. It will be conducted in Salzburg and Werfenweng, Austria, as well as in Prien am Chiemsee and Aschau im Chiemgau, Germany. The first work package establishes and validates a 1-km CTTT. The second work package analyzes the physiological aspects of an 8-km trekking trail (Figure 1). In the third work package, developing an algorithm to calculate exercise intensity based on the results of the CTTT is the main task. This work package includes the cartography of intensities over the 8-km trekking trail. The first and second work packages will be performed by the Ludwig Boltzmann Institute for Digital Health and Prevention Salzburg and the Technical University Munich, and the third work package will be performed by Salzburg Research. The laboratory testing and medical assessment of the Austrian participants will be performed at the University Institute of Sports Medicine, Prevention and Rehabilitation, Paracelsus Medical University Salzburg, Austria, and the testing and assessment of the German participants will be performed at St. Irmingard Klinik in Prien am Chiemsee, Germany.

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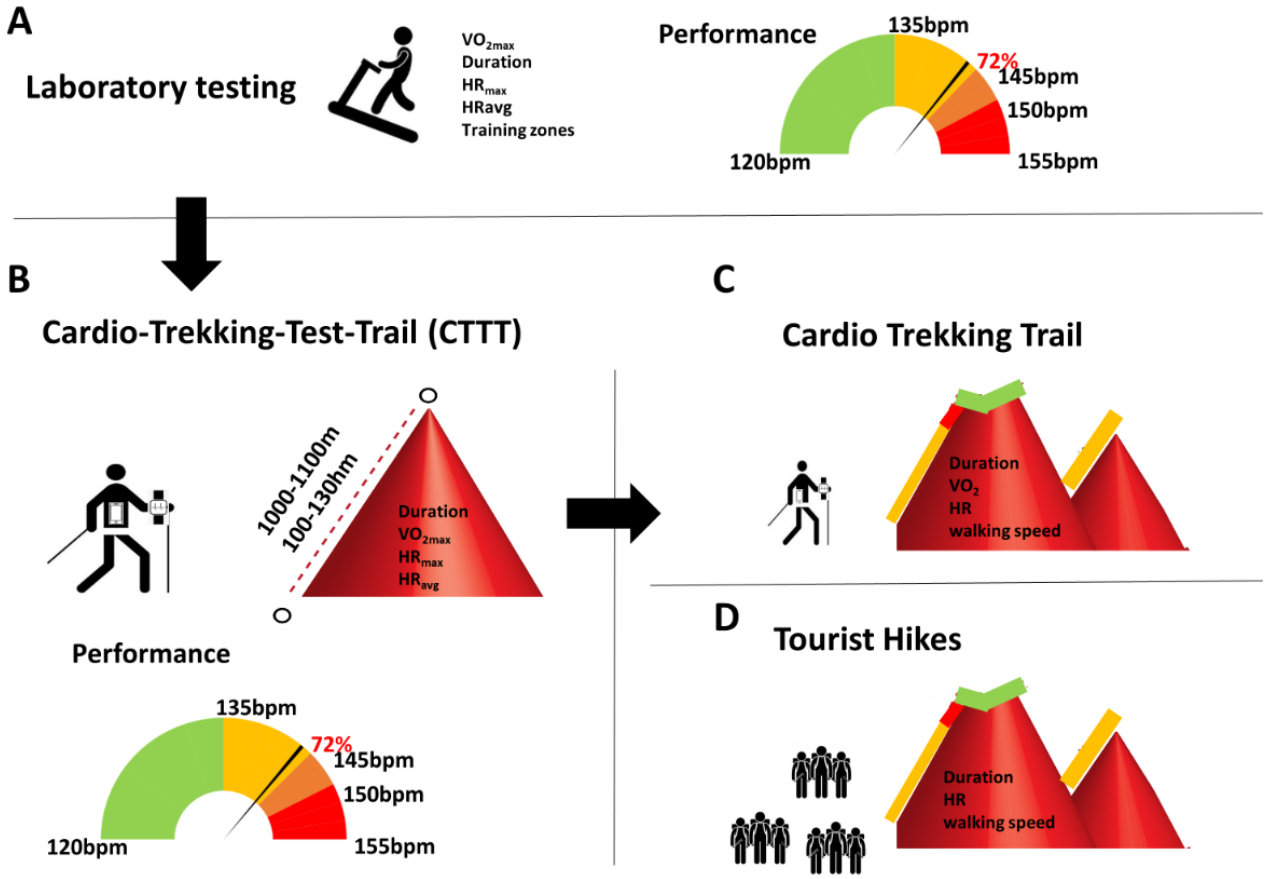
Figure 1. From laboratory testing to tourist hikes. (A) Laboratory treadmill test. Evaluation of maximal exercise capacity and training zones. (B) 1-km cardio trekking test trail. Evaluation of exercise capacity in a standardized outdoor setting. (C) 8-km cardio trekking trail. Guided hikes with study participants, with measurement of exercise capacity and heart rate during the hike. (D) Cartography of the 8-km cardio trekking trail with the help of guided tourist hikes. bpm: beats per minute; HR: heart rate; HR_{avg}: average heart rate; HR_{max}: maximal heart rate; VO_2: oxygen uptake; VO_{2max}: maximal oxygen uptake.



Ethics Approval

Inclusion and exclusion criteria are described in Textbox 1. Participants will have to provide written informed consent before participating in the study. The Ethics Committee of the State of Salzburg (EK-Nr.: 1090/2020) and the Ethics Committee of the Medical Faculty of the Technical University of Munich (527/20S) have approved this study. Further, the study has been registered at ClinicalTrials.gov (NCT05226806). The study will be conducted following the ethical guidelines of the Declaration of Helsinki.

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Textbox 1. Inclusion and exclusion criteria.

Inclusion criteria

- Age >45 years
- Any sex
- Signed informed consent
- No relevant pathologies found during initial laboratory testing

Exclusion criteria

- Acute or chronic cardiovascular diseases, including untreated or insufficiently treated arterial hypertension (systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg)
- Acute or chronic lung diseases
- Liver diseases
- Kidney diseases
- Diabetes mellitus
- Alcohol (>30 g/day) or drug abuse
- BMI >35
- Orthopedic restriction precluding physical activities performed during the study
- Pregnancy

Recruitment Process and Measurement Process

The recruitment of participants will be conducted using the different information channels of the included institutes via the project website, recruitment flyers, and word-of-mouth advertising. If potential participants are >45 years of age, they will be informed about the study objectives, evaluation protocol, and procedures. On agreeing to participate, they will be invited to the initial laboratory testing at 1 of the 2 testing sites. At the beginning of the initial testing, researchers will provide detailed information about the study again, and the participants will be asked to read and sign written informed consent.

Participants will have to perform 3 different exercise testing procedures to complete the study, including 1 laboratory test on a treadmill and 2 field tests (1-km CTTT and 8-km hikes) in Werfenweng, Austria, or Aschau im Chiemgau, Germany. There will be at least 1 full day of rest between the laboratory test and the first field test. The 1-km CTTT and 8-km hikes will be performed on 2 days. If the scheduling of 2 days is not possible, the 1-km CTTT and 8-km hikes will be conducted on the same day with at least 1 hour of rest in between. Half of the study population will participate in Austria, and the other half will participate in Germany.

Laboratory Testing

The baseline testing will start with a detailed examination by a specialist in internal medicine. Measurements will include anthropometrics (weight, height, and BMI), pulmonary function testing (spirometry), resting electrocardiography (ECG), blood pressure, patient history, echocardiography, and blood testing (lipids, electrolytes, markers of kidney and liver function, thyroid hormones, glucose, and blood count), as well as risk scores for cardiac events in the next 10 years, including the prospective cardiovascular Münster study (PROCAM) Score [9], Framingham Score [10], and European Society of Cardiology (ESC) Score [11]. Other health information will be collected via a face-to-face interview by trained staff. It will include personal questions regarding smoking and alcohol consumption, and sociodemographic data (education, employment status, and marital status). Participants will be asked to fill out standardized questionnaires on physical activity (International Physical Activity Questionnaire [IPAQ] short form [12]) and health (Health Survey Questionnaire: 36-Item Short Form Health Survey [SF-36] [13]). Before exercise capacity is measured, it will be estimated based on a resting test protocol called the Polar Fitness Test, using the Polar beat app and a chest-strap ECG-based heart rate monitor (Polar Electro). The last part of the baseline testing will be an all-out spiroergometry test on a treadmill. The participants will wear the portable spirometry device K5 (Cosmed) to measure respiratory gas exchange throughout the test. The gas analysis will occur in the K5's dynamic mixing chamber (DMC) mode. Heart rate will be measured using a Garmin chest strap. In addition, the participants will wear a 12-lead ECG device (Amedtec Medizintechnik Aue GmbH) for evaluation of exercise-dependent ECG changes, as well as a Garmin Vivoactive 4 smartwatch, which will measure wrist-based heart rate values from an optical sensor throughout the treadmill test. All 3 measurement methods for heart rate will be started simultaneously. The modified Bruce protocol [14] will be used as the treadmill test protocol and will start with 3 min at 2.4 km/h and 0% incline, followed by 3 min at 2.4 km/h and 5% incline. After the first 2 stages, the traditional Bruce protocol will be followed. The test will be stopped if participants reach maximal exhaustion or start running. At the end of each stage, the participants will be asked to indicate their rate of perceived exertion (RPE) on a printed 6-20 Borg scale [15], including a maximum value at test termination. Based on the spiroergometry results measured via the K5 device, ventilatory thresholds for each participant will be determined by the V-slope method [16].

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Exercise recommendations (heart rate zones) for the 8-km hike will be made based on these thresholds.

Environmental Factors During Field Tests

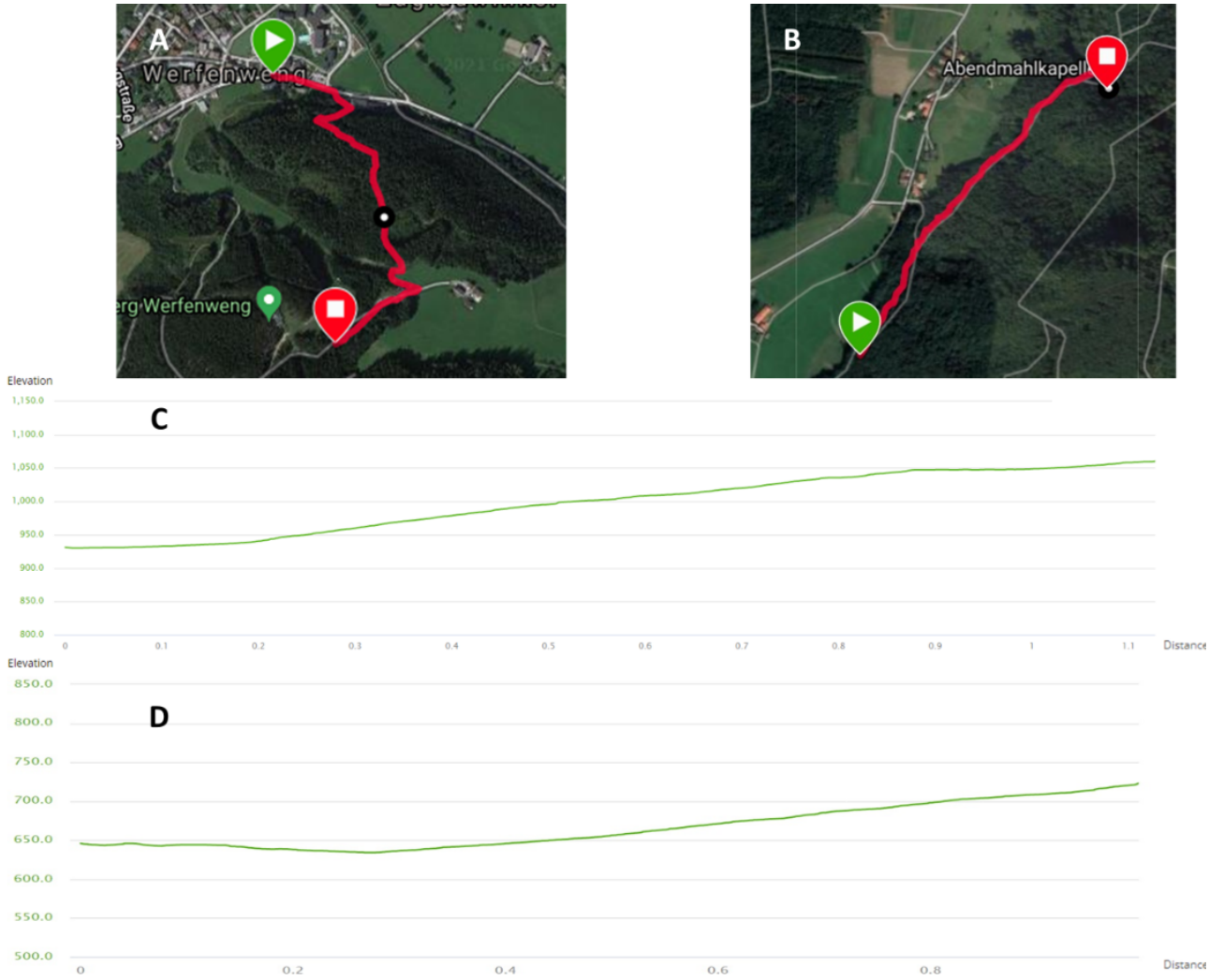
To keep the temperature difference between the field tests and the spiroergometry in the laboratory as little as possible, the laboratory test will be carried out at a standardized room temperature of 20°C, which corresponds with the expected average daily temperature of the study months in the test regions. Should temperatures exceed 26°C, the tests will be postponed since a relevant impact on the heart rate response would be expected [17]. Moreover, humidity will be recorded.

CTTT (1 km)

The CTTT will be implemented outdoors in Werfenweng, Austria, and Aschau im Chiemgau, Germany. The maps and height profiles of the chosen trails for the CTTT are shown in Figure 2. The CTTT includes an easily accessible path with a length of 1000 (SD 100) meters and an elevation of 100 (SD 30) vertical meters, as well as a gradient of up to 26%.

After completing the laboratory test, all participants who have passed the baseline examination (no relevant heart diseases found during testing) will be invited for the field testing. This submaximal cardiorespiratory fitness test will be performed on the 1-km CTTT by each participant alone, with a researcher walking beside the participant. After an explanation of the route, as well as how to walk the track, the participants will get equipped with the measuring devices using the same setup as that during the treadmill test, except for the 12-lead ECG device. They will be wearing the portable K5 device operating in DMC mode, the Garmin chest strap, which will send their heart rate to the K5 device, and the Garmin Vivoactive 4 smartwatch set for wrist-based heart rate measurement. The outdoor exercise test should not be an all-out assessment but rather a submaximal assessment. A researcher will individually accompany participants (walk by their side) and guide their intensity via the Borg scale. Participants will be instructed to hike at a brisk pace and adjust their walking speed according to the trail's steepness. They will be further required not to reach >15 RPE on the Borg scale. Individual Borg values will be assessed at multiple stages of the CTTT, and the pace will be adjusted accordingly if the RPE value exceeds 15 or falls below 11.

Figure 2. Cardio trekking test trail profiles. (A) Map of the cardio trekking test trail in Werfenweng, Austria. (B) Map of the cardio trekking test trail in Aschau im Chiemgau, Germany. (C) Profile of the Austrian trail. (D) Profile of the German trail.



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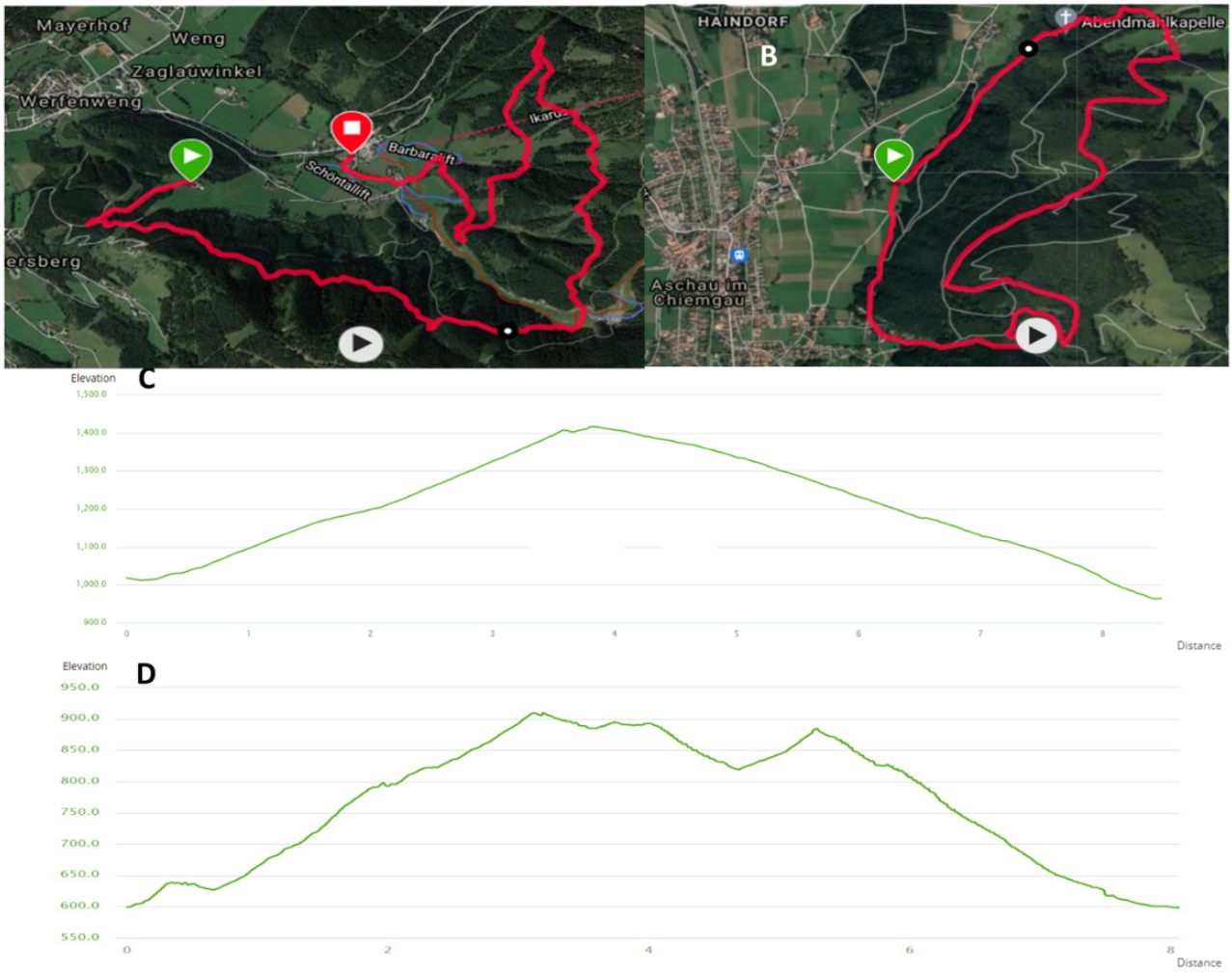
Field Test Involving 8-km Hikes

The 8-km hikes were selected based on touristic, sport scientific, and medical aspects like accessibility, visitor frequency, difficulty, soil texture, important landmarks for sightseeing, etc. Moreover, proximity to the selected CTTT plays an essential role in choosing the tracks. The maps and height profiles of the chosen trails for the long hikes are shown in Figure 3. The selected course in Austria has a length of approximately 8400 m, with 402 vertical meters uphill and 461 vertical meters downhill, and the steepest passage has a 37% gradient. The German trail has a length of approximately 8200 m, with 415 vertical meters uphill and 410 vertical meters downhill, and the steepest passage has a 26% gradient.

For the clinical study, we plan for at least one-third of all participants to hike the 8-km trail wearing the portable K5 device in the DMC mode. The Garmin chest strap sends heart rate data to the K5 device, and the Garmin Vivoactive 4 smartwatch is set for wrist-based heart rate measurement. All participants, who will hike the long trail without the K5 device, will track their hike using a Garmin chest strap connected to the Garmin Vivoactive 4 smartwatch. The groups for the long hike will vary in group size from 2 (1 researcher and 1 participant) to 6 (1 researcher and up to 5 participants). Intensity on the 8-km hike will be moderate. The participants will get individual heart rate ranges based on their ventilatory thresholds assessed during the laboratory treadmill test. Throughout the hike, the heart rate should remain in that range. In addition, the researcher will determine RPE occasionally, which should not exceed a value of 15 on the Borg scale.

Figure 3. Cardio trekking trail profiles. (A) Map of the cardio trekking trail in Werfenweng, Austria. (B) Map of the cardio trekking trail in Aschau im Chiemgau, Germany. (C) Profile of the Austrian trail. (D) Profile of the German trail.



Cartography of the 8-km Cardio Trekking Trails

Subsequent to the 8-km hikes with the study participants, we will perform additional "cardio hikes" for tourists to gain further data for georeferencing and cartography of the selected hikes. We aim to complete guided hikes for 250 willing participants in both countries. All participants will be outfitted with heart rate sensors (Polar Verity Sense arm strap or Garmin Vivoactive 4 smartwatch) for tracking their heart rate, speed, etc, during the hikes. The selected 8-km cardio hikes in Austria and Germany will be newly mapped based on the data from our study participants. This part of the project will aim to tone the hike sections according to heart rate.

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Primary and Secondary Outcomes

Primary Outcome

The primary outcome is estimating the exercise capacity based on physiological features, subjective performance parameters, and route characteristics collected for 2 cardio trekking test routes in Werfenweng, Austria, and Aschau im Chiemgau, Germany. The 2 test routes have a length of approximately 1 km and a gradient of up to 26%. Participants will hike 1 of the 2 test routes shortly after the laboratory measurement. Based on these data and in combination with the capacity of maximal oxygen uptake (VO_{2max}) derived in the laboratory setting, a statistical model for the prediction of VO_{2max} will be developed.

Secondary Outcome

During the 8-km hiking tour, the cardiovascular load will be measured on defined hiking sections (ascents, descent, and plain levels). Based on the individually predicted VO_{2max} on the 1-km CTTT, the estimated cardiovascular load (heart rate or oxygen cost) will be defined and visualized in a digital map using 3 different intensity levels (low, moderate, and high intensity).

Accuracy of Heart Rate Measurements

Each participant's heart rate will be measured simultaneously from at least two different sources during every part of the study. We aim to evaluate the accuracy of the wrist-based Garmin Vivoactive 4 smartwatch data and Garmin chest strap data considering the gold standard 12-lead ECG data measured during the treadmill test. Further, the wrist-based measurement accuracy during the field tests will be compared with the chest strap measurement accuracy.

Comparison of Resting Evaluation Versus Exercise Test for Exercise Capacity

We will measure the maximal exercise capacity (VO_{2max}) during the use of the modified Bruce protocol on the treadmill. As we will use the portable spirometry device K5 from Cosmed, we will be able to use the DMC method instead of the breath-by-breath measurement.

As we will obtain measured VO_{2max} values, we will be able to compare those results with estimations for this parameter, which we will obtain with the Polar Fitness Test. This test is a 5-min resting evaluation performed with a chest strap and the Polar beat app. Based on the measured heart rate variability and added data like age, gender, weight, height, and fitness classification, the app will estimate the individual's VO_{2max}.

In addition, we will obtain VO_{2max} estimation based on the outdoor hikes that involve recording with the Garmin Vivoactive 4 smartwatch.

We aim to evaluate the validity of the 2 VO_{2max} estimations.

Physical Activity and Quality of Life

We will use the IPAQ short form to assess participants' physical activity levels. The questionnaire captures vigorous, moderate, and walking activities and sitting times of the previous 7 days.

The SF-36 will be used to assess health-related quality of life. It contains 36 items grouped into the following 8 dimensions: physical functioning, physical role, body pain, general health, vitality, social functioning, emotional function, and mental health.

Statistical Analysis

Sample Size Calculation

The sample size calculation was done with G*Power Software (Version 3.1.9.7; Heinrich-Heine University) [18,19]. With α=.05, β=.1, and a middle effect size of f^2=0.15, a strong model should be created. The calculation of maximal oxygen uptake could be performed using a linear multiple regression model with 6 predictors. For a model power of 0.90, 123 participants would be required to finish the study. To make sure we reach the number we chose, we added a 15% dropout rate and set the target sample size to 144 participants, with a balanced distribution in Austria and Germany.

Descriptive and Statistical Significance

Statistical evaluations of the hikes (per region or participant) will be performed. Since this study aims to develop a model for calculating exercise capacity during a hiking field test, the statistical analysis will be performed on a per protocol basis, thus including only participants who complete the lab test, the 1-km CTTT, and the 8-km hike. Statistical analyses will be performed using SPSS version 24.0 (SPSS Inc) and R version 4.1.0 (The R Project for Statistical Computing).

Visualization of Exercise Capacity on Hiking Trails

To visualize the analysis results, the collected data on the 8-km hiking trails in Austria and Germany will be used to determine the average exercise capacity for defined hiking trail sections. Therefore, accumulated heart rate and maximal oxygen uptake will be map matched on the hiking trail sections representing different intensities during the hike.

Algorithm Development

Algorithm development is based on the objectives of the analyses, which are as follows: (1) The implementation of an estimation model for exercise capacity; (2) The definition of the hiking trail sections; and (3) The recommendation of intensity ranges via visualization of the hiking trail sections of the 8-km hike based on the capacity estimation of the 1-km CTTT.

Estimation Model for Exercise Capacity

As the first step in model development, the data collected in the laboratory and the results from the 1-km CTTT and 8-km hike will be analyzed descriptively to identify anomalies in the data, such as outliers or data loss due to possible device crashes. Based on these analyses, the data for Austria and Germany will be cleaned.

Following the principle "from the lab to the field," the first estimation model will be developed based on features collected in the laboratory to verify how accurate and reliable VO_{2max} can be estimated. When the proof of concept works on the laboratory data, an in-field estimation model will be created based on the CTTT measurements to see if VO_{2max} from the laboratory can be determined based on the data collected on the

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CTTT. The derived estimation models will be validated with cross-validation and evaluation metrics (eg, adjusted R-squared and mean absolute error).

Definition of Hiking Trail Sections

The definition of hiking trail sections will be a combination of expert-based labeling and a data-driven approach. Sports scientists will mark relevant waypoints due to their expected change in intensity. The data-driven approach will use data from some participants on the 8-km hikes to determine the remarkable difference in intensities. The final definition will combine both approaches and will determine the section points.

Visualization of Hiking Trail Sections With Recommended Intensity

For each 8-km hike, the recommendations will include the impersonalized visualization of expected intensities and the personalized recommended intensity. The collected study data will determine the expected intensities and will be georeferenced to the hiking trail sections. The recommended intensity ranges for each hiking trail section of the 8-km hikes will be determined based on the capacity estimation of the CTTT.

Results

The project "Connect2Move" was funded in December 2019 by the European Regional Development Fund (INTERREG V-A Programme Austria-Bavaria – 2014-2020; Project Number AB296). "Connect2Move" started in January 2020 and runs until the end of June 2022. By the end of April 2022, 162 participants were tested in the laboratory, and of these, 144 were tested outdoors. The data analysis will be completed by the end of June 2022, and results are expected to be published by the end of 2022.

Discussion

This paper describes a protocol created by a multidisciplinary team of physicians, sports scientists, data scientists, and tourist experts to develop a standardized CTTT, which can evaluate the hiking-specific exercise capacity and hence the fitness level of hikers. This project focuses on hiking, as it is one of the most common outdoor activities in the alpine region and can be performed throughout the year. This outdoor activity encourages people to be physically active while spending time in nature. Besides greater physical fitness, hikers may also experience benefits from spending time in a natural environment, such as decreased blood pressure and stress levels, enhanced immune system, restored mental and emotional well-being, and improved general well-being [20,21]. To further promote this form of outdoor activity and raise awareness of the prevention of the overestimation of one's fitness level, this study aims to develop an easy-to-performance fitness test located directly in popular hiking areas. Why should a new physical fitness test be developed when the literature reports several test protocols for field tests to evaluate physical fitness or exercise capacity (VO_{2max})? Tests like the 6-min walking test [22,23] and the Urho Kaleva Kekkonen (UKK) walking test [24] are regularly used by numerous professionals (physicians, sports scientists, coaches, etc) and are well established in the clinical setting. However, these tests are used mainly for patients with underlying diseases like cardiovascular or pulmonary diseases. Existing walking tests are usually performed on flat surfaces (eg, athletic tracks) and not on an inclined slope, making it hard to give recommendations for hiking exercises, since hiking track profiles range from plain surfaces to inclining and declining surfaces. Furthermore, most popular hiking areas cannot provide long enough flat tracks to perform such tests. Therefore, this study aims to develop a hiking-specific CTTT, which will be validated with a standardized laboratory exercise test.

Similar to our study, Chiaranda et al [25] developed an equation for a 1-km submaximal treadmill test for patients with cardiovascular diseases. They recommend it as a possible substitute for maximal exercise testing at laboratories in rehabilitation and health and fitness facilities where expense, space, time, and personnel needed to carry out these cardiopulmonary tests are limited. They also tried to reproduce this 1-km flat submaximal walking test in an outdoor setting with similar results [26]. However, their equations only apply to cardiac patients. We set out to develop an equation for healthy individuals interested in hiking, which is one of the most common leisure activities in mountainous areas. We aim a step further as we hope to integrate this equation into existing hiking apps to deliver individual recommendations based on the performance at a standardized CTTT. In addition, the Connect2Move project hopes to disseminate the characteristics of the developed equation and CTTT throughout interested mountainous areas.

As the interest in green tourism and holidays focusing on health increases, we aim to deliver cost-effective easily accessible tools that facilitate individual recommendations for hiking tours and help avoid overexertion, resulting in fewer cardiovascular events while hiking.

Acknowledgments

We would like to thank all subjects for their enthusiasm and their time dedicated to the study.

Conflicts of Interest

None declared.

Multimedia Appendix 1

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External peer-review report from the ESI Funds 2014-2020, INTERREG V-A Austria-Germany/Bavaria 2014-2020 (Munich, Germany).
[PDF File (Adobe PDF File), 55 KB - resprot_v11i7e39038_app1.pdf]

Multimedia Appendix 2
Machine translation (by Google) of the external peer-review report.
[PDF File (Adobe PDF File), 315 KB - resprot_v11i7e39038_app2.pdf]

References

1. Niebauer J, Hambrecht R, Velich T, Hauer K, Marburger C, Kälberer B, et al. Attenuated progression of coronary artery disease after 6 years of multifactorial risk intervention: role of physical exercise. Circulation 1997 Oct 21;96(8):2534-2541. [doi: 10.1161/01.cir.96.8.2534] [Medline: 9355890]
2. Tschentscher M, Eichinger J, Egger A, Droese S, Schönfelder M, Niebauer J. High-intensity interval training is not superior to other forms of endurance training during cardiac rehabilitation. Eur J Prev Cardiol 2016 Jan;23(1):14-20. [doi: 10.1177/2047487314560100] [Medline: 25404752]
3. Sixt S, Beer S, Blüher M, Korff N, Peschel T, Sonnabend M, et al. Long- but not short-term multifactorial intervention with focus on exercise training improves coronary endothelial dysfunction in diabetes mellitus type 2 and coronary artery disease. Eur Heart J 2010 Jan;31(1):112-119. [doi: 10.1093/eurheartj/ehp398] [Medline: 19793768]
4. Reich B, Schönfelder M, Lampl K, Mueller EE, Egger A, Niebauer J. Comparable anti-glycaemic effects of hypertrophy versus endurance resistance training in type 2 diabetes mellitus. Eur J Prev Cardiol 2020 Sep;27(14):1564-1565. [doi: 10.1177/2047487319859971] [Medline: 31219701]
5. Strauss-Blasche G, Riedmann B, Schobersberger W, Ekmekcioglu C, Riedmann G, Waanders R, et al. Vacation at moderate and low altitude improves perceived health in individuals with metabolic syndrome. J Travel Med 2004;11(5):300-304 [FREE Full text] [doi: 10.2310/7060.2004.19106] [Medline: 15544714]
6. Burtscher M. Risk of cardiovascular events during mountain activities. Adv Exp Med Biol 2007;618:1-11. [doi: 10.1007/978-0-387-75434-5_1] [Medline: 18269184]
7. Willich SN, Lewis M, Löwel H, Arntz HR, Schubert F, Schröder R. Physical exertion as a trigger of acute myocardial infarction. Triggers and Mechanisms of Myocardial Infarction Study Group. N Engl J Med 1993 Dec 02;329(23):1684-1690. [doi: 10.1056/NEJM199312023292302] [Medline: 8232457]
8. Mittleman MA, Maclure M, Tofler GH, Sherwood JB, Goldberg RJ, Muller JE. Triggering of acute myocardial infarction by heavy physical exertion. Protection against triggering by regular exertion. Determinants of Myocardial Infarction Onset Study Investigators. N Engl J Med 1993 Dec 02;329(23):1677-1683. [doi: 10.1056/NEJM199312023292301] [Medline: 8232456]
9. Assmann G, Cullen P, Schulte H. Simple scoring scheme for calculating the risk of acute coronary events based on the 10-year follow-up of the prospective cardiovascular Münster (PROCAM) study. Circulation 2002 Jan 22;105(3):310-315. [doi: 10.1161/hc0302.102575] [Medline: 11804985]
10. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive summary of the third report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). JAMA 2001 May 16;285(19):2486-2497. [doi: 10.1001/jama.285.19.2486] [Medline: 11368702]
11. Perk J, De Backer G, Gohlke H, Graham I, Reiner Z, Verschuren M, ESC Committee for Practice Guidelines (CPG). European Guidelines on cardiovascular disease prevention in clinical practice (version 2012). The Fifth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of nine societies and by invited experts). Eur Heart J 2012 Jul;33(13):1635-1701 [FREE Full text] [doi: 10.1093/eurheartj/ehs092] [Medline: 22555213]
12. Craig CL, Marshall AL, Sjöström M, Bauman AE, Booth ML, Ainsworth BE, et al. International physical activity questionnaire: 12-country reliability and validity. Med Sci Sports Exerc 2003 Aug;35(8):1381-1395. [doi: 10.1249/01.MSS.0000078924.61453.FB] [Medline: 12900694]
13. Bullinger M. German translation and psychometric testing of the SF-36 Health Survey: Preliminary results from the IQOLA project. Social Science & Medicine 1995 Nov;41(10):1359-1366. [doi: 10.1016/0277-9536(95)00115-N]
14. Bruce RA, Kusumi F, Hosmer D. Maximal oxygen intake and nomographic assessment of functional aerobic impairment in cardiovascular disease. Am Heart J 1973 Apr;85(4):546-562. [doi: 10.1016/0002-8703(73)90502-4] [Medline: 4632004]
15. Borg GA. Psychophysical bases of perceived exertion. Med Sci Sports Exerc 1982;14(5):377-381. [Medline: 7154893]
16. Schneider DA, Phillips SE, Stoffolano S. The simplified V-slope method of detecting the gas exchange threshold. Med Sci Sports Exerc 1993 Oct;25(10):1180-1184. [Medline: 8231764]
17. American College of Sports Medicine, Armstrong LE, Casa DJ, Millard-Stafford M, Moran DS, Pyne SW, et al. American College of Sports Medicine position stand. Exertional heat illness during training and competition. Med Sci Sports Exerc 2007 Mar;39(3):556-572. [doi: 10.1249/MSS.0b013e31802fa199] [Medline: 17473783]

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18. Faul F, Erdfelder E, Buchner A, Lang A. Statistical power analyses using G*Power 3.1: tests for correlation and regression analyses. Behav Res Methods 2009 Nov;41(4):1149-1160. [doi: 10.3758/BRM.41.4.1149] [Medline: 19897823]
19. Faul F, Erdfelder E, Lang A, Buchner A. G*Power 3: a flexible statistical power analysis program for the social, behavioral, and biomedical sciences. Behav Res Methods 2007 May;39(2):175-191. [doi: 10.3758/bf03193146] [Medline: 17695343]
20. Mitten D, Overholt JR, Haynes FI, D'Amore CC, Ady JC. Hiking: a low-cost, accessible intervention to promote health benefits. Am J Lifestyle Med 2018;12(4):302-310 [FREE Full text] [doi: 10.1177/1559827616658229] [Medline: 32063815]
21. Neunhäuserer D, Sturm J, Baumgartlinger MM, Niederseer D, Ledl-Kurkowski E, Steidle E, et al. Hiking in suicidal patients: neutral effects on markers of suicidality. Am J Med 2013 Oct;126(10):927-930. [doi: 10.1016/j.amjmed.2013.05.008] [Medline: 23953873]
22. Ross RM, Murthy JN, Wollak ID, Jackson AS. The six minute walk test accurately estimates mean peak oxygen uptake. BMC Pulm Med 2010 May 26;10:31 [FREE Full text] [doi: 10.1186/1471-2466-10-31] [Medline: 20504351]
23. Casanova C, Celli BR, Barria P, Casas A, Cote C, de Torres JP, Six Minute Walk Distance Project (ALAT). The 6-min walk distance in healthy subjects: reference standards from seven countries. Eur Respir J 2011 Jan;37(1):150-156 [FREE Full text] [doi: 10.1183/09031936.00194909] [Medline: 20525717]
24. Oja P, Laukkanen R, Pasanen M, Tyry T, Vuori I. A 2-km walking test for assessing the cardiorespiratory fitness of healthy adults. Int J Sports Med 1991 Aug 14;12(4):356-362. [doi: 10.1055/s-2007-1024694] [Medline: 1917218]
25. Chiaranda G, Myers J, Mazzoni G, Terranova F, Bernardi E, Grossi G, et al. Peak oxygen uptake prediction from a moderate, perceptually regulated, 1-km treadmill walk in male cardiac patients. J Cardiopulm Rehabil Prev 2012;32(5):262-269. [doi: 10.1097/HCR.0b013e3182663507] [Medline: 22936157]
26. Grazzi G, Chiaranda G, Myers J, Pasanisi G, Lordi R, Conconi F, et al. Outdoor Reproducibility of a 1-km Treadmill Walking Test to Predict Peak Oxygen Uptake in Cardiac Patients. J Cardiopulm Rehabil Prev 2017 Sep;37(5):347-349. [doi: 10.1097/HCR.0000000000000266] [Medline: 28671933]

Abbreviations

CTTT: cardio trekking test trail
DMC: dynamic mixing chamber
ECG: electrocardiography
IPAQ: International Physical Activity Questionnaire
RPE: rate of perceived exertion
SF-36: 36-Item Short Form Health Survey

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Protocol

Intervention in Older Urban-Dwelling Veterans With Dysmobility: Protocol for a Pilot Feasibility Clinical Trial

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Abstract

Background: The majority of older veterans do not meet the minimum healthy diet or physical activity recommendations despite known benefits. Identifying ways to increase adherence to programs that improve dietary quality and physical activity may reduce the risk of disability in older veterans. Peer-based interventions may be one method for facilitating lasting behavior change because peers often share a common culture and knowledge regarding problems their community experiences.

Objective: This study aims to develop, pilot, and evaluate a theory-driven, 12-week, peer-led nutrition and exercise intervention that targets older veterans with dysmobility and assess its feasibility in 2 diverse urban areas with underrepresented populations.

Methods: Community-dwelling veterans aged >65 years with self-reported dysmobility (defined as difficulty in at least 1 of the following: walking quickly across a street, walking a mile, ascending a flight of stairs, rising from a chair without the use of arms, or a fear of falling) from 2 Department of Veterans Affairs Geriatric Research, Education, and Clinic Centers (Baltimore, Maryland, and San Antonio, Texas) will be eligible to participate. First, this study will use validated mixed methods via web-based surveys (n=50 per site) to assess potential physical, social or environmental, and behavioral or lifestyle barriers that affect physical activity and dietary quality (phase 1). Next, we will use knowledge gained from these assessments and feedback from a focus group (n=10 per site) to adapt established Department of Veterans Affairs diet and exercise program materials to develop peer-led intervention materials and train peer leaders (n=3 per site). Finally, we will determine the feasibility and acceptability of the intervention to assess reach (recruitment and retention), adoption (satisfaction, perceived utility, attendance, and engagement), and implementation (fidelity of intervention), as well as the estimated magnitude and potential impact on selected outcomes (ie, diet quality and mobility) in 20 older veterans with dysmobility (n=10 per site).

Results: The study was funded on January 1, 2022, with a projected data collection period of June 1, 2022, to December 31, 2023.

Conclusions: This study offers an innovative approach to identifying strategies that increase long-term adherence to lifestyle modification programs that improve dietary quality and physical activity in older veterans with dysmobility.

Trial Registration: ClinicalTrials.gov NCT04994938; https://clinicaltrials.gov/ct2/show/NCT04994938

International Registered Report Identifier (IRRID): PRR1-10.2196/39192

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(JMIR Res Protoc 2022;11(7):e39192) doi:10.2196/39192

KEYWORDS

peer-led; veterans; dysmobility; lifestyle modification programs

Introduction

Background

US veterans are a multifaceted population with unique health challenges. The veteran population is disproportionately older men (>50% are aged >65 years) [1] who have a higher prevalence of obesity [2], multimorbidity [3], and self-reported disability or dysmobility [4] and have suboptimal dietary quality and perform less physical activity than nonveterans [5]. Decades of research has demonstrated that exercise is an effective intervention to improve mobility and overall health [6]. Despite these known benefits, the majority of older veterans do not meet the minimum physical activity recommendations for either aerobic or resistance exercises [7]. The ability to safely maintain mobility with age is critical, as immobility is the leading cause of long-term care admissions and increases fall risk, health care use, and expenditure [8]. Older adults with mobility limitations are also more likely to have poor diet quality [9]. Furthermore, as veterans are at increased risk of obesity and dysmobility, they are also more likely to have lower diet quality and deviate further from dietary guidelines than nonveterans [10]. Poor diet quality is primarily due to high consumption of empty calories from added sugar and solid fats and lower intake of fruits, vegetables, whole grains, and dairy [10]. Many well-established factors contribute to poor nutrition in aging, including physiological, social, emotional, and environmental changes [11-13]. Among older veterans with mobility limitations, these factors are further compounded by accessibility limitations and the inability to complete instrumental activities of daily living such as shopping or cooking [14].

Chronic disease and frailty are likely to develop with age, and these outcomes are associated with an increased risk of poor quality of life [15]. A recent systematic review reported strong and consistent observational evidence for a link between *healthier* diets and a lower risk of decline in physical performance [16]. Furthermore, exercise interventions in veterans have consistently been shown to improve physical performance [17]. Veteran participation in the Department of Veterans Affairs (VA) MOVE! Weight Management Program, the largest weight management program in the United States, is associated with successful short-term weight loss and greater weight loss as participation engagement increases [18]. Participation in Gerofit, a national VA exercise and health promotion program targeting older veterans with dysmobility, is associated with improved mobility [17]. Even professionally led, evidence-based lifestyle intervention programs that have a positive impact on weight management and mobility have low long-term adherence rates [19]. Therefore, identifying strategies that increase long-term adherence to programs that improve the dietary intake quality and physical activity of older veterans may reduce the risk of disability by maintaining mobility and preserving cardiovascular health with advancing age.

Objective

Peer-based interventions may be one method of facilitating lasting health behavior change, because peers often share a common culture, language, and knowledge about the problems their community experiences [20]. Group-based, peer-led lifestyle interventions are particularly well suited for older veterans, as social interaction is a powerful motivator [21]. Although previous peer-led diet and exercise interventions have been successfully implemented [22], there are numerous limitations in their design that make them suboptimal for older veterans with dysmobility. The majority of these studies targeted only diet or exercise and did not emphasize the achievement of national dietary guidelines [22]. In addition, few studies have focused directly on the unique needs of older veterans who often live in underserved areas without access to professional resources [22]. This is especially important to address, as underrepresented minority populations are projected to constitute >35% of the veteran population by 2040 [23]. These gaps in the literature provide opportunities for improvement in peer-led interventions. Our central hypothesis is that we can develop, pilot, and evaluate a 12-week, peer-led lifestyle intervention targeting older veterans in underserved minority populations with dysmobility.

Methods

Study Design and Overview

This is a multisite feasibility clinical trial pilot study. Figure 1 shows the study design, and Table 1 shows the study timeline. The study protocol follows the SPIRIT (Standard Protocol Items: Recommendations for Interventional Trials) guidelines [24]. Any deviations from the protocol, breaches of confidentiality, and reportable adverse events will be reported to the respective institutional review boards (IRBs) and data safety monitoring boards according to local policies. In addition, the data safety monitoring boards will review study-related materials at least annually and review the collected data to ensure data integrity, security, and control for quality assurance. The study is registered at *ClinicalTrials.gov* (NCT04994938). The proposed study will develop a peer-led nutrition and exercise intervention (aim 1) and will pilot and evaluate its feasibility, acceptance, and impact (aim 2) in 2 diverse urban areas with high underrepresented populations of older veterans (Baltimore, Maryland, and San Antonio, Texas). Each site will conduct the study in parallel, and the study protocol has been approved by the local IRB and the VA Research and Development Committees. As seen in Figure 1, the study is designed to be conducted over 2 stages. Stage 1 will develop a theory-driven, peer-led nutrition and exercise intervention tailored for older veterans with dysmobility (aim 1), whereas stage 2 will evaluate the feasibility, acceptability, and impact of a peer-led pilot intervention (aim 2).

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Figure 1. Study design.

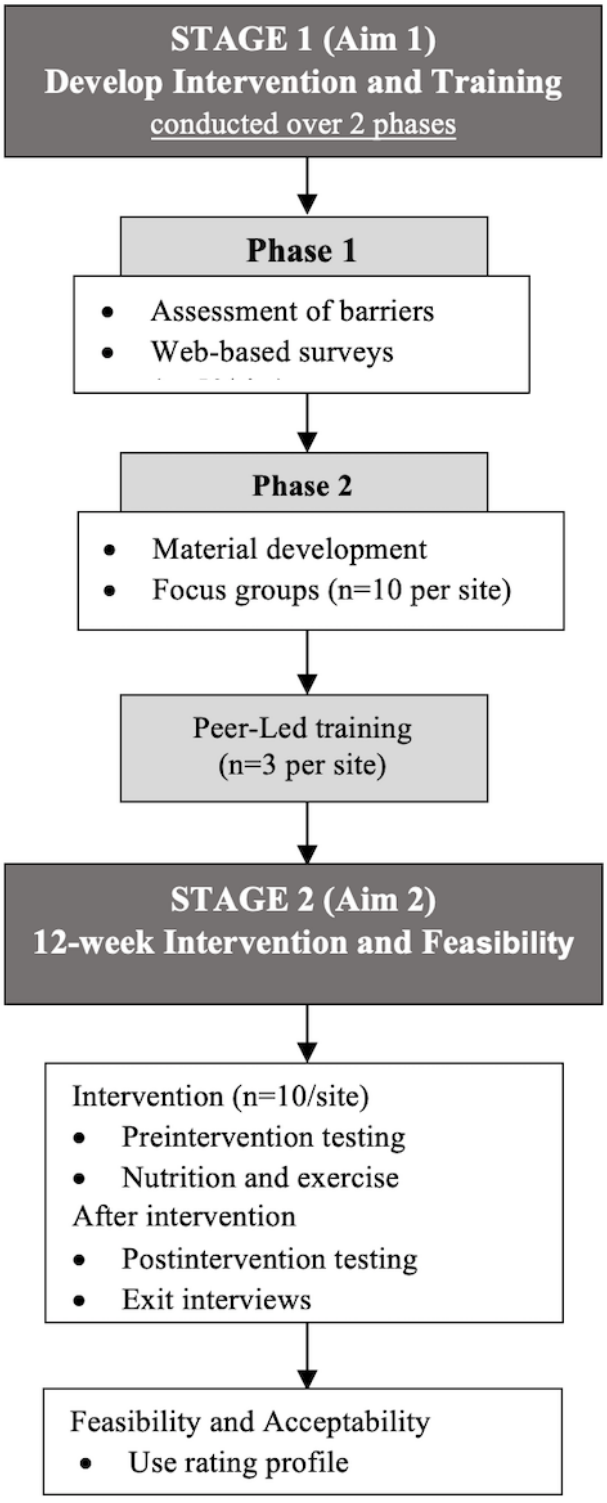

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Table 1. Study timeline.

	Yearly quarters							
	1 (n=10 per site)	2 (n=20 per site)	3 (n=20 per site)	4 (n=10 per site)	5 (n=3 per site)	6 (n=5 per site)	7 (n=5 per site)	8
Stage 1 (aim 1)								
Phase 1: web-based survey	✓	✓	✓					
Phase 2								
Material development	✓	✓	✓					
Focus groups				✓				
Peer training					✓			
Stage 2 (aim 2)								
Pretesting						✓		
Intervention						✓	✓	
Posttesting							✓	
Feasibility								✓

Study Design Stage 1 (Aim 1)

Overview

In stage 1, peer-led nutrition and exercise intervention will be achieved through a mixed methods approach that uses a concurrent nested design [25] over the following two phases: (1) phase 1 (Assessment of Barriers): using validated quantitative and qualitative assessments implemented via web-based surveys, potential physical, social or environmental, and behavioral or lifestyle barriers and facilitators that affect activity and nutrition will be assessed and (2) phase 2 (Program Adaptation and Peer Leader Training): using a task-shifting approach [26], the current VA MOVE! and Gerofit programs will be adapted based on knowledge gained in phase 1 and through focus groups to develop peer-led training materials and train peer leaders.

Phase 1: Assessment of Barriers and Facilitators

Participants and Inclusion and Exclusion Criteria

Given the web-based nature of this aim, the inclusion and exclusion criteria are minimal, and anonymous web-based surveys are exempt under local IRB guidelines. Community-dwelling veterans (male and female) aged >65 years (n=50 per site) with self-reported dysmobility (defined as difficulty in at least 1 of the following activities: walking quickly across a street, walking a mile, ascending a flight of stairs, rising from a chair without the use of arms, or a fear of falling) and the ability to take the survey in English will be recruited to complete web-based surveys.

Recruitment and Screening

Participants will be recruited from the Baltimore (Baltimore, Maryland) and Audie Murphy (San Antonio, Texas) Veterans Administration Medical Centers (VAMCs), local Geriatric Research Education Clinics Centers' registries and contacts, local veteran groups, posts in web-based forums, media advertisements, and finally through word of mouth. Those responding to recruitment efforts will be telephonically screened and asked a series of questions to determine eligibility. Individuals who meet the eligibility criteria will be invited to complete the web-based surveys.

Web-Based Surveys, Questionnaires, and Assessments

Eligible participants will provide demographic information and will self-report their medical history, current medications, and height and weight. Participants will also complete 25 to 30 minutes of validated questionnaires (Table 2) administered via the VA-approved Federal Risk and Authorization Management Program version of Qualtrics to assess potential physical (medical morbidities and physical mobility), social or environmental (food insecurity and access to exercise or recreation), and behavioral or lifestyle (physical activity, sleep disturbances, and use of television, internet, and alcohol) barriers and facilitators that may affect physical activity and dietary quality in older adults with dysmobility. In addition, participants will be provided with log-in information and asked to complete a 24-hour dietary recall [27] for the previous day using the Automated Self-Administered 24-Hour Dietary Assessment Tool [28]. Food records will be used to calculate the Healthy Eating Index score, a measure of dietary quality used to assess adherence to national dietary guidelines [29].

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Table 2. Aim 1: quantitative and qualitative measures.

Assessment measures	Description
Primary correlates	
Physical activity (Physical Activity Scale for the Elderly)	A 11-item self-report of physical activity: leisure time and household activities and optional work and volunteer activities. Good reliability, validity; brief to reduce participant burden [30].
Dietary intake quality (Automated Self-Administered 24-hour Dietary Assessment)	Validated web-based tool developed by the National Cancer Institute that enables multiple, automatically coded, and self-administered 24-hour diet recalls. The recall will be used to calculate the HEI[a]. HEI scores range from 0 to 100, with higher scores indicating better adherence to the Dietary Guidelines for Americans [28,31].
Quantitative assessments	
BMI	Self-reported height and weight (owing to survey nature of study); calculated as weight (kg) and height squared (m^2).
Demographics and history	Self-reported annual household income, education, and marital status and medical history or comorbidity, polypharmacy (ie, number of current medications), and surgeries.
Eating behaviors	
Short Healthy Eating Index	Measure of diet quality used to assess how well dietary patterns align with key recommendations of the Dietary Guidelines for Americans [32].
A 3-factor eating questionnaire	A 21-item questionnaire that measures 3 domains of eating behavior: cognitive restraint, uncontrolled eating, and emotional eating [33].
Department of Veterans Affairs binge eating screener	A single question, validated in veterans, that assesses the frequency of binge eating [33].
Barriers to diet and exercise	A total of 12 questions used in the Life Trial that assessed potential barriers and the extent of those barriers that make it difficult to change eating and exercise habits [34].
Short Food Security Scale	A 6-item survey, developed by the USDA[b] that identifies food-insecure households and households with very low food security [35].
Health and lifestyle behaviors	
Short Form Survey-12	A 12-item validated Quality of Life Questionnaire that measures 8 health domains: physical function, pain, role limitations owing to physical health problems, personal or emotional problems, emotional well-being, social functioning, energy and fatigue, and general health perceptions [36].
Alcohol Use Disorders Identification Test-3	A 10-item screening tool to assess alcohol consumption, drinking behaviors, and alcohol-related problems [37].
Television and internet use	Will be assessed through 2 multiple-choice questions: (1) On average, how long do you spend using a computer, tablet, or phone to be on the internet (eg, reading news, playing games, or watching shows) per day? and (2) How long do you spend watching television or movies per day? Response options range from none to >12 hours.
Sleep disturbance (Insomnia Severity Index-7)	A 7-item questionnaire to assess the nature, severity, and impact of insomnia and monitor treatment response in adults [38].
Depression (Center for Epidemiologic Studies Depression Scale)	A 20-item screening test for depression and depressive disorder. The CES-D[c] measures symptoms defined by the American Psychiatric Association Diagnostic and Statistical Manual for a major depressive episode [39].
Qualitative assessments	
Eating and physical activity [40]	What were the eating and physical activity habits you had before, during, and after your military service? While thinking of all these times in your life before, during, and after your military service, what eating and physical activity habits stand out to you? What do you think would help you to be more physically active? Some veterans say that they eat when they experience stress or think of things that are hard to deal with; has this ever happened to you? Can you tell me about it? What helps you the most to eat healthy and exercise? What is the biggest barrier to eating healthy and exercising?

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Assessment measures	Description
Cultural or contextual factors	What are the local norms around the perceptions of food (or meals) and physical activity in your community? How are *favorite* foods prepared and served? What are local meal patterns and food preferences? What are local perceptions of preferred body size? What value is placed on fatness?

[a]HEI: Healthy Eating Index.

[b]USDA: United States Department of Agriculture.

[c]CES-D: Center for Epidemiologic Studies Depression Scale.

At the end of the web-based quantitative assessment, participants will also be asked to schedule an interview with a research team member (MSC, LSK, or OA) to complete a qualitative assessment. The qualitative interview will occur via telephone or web-based assessment and will provide an opportunity to delve deeper into individual barriers and facilitators of healthy diet and exercise habits. The qualitative assessment questions are presented in Table 2. A concurrent nested mixed methods design will be used to conduct both quantitative and qualitative assessments in the same phase. This embedded design will allow the gathering of quantitative data on the constructs of interest, and then, using open-ended qualitative questions, more in-depth information about the data will be gathered. This embedded design uses qualitative data in a supportive role to better explain the relationships gathered from quantitative data [25].

Phase 1 Outcomes and Analysis

We will identify quantitative factors in Table 2 that correlate with low physical activity (assessed via the Physical Activity Scale for the Elderly) [30] and poor diet quality (Healthy Eating Index assessed via a validated questionnaire [32] and calculated from the Automated Self-Administered 24-Hour Dietary Assessment Tool) [28] using multiple linear regression. Qualitative analysis will be used to identify themes (see *Phase 2: Program Adaptation and Peer Leader Training* for further details). Integration of this aim will involve connecting quantitative results with qualitative findings.

Phase 2: Program Adaptation and Peer Leader Training

Overview

On the basis of the knowledge gained from phase 1, the VA MOVE! and Gerofit programs, which are currently running successfully at the Baltimore and San Antonio sites, will be adapted to develop peer leader training materials that target older veterans. Using a task-shifting approach [41], we will modify available handouts and participant resources from the MOVE! and Gerofit. Once the materials are drafted, focus groups will be conducted to provide feedback on the developed program.

Focus Group Inclusion and Exclusion Criteria, Recruitment, and Screening

A mixed group of veterans (male and female; aged >65 years) who are actively engaged in lifestyle change programs such as MOVE! or Gerofit (n=10 per site) and meet the inclusion criteria in phase 1 will be recruited to participate in the focus groups.

Focus Groups

Before completing any data collection, all focus group participants will provide written informed consent and complete the Health Insurance Portability and Accountability Act (HIPAA) authorization form. Focus groups will be led by the investigators (in-person when on-site and web-based when off-site) and will gather feedback using evidence-based materials on the content and presentation of materials, rating of acceptability, and relevance. We will ask for their input on the positives, negatives, and what was left out. In addition, we will ask them to share their favorite and least favorite parts (defined as what they liked, thought was most relevant, or thought would be most helpful and vice versa for least favorite options). Finally, we gather information on logistical considerations (eg, group vs one-on-one, in-person vs virtual, apps or trackers, frequency of meetings, and duration).

For cultural tailoring, we will consider family and community dynamics, access to resources (food and activity), materials goodness of fit (eg, written words sit better with some, whereas graphics with others or individualistic vs collectivistic cultural approaches to interventions), ways to reach the communities of interest, and language.

Outcomes and Analysis

Focus group interviews will be recorded and transcribed, and a summary template will be developed to gather key points from the interview guide. The transcripts will be coded to identify themes (eg, reported experiences) using qualitative analysis software (Atlas.ti; Scientific Software Development GmbH), review patterns in core themes, determine the degree of overlap, and develop a network diagram of interrelationships between themes. The themes will be used to describe the barriers and facilitators of diet quality, energy balance, and physical activity (Table 2) that may influence treatment.

Peer Leader Inclusion and Exclusion Criteria, Recruitment, and Training

Once materials are finalized according to focus group feedback, peer leaders (n=3 per site) will be recruited at each site from the focus groups to undergo training. Peer leaders will be selected based on (1) prior participation in a VA-directed lifestyle program for at least six months, (2) demonstration of an understanding of the importance of diet and exercise determined by a successful diet change, and (3) expression of a desire for further training in the peer leader role when approached [42]. In addition, because peer leaders will serve as aspirational behavioral role models [43], they will be selected from veterans who have been successful in making and maintaining positive changes to their diet and exercise habits and are familiar with community networks and group facilitation. Furthermore, studies suggest that peer leaders of older adults should be optimistic, inclusive, and compassionate

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[44]; therefore, we will use these qualities along with the inclusion criteria listed earlier to select and train peer leaders using need-supportive motivation strategies [43].

Peer Leader Training

Once chosen, peer leaders will provide written informed consent, complete a HIPAA authorization form, and attend a full-day virtual training workshop with peer leaders and research team members from both sites. Training will be web-based and informal, with emphasis on the provision of social support to encourage positive behavior change. A research team member with expertise in developing peer interventions will oversee the development of peer training. Peer leaders will learn the importance of physical activity and healthy eating. They will learn about the social determinants of health and discuss solutions to overcome potential physical, social or environmental, and behavioral or lifestyle barriers described among older veterans in their communities (Table 2). They will also be provided with key safety information necessary for working with older veterans with comorbid conditions (eg, diabetes) and indicators that an exercise intervention should be discontinued (eg, signs of low blood sugar). In addition, peer leaders will learn key communication skills to convey information to their peers as advocates of change. Training will consist of leading mock sessions and receiving supervision from a research team member. Mock sessions will be recorded, and the sessions will be rated against an adherence checklist.

Study Design Stage 2 (Aim 2)

Stage 2 will determine the feasibility and acceptability and the estimated magnitude of the potential impact on selected primary and secondary outcomes of the peer-led diet and exercise pilot intervention in older veterans with dysmobility.

Participants and Inclusion and Exclusion Criteria

Community-dwelling veterans (male and female) aged >65 years (n=10 per site) who self-identify as having dysmobility (same inclusion as phase 1) will be included. Exclusion criteria include (1) high cardiovascular risk (poorly controlled hypertension >160/100 mm Hg, class IV chronic heart failure, symptomatic angina at rest, or syncope in the past year without known resolution of cause); (2) use of home oxygen; (3) contraindications to an exercise intervention; (4) dementia (on medical record review or a mini-mental status exam score <25); (5) currently regularly exercising or participating in a diet or weight loss intervention; and (6) behavior that prevents group interaction.

Recruitment and Screening

Participants will be recruited using the same strategies as in phase 1. Individuals responding to recruitment efforts will initially be telephonically screened to assess their eligibility and potential interest in enrollment in the study. Individuals who pass the screening will be invited to the respective facility to sign informed consent; complete a HIPAA authorization form; provide demographics, brief medical history, and medications; and then undergo a physical examination. A Montreal Cognitive Assessment examination will be performed as part of the physical examination to screen for dementia. Participants with a Montreal Cognitive Assessment score <25 will be excluded. Participants who remain eligible will be scheduled for baseline assessments.

Baseline Assessments Measures and Subjective Assessments

A baseline assessment battery will occur before the beginning of and after the 12-week, peer-led nutrition and exercise pilot intervention. All baseline assessments and tests will be conducted at the respective facilities (Baltimore and Audie Murphy VAMCs) over 1 to 2 visits during a 1-week period and will be collected using standardized protocols and trained research team members. These assessments are described in detail in Textbox 1 and include the following domains: body composition, caloric balance, and physical function. Assistive devices will be used during the assessments of physical function as needed, with the same device used at baseline and follow-up assessments. In addition, participants will complete web-based subjective assessments (eg, surveys and questionnaires) administered via VA-approved Federal Risk and Authorization Management Program version of Qualtrics to assess potential physical, social or environmental, and behavioral or lifestyle barriers and facilitators that may affect physical activity and dietary intake quality in older adults with dysmobility. The same uestionnnaires outlined in stage 1 will be used in stage 2 (Table 2).

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Textbox 1. Aim 2: baseline and postintervention assessment measures. Assistive devices will be used as needed, with the same device used at baseline and the follow-up assessment.

Assessment measure and description

- BMI: weight (kg) will be determined at baseline and weekly during the 12-week intervention with participants dressed in light clothing without shoes. Standing height and weight will be measured using a calibrated digital scale and calculated as weight (kg)/height squared (m^2).
- Dual-energy x-ray absorptiometry: assessment of total and regional fat mass, lean tissue mass, % body fat, bone mineral content, and bone density will be completed with a whole-body dual-energy x-ray absorptiometry scan [45].
- Waist and hip circumference: will be measured using standardized techniques [46].
- Resting blood pressure: will be measured after a 10-minute rest using standardized techniques [47].
- Food recalls: instruction on completing a 24-hour dietary recall will be provided to participants by a registered dietitian. Food records will be entered and analyzed for macronutrient and micronutrient composition by using the Automated Self-Administered 24-Hour Dietary Assessment program [28].
- Physical activity: Physical Activity Scale for the Elderly 11-item self-report of physical activity: leisure time and household activities and optional work or volunteer activities. Good reliability and validity; brief to reduce participant burden [30].
- A 6-minute walk distance: assessment of submaximal aerobic capacity, measured as the distance walked quickly during a period of 6 minutes [48].
- Gait speed: assessment of functional mobility, calculated from a 4-meter walk performed at self-selected and fast walking speeds, with the average of 3 trials used [49].
- A 30-second chair stand: assessment of functional lower extremity strength. Chair stand number will be recorded as the number of chair stands achieved in 30 seconds [50].
- Timed Get Up and Go Test: assessment of mobility, balance, walking ability, and fall risk. Measured by recording the time to get up from a fully seated position, walk around a cone placed 3 meters away, and return to a seated position, with the fastest of 2 trials used [49].
- Short physical performance battery: assessment of lower extremity function. A group of measures that combines the results of the gait speed, chair stand, and balance tests [51].
- Four-Square Step Test: test of dynamic balance and lateral mobility will be used to assess fall risk and dynamic balance [52]. Measured by the time to step over 4 canes set-up in a cross on the floor with the fastest of 2 trials used.
- Handgrip strength: Measure of isometric strength level of the hand and forearm. Hand grip strength of both arms will be assessed using a handheld dynamometer. Measures will be taken in triplicate to take the average of the 3 measures [53].

Peer-Led Diet and Exercise Intervention Procedures

Peer leaders at each site will serve as event organizers, offer guidance, and demonstrate healthy eating and exercise techniques at their respective sites. Participants will meet in groups biweekly for 12 weeks with the peer leaders to learn and discuss various content dealing with diet, exercise, and managing comorbidities (approximately 20-30 minutes per session) and to participate in a group exercise session (approximately 45-50 minutes per session). To ensure peer leaders implement the diet and exercise intervention as developed and the results reflect the true test of the program, peer leaders will complete weekly fidelity checks to document adherence to topics discussed, quality of delivery, major issues, component differentiation, and participant engagement [54]. Anticipated diet themes include budget-friendly nutrition for optimal aging: nutrition basics (ie, healthy dietary patterns and hydration), recipe modification, and mindful eating. Anticipated physical activity themes include American College of Sports Medicine (ACSM) physical activity recommendations (duration, intensity, and mode), as well as problem solving focused on how to safely exercise in their home environments. Other topics included are managing common comorbidities (ie, sleep behaviors, preventing and managing diabetes, avoiding excessive sitting, and managing stress) and available community resources. Sessions will be structured as a brief overview of the topic, followed by group discussion to allow the group to openly discuss the barriers to consuming a healthy diet and following the ACSM physical activity guidelines, as well as exchange ideas to improve their diet and exercise behaviors. This group dynamic provides the participating older adults an opportunity to build their social networks and provides supportive relationships to facilitate behavior change by meeting self-selected goals. These themes will not be prescriptive and will focus on topics for each week of the program.

Postintervention Assessments Measures and Subjective Surveys

All assessment battery measures described in Textbox 1 and web-based subjective assessments (surveys and questionnaires) described in Table 2 will be repeated after the 12-week intervention period. In addition, a postintervention exit interview (both quantitative and qualitative assessments) will be conducted by a research team member to obtain direct feedback on participant experience (ie, program enjoyment, lesson applicability, confidence and willingness to implement behavior changes, and identification of additional barriers not addressed).

Outcomes and Analysis

The primary outcome will determine the feasibility and acceptability of the 12-week, peer-led intervention in older veterans with dysmobility (n=10 per site). Feasibility and

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acceptability of the peer-led intervention will be determined by assessing (1) reach (recruitment and retention), (2) adoption (satisfaction, perceived utility attendance, and engagement), (3) implementation (fidelity of intervention), and (4) estimated magnitude of potential impact on select outcomes (ie, energy balance, diet quality, and mobility). Secondary outcomes will assess (1) mobility using a standard battery of functional assessments (strength, balance, and endurance), (2) cardiometabolic risk factors (BMI, body composition, and resting blood pressure), and (3) psychological health (quality of life, fatigue, sleep quality, dietary intake and physical activity, and depression) before and after the 12-week intervention. Refer to Table 2 for web-based subjective assessments (surveys and questionnaires) and Textbox 1 for baseline and postintervention secondary outcome assessment measures.

The analysis plan includes feasibility (eg, recruitment, retention, and adherence) and acceptability using the RE-AIM (Reach, Effectiveness, Adoption, Implementation, Maintenance) framework [55]. A flowchart (ie, CONSORT [Consolidated Standards of Reporting Trials] chart) will be prepared to identify and summarize issues in recruitment and retention (record total numbers screened, numbers excluded with reasons for nonparticipation, timing and frequency of dropout, etc). Acceptable recruitment will be defined as 100% of the total targeted enrollment within 2 months of initiating recruitment efforts. Retention will be assessed by the frequency of dropouts; overall, 80% retention will be considered acceptable. An examination of attrition and exit interviews (quantitative and qualitative) will be conducted. The Usage Rating Profile-Intervention acceptability and feasibility subscales will be used to assess both peer leaders' and participants' responses to the intervention [56]. Successful adherence will be defined as participants completing at least 75% of all sessions. A random sampling of 30% of peer leader sessions will also be evaluated to determine whether peer leaders accurately covered all prescribed materials for each topic. The focus of a feasibility pilot study is to estimate the magnitude of the potential impact. Data will be inspected for out-of-range values, missing data, and internal consistency (when relevant). The clinical outcomes of interest are changes in diet quality and physical mobility after the 12-week intervention period. Similar changes in mobility with higher adherence and retention will indicate that long-term success is feasible for the program and warrants a trial with a longer duration. Summary statistics with CIs will be calculated to describe the average levels and trajectories of clinical outcomes over time. Baseline variables will be summarized, and frequency distributions will be examined for unusual data distributions or data points.

Participant Safety and Minimizing Potential Risk

The risks of participating in the research program involve minor discomforts, but these are transient. The participants will undergo procedures that involve a mild to moderate degree of risk, including questionnaires, exercise training, weight loss, mobility assessment, and dual-energy x-ray absorptiometry scans. The interviews and questionnaires in this study are time-consuming but of minimal risk. Completion of physical activity is associated with the risk of cardiovascular complications such as chest pain, heart attack, or sudden death and complications related to stress and strain of muscles, twisted ankles, or falls. The American Heart Association consensus statement on exercise standards estimates that the acute risk of sudden cardiac arrest during exercise training in participants with known cardiac disease is approximately 1 event per 60,000 hours of aerobic exercise. The risk of exercise training is greater at higher exercise intensities. This risk can be offset by prescreening the participants with medical evaluations before exercise. In addition, all leaders will undergo a competency evaluation before leading any class. Competencies will include identifying signs and symptoms of a medical emergency, how and when to call VA emergency services in the gym setting, and who should be contacted for any adverse events that are not medical emergencies and for common injuries that occur during exercise. In addition, a trained research team member (exercise physiologist or other medical professional), certified by the American Heart Association Basic Life Support, will be present during all diet and exercise sessions. The research team member will step in to assist if the health or safety of participants or peer leaders is at risk. All instances of the research team members assisting peer leaders will be documented and assessed as part of the feasibility of the study. Minimal risks associated with weight loss and body weight will be monitored to ensure that the BMI does not fall below a healthy BMI of 18.5 kg/m^2. Proper hydration guidelines will also be provided. In addition, there is a minimal risk of falling during the walking and mobility tests. A standby aid will always be present, and a gait belt will be used to increase safety when necessary. Ample rest periods will be provided to limit fatigue during testing. Finally, the 2 dual-energy x-ray absorptiometry scans will expose participants to a very small dose of ionizing radiation (0.6 mrem total) [45], which is well below the dose of a standard chest x-ray (8 mrem) [57]. Any dose of radiation could be potentially harmful; however, the radiation risk for the measurement of body composition is well within the established dosimetry of radiation guidelines and is not harmful to health or life [45].

Data Management

All participants from stages 1 and 2 will be assigned a unique code stored in a password-protected database on a VA server that has a level and scope of security that equals or exceeds that established by the HIPAA Security Rules. Data collected during the study that is not captured electronically will be entered and stored in the VA Research Electronic Data Capture. The participants' charts will be held in a locked room inside a locked cabinet at their respective facilities (Baltimore and Audie Murphy VAMCs). Access to individual participant numbers or personal identifiers will be limited to research team members who need these data to perform their roles in this study.

Ethics Approval

Each site has been approved by the local Institutional Review Board (University of Maryland School of Medicine, HP-00097187; UT Health San Antonio, 21-890E) and VA Research and Development Committees in accordance with the ethical standards of the responsible committees on human experimentation and the Declaration of Helsinki. In addition, informed consent will be obtained from each participant, and

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they will be allowed to opt out. Phase 1 (Assessment of Barriers and Facilitators) is exempt from IRB approval under local IRB guidelines because of its web-based nature, minimal inclusion and exclusion criteria, and anonymous web-based surveys [58,59].

Dissemination

The results of this study will be made available to health care professionals and the public through the National Library of Medicine PubMed Central website within 1 year after the date of publication. In addition, the findings of this study will be presented at scientific meetings. The study investigators will be responsible for writing all publications and will not use the services of professional writers.

Results

The study was funded on January 1, 2022, with a projected data collection period of June 1, 2022, to December 31, 2023. Screening and enrollment of participants for stage 1 began on June 1, 2022.

Discussion

Overview

The purpose of this study is to develop and evaluate a novel, culturally tailored 12-week, peer-led diet and exercise intervention using a mixed methods approach that targets older veterans with dysmobility in 2 diverse urban areas with a high percentage of underrepresented minority veteran populations (Baltimore, Maryland, and San Antonio, Texas). Specifically, we anticipate that the results of this pilot study will identify barriers and facilitators of physical activity and dietary intake, develop a culturally sensitive peer-led diet and exercise intervention, and determine its feasibility in older veterans with dysmobility.

Previous peer-led diet and exercise interventions have been successfully implemented [18]; however, there are numerous limitations in their targeted population and design that make them suboptimal for older veterans with dysmobility. The multitude of interventions that have attempted to address diet and physical activity in older adults were not based on professionally led, evidence-based interventions with available long-term follow-up data. They have targeted only diet (mainly weight loss) or exercise (as opposed to both) and have emphasized walking but not following the United States Department of Agriculture dietary or ACSM exercise guidelines (ie, strength, endurance, and flexibility) for older adults [22]. Participants in these interventions are predominantly female [22], which may not translate to the veteran population, which is disproportionately older men [1]. Furthermore, few have focused directly on the unique needs of older veterans who often live in underserved areas without access to professional resources [60-62]. In addition, in many of these studies, minority populations are underrepresented. Because of the unique challenges faced by this population, including equitable access to high-quality foods (ie, food insecurity and food deserts) and high obesity rates [63], the ability to translate these interventions to other populations is challenging. Inclusion of minority populations who live in underresourced areas is critical to the development of a diet and exercise program because peer-led interventions targeting this population may require a different approach compared with predominately White or nonminority populations [64]. Furthermore, few studies have examined the determinants of dietary intake and physical activity among older veterans with limited physical functioning or dysmobility. Therefore, this study is designed to specifically assess the numerous limitations of previous studies. To our knowledge, this will be the first study to develop and implement a peer-led diet and exercise intervention that uses evidence-based interventions with long-term follow-up data that target both diet quality and physical activity in older veterans living in underserved areas with dysmobility, thus filling a significant knowledge gap in the current literature.

Physicians often have little time to offer support for lifestyle counseling, especially among older adults who often have multiple chronic conditions that require time-consuming medical management. Furthermore, diet and physical activity support from other trained professionals such as registered dietitians and exercise physiologists are often not readily available in low-income urban communities [60-62]. Peer-led interventions have been used in a variety of settings including support groups with people who share life experiences (eg, substance abuse and common illness), peer mentoring or coaching, and health promotion (eg, physical activity) [43] and have been shown to effectively help individuals achieve their desired goals [65]. Peer-based interventions have the potential to facilitate long-term health behavior changes, because peers often understand the obstacles that affect their communities [20]. In addition, peer leaders can serve as relatable role models and provide emotional and social support [26] to better connect and empathize with individuals of equal status and of similar age, background, and abilities [66]. Peer leaders offer a cost-effective opportunity to promote physical activity, healthy diet behaviors, and well-being in older adults by facilitating attention, retention, and motivation in recipients [67]. We have previously shown that using experienced, doctoral-level trainers to implement a diet modification intervention did not yield superior participant outcomes compared with training implemented by trained peer leaders [26]. Studies have also shown that peer-led interventions are as effective as professionally led interventions [67] and can lead to better program retention and adherence in older adults [68]. These data support the use of peer leaders to disseminate impactful education via lifestyle programs in a cost-effective manner. Therefore, the results of this study may identify a cost-effective and easily scalable strategy that increases long-term adherence to a program that improves the dietary quality and physical activity of older veterans and may reduce the risk of disability by maintaining mobility and preserving cardiovascular health with advancing age.

Limitations

Despite its strengths, this study has potential limitations that should be considered. The behavior changes in diet and physical activity could possibly result from the veterans' knowledge of participating in the intervention. Participants could change their behavior solely because of study participation, thus skewing the results positively. Selection bias is another limitation that

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could affect the results. Individuals willing to participate in the intervention would be aware of the health benefits of a healthy diet and exercise, and thus, they may be more prone to changing behaviors. This could result in the study findings not representing the true relationship between the intervention and outcomes within the average older veteran population with dysmobility. Recruitment of peer leaders may be difficult; therefore, we will recruit the current Gerofit and MOVE! participants who successfully made and maintained positive changes in their diet and exercise habits. The selected peer leaders may be concerned about the time commitment to learn the information and lead diet and exercise sessions. Developing the materials, resources, and training modules used in diet and exercise sessions will help mitigate the perceived time requirements. In addition, we will recruit 3 peer leaders per site to help distribute time commitments and prepare for possible peer leader attention. Another limitation is the response and sampling biases associated with self-reported subjective assessments (surveys and questionnaires). To minimize these biases, we will use a multimodal approach to clinical assessment measures and validated questionnaires that have demonstrated responses that measure what they claim to measure. Finally, the underlying design of a pilot study limits the interpretation of feasibility to only the participant's characteristics and cannot be generalized beyond the inclusion and exclusion criteria.

Future Directions

This pilot study will provide preliminary evidence for a larger grant application to examine the long-term effects and maintenance of health behaviors of a peer-led intervention trial on diet quality, energy balance, and mobility in a diverse sample of older veterans, a population more likely to self-report physical disability [14] and experience higher rates of obesity and comorbid conditions than the general population [14,15]. On the basis of the findings from this project, future clinical studies may address a broader array of clinical outcomes, as well as examine the potential impact on reductions in VA health care expenditure and use owing to improvements in health. Future trials are needed to validate these findings before broad-based acceptance and dissemination across VAs can occur. Thus, the proposed research will not only provide information to the veterans participating in this study but will also lay a foundation for future research targeting underrepresented minority veterans who lack access to specialty health care and are at increased risk of dysmobility and loss of independence.

Conclusions

Our study design allows for a comprehensive assessment of complex personal and social phenomena. In doing so, the proposed study fills a critical knowledge gap in aging research by identifying and elaborating on barriers to a healthy lifestyle that may not have been captured previously in older veterans with dysmobility. Furthermore, peer-led interventions offer a potentially low-cost and easily scalable approach. This approach will encourage dietary and physical activity changes, with the goal of improving energy balance and ultimately increasing mobility in this at-risk population. As Baltimore, Maryland, and San Antonio, Texas, have a large number of typically understudied minority populations, the 2 sites will allow us to develop a program that specifically targets a group of older veterans typically excluded from lifestyle intervention trials (older urban men from minority populations with dysmobility).

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Data Availability

The final data sets underlying all publications resulting from the proposed research will be shared outside Department of Veterans Affairs. On request, a deidentified, anonymized data set will be created and shared pursuant to a data use agreement, appropriately limiting the use of the data set and prohibiting the recipient from identifying or reidentifying (or taking steps to identify or reidentify) any individual whose data are included in the data set.

Authors' Contributions

The authors RNR, MCS, and OA wrote the initial draft of the manuscript. All the other authors have reviewed and edited the manuscript. All the authors have approved the manuscript for publication.

Conflicts of Interest

None declared.

Multimedia Appendix 1
Peer-review summary statement by Rehabilitation Research and Development SPiRE Program - Rehabilitation Research and Development Parent IRG - Office of Research & Development (RRDS) (National Institutes of Health, USA).
[PDF File (Adobe PDF File), 134 KB - resprot_v11i7e39192_app1.pdf]

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References

1. Farmer C, Hosek S, Adamson D. Balancing demand and supply for veterans' health care: a summary of three RAND assessments conducted under the veterans choice act. Rand Health Q 2016 Jun 20;6(1):12 [FREE Full text] [Medline: 28083440]
2. Breland JY, Phibbs CS, Hoggatt KJ, Washington DL, Lee J, Haskell S, et al. The obesity epidemic in the veterans health administration: prevalence among key populations of women and men veterans. J Gen Intern Med 2017 Apr;32(Suppl 1):11-17 [FREE Full text] [doi: 10.1007/s11606-016-3962-1] [Medline: 28271422]
3. Boersma P, Cohen RA, Zelaya CE, Moy E. Multiple chronic conditions among veterans and nonveterans: United States, 2015-2018. Natl Health Stat Report 2021 Feb(153):1-13. [Medline: 33663648]
4. Ben-Shalom Y, Tennant JR, Stapleton DC. Trends in disability and program participation among U.S. veterans. Disabil Health J 2016 Jul;9(3):449-456. [doi: 10.1016/j.dhjo.2015.12.008] [Medline: 26847668]
5. Park S, Zhu K, Potter JF, Kolonel LN. Health-related characteristics and dietary intakes of male veterans and non-veterans in the Multiethnic Cohort Study (United States). J Mil Veterans Health 2011 Apr;19(2):4-9 [FREE Full text] [Medline: 22623947]
6. American College of Sports Medicine, Chodzko-Zajko WJ, Proctor DN, Fiatarone Singh MA, Minson CT, Nigg CR, et al. American college of sports medicine position stand. Exercise and physical activity for older adults. Med Sci Sports Exerc 2009 Jul;41(7):1510-1530. [doi: 10.1249/MSS.0b013e3181a0c95c] [Medline: 19516148]
7. Blackwell D, Lucas J. Participation in leisure-time aerobic and muscle-strengthening activities that meet the federal 2008 Physical Activity Guidelines for Americans among adults aged 18 and over, by selected characteristics: United States, selected years 1998–2014. Centers for Disease Control and Prevention. URL: https://www.cdc.gov/nchs/data/hus/2015/057.pdf [accessed 2022-06-21]
8. Gaugler JE, Duval S, Anderson KA, Kane RL. Predicting nursing home admission in the U.S: a meta-analysis. BMC Geriatr 2007 Jun 19;7(1):13 [FREE Full text] [doi: 10.1186/1471-2318-7-13] [Medline: 17578574]
9. Musich S, Wang SS, Ruiz J, Hawkins K, Wicker E. The impact of mobility limitations on health outcomes among older adults. Geriatr Nurs 2018;39(2):162-169 [FREE Full text] [doi: 10.1016/j.gerinurse.2017.08.002] [Medline: 28866316]
10. An examination of Veterans' diet quality. United States Department of Agriculture. URL: https://www.ers.usda.gov/webdocs/publications/95609/err-271.pdf?v=9205 [accessed 2022-04-05]
11. Pucciarelli D, Thomas A. Determinates that influence food comsumption among older members of a midwest community. FNS 2011;02(09):1018-1026. [doi: 10.4236/fns.2011.29136]
12. Drewnowski A, Shultz JM. Impact of aging on eating behaviors, food choices, nutrition, and health status. J Nutr Health Aging 2001;5(2):75-79. [Medline: 11426286]
13. Elsner RJ. Changes in eating behavior during the aging process. Eat Behav 2002 Mar;3(1):15-43. [doi: 10.1016/s1471-0153(01)00041-1] [Medline: 15001018]
14. Locher JL, Ritchie CS, Roth DL, Baker PS, Bodner EV, Allman RM. Social isolation, support, and capital and nutritional risk in an older sample: ethnic and gender differences. Soc Sci Med 2005 Feb;60(4):747-761 [FREE Full text] [doi: 10.1016/j.socscimed.2004.06.023] [Medline: 15571893]
15. Lee L, Heckman G, Molnar FJ. Frailty: identifying elderly patients at high risk of poor outcomes. Can Fam Physician 2015 Mar;61(3):227-231 [FREE Full text] [Medline: 25767167]
16. Bloom I, Shand C, Cooper C, Robinson S, Baird J. Diet quality and sarcopenia in older adults: a systematic review. Nutrients 2018 Mar 05;10(3):308 [FREE Full text] [doi: 10.3390/nu10030308] [Medline: 29510572]
17. Peterson MJ, Crowley GM, Sullivan RJ, Morey MC. Physical function in sedentary and exercising older veterans as compared to national norms. J Rehabil Res Dev 2004 Sep;41(5):653-658 [FREE Full text] [doi: 10.1682/jrrd.2003.09.0141] [Medline: 15558394]
18. Jackson SL, Long Q, Rhee MK, Olson DE, Tomolo AM, Cunningham SA, et al. Weight loss and incidence of diabetes with the Veterans Health Administration MOVE! lifestyle change programme: an observational study. Lancet Diabetes Endocrinol 2015 Mar;3(3):173-180 [FREE Full text] [doi: 10.1016/S2213-8587(14)70267-0] [Medline: 25652129]
19. Addison O, Serra MC, Katzel L, Giffuni J, Lee CC, Castle S, et al. Mobility improvements are found in older veterans after 6-months of gerofit regardless of BMI classification. J Aging Phys Act 2019 Dec 01;27(4):848-854 [FREE Full text] [doi: 10.1123/japa.2018-0317] [Medline: 31170861]
20. Webel AR, Okonsky J, Trompeta J, Holzemer WL. A systematic review of the effectiveness of peer-based interventions on health-related behaviors in adults. Am J Public Health 2010 Feb;100(2):247-253 [FREE Full text] [doi: 10.2105/AJPH.2008.149419] [Medline: 20019321]
21. Zubala A, MacGillivray S, Frost H, Kroll T, Skelton DA, Gavine A, et al. Promotion of physical activity interventions for community dwelling older adults: a systematic review of reviews. PLoS One 2017;12(7):e0180902 [FREE Full text] [doi: 10.1371/journal.pone.0180902] [Medline: 28700754]
22. Burton E, Farrier K, Hill KD, Codde J, Airey P, Hill A. Effectiveness of peers in delivering programs or motivating older people to increase their participation in physical activity: systematic review and meta-analysis. J Sports Sci 2018 Mar;36(6):666-678. [doi: 10.1080/02640414.2017.1329549] [Medline: 28535358]

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23. Minority Veterans report: military service history and VA benefits utilization statistics. U.S. Department of Veterans Affairs, National Center for Veterans Analysis and Statistics. 2017. URL: https://www.va.gov/vetdata/docs/SpecialReports/Minority_Veterans_Report.pdfAccessed [accessed 2022-04-04]
24. Chan A, Tetzlaff JM, Gøtzsche PC, Altman DG, Mann H, Berlin JA, et al. SPIRIT 2013 explanation and elaboration: guidance for protocols of clinical trials. BMJ 2013 Jan 08;346:e7586 [FREE Full text] [doi: 10.1136/bmj.e7586] [Medline: 23303884]
25. Advances in mixed methods research designs. In: SAGE Handbook of Mixed Methods in Social & Behavioral Research. Thousand Oaks, California: SAGE Publications; 2010.
26. Kilpela LS, Hill K, Kelly MC, Elmquist J, Ottoson P, Keith D, et al. Reducing eating disorder risk factors: a controlled investigation of a blended task-shifting/train-the-trainer approach to dissemination and implementation. Behav Res Ther 2014 Dec;63:70-82 [FREE Full text] [doi: 10.1016/j.brat.2014.09.005] [Medline: 25305538]
27. Salvador Castell G, Serra-Majem L, Ribas-Barba L. What and how much do we eat? 24-hour dietary recall method. Nutr Hosp 2015 Feb 26;31 Suppl 3:46-48 [FREE Full text] [doi: 10.3305/nh.2015.31.sup3.8750] [Medline: 25719770]
28. Kirkpatrick S, Subar A, Douglass D, Zimmerman T, Thompson F, Kahle L, et al. Performance of the Automated Self-Administered 24-hour Recall relative to a measure of true intakes and to an interviewer-administered 24-h recall. Am J Clin Nutr 2014 Jul;100(1):233-240 [FREE Full text] [doi: 10.3945/ajcn.114.083238] [Medline: 24787491]
29. Krebs-Smith SM, Pannucci TE, Subar AF, Kirkpatrick SI, Lerman JL, Tooze JA, et al. Update of the Healthy Eating Index: HEI-2015. J Acad Nutr Diet 2018 Sep;118(9):1591-1602 [FREE Full text] [doi: 10.1016/j.jand.2018.05.021] [Medline: 30146071]
30. Washburn RA, Smith KW, Jette AM, Janney CA. The Physical Activity Scale for the Elderly (PASE): development and evaluation. J Clin Epidemiol 1993 Feb;46(2):153-162. [doi: 10.1016/0895-4356(93)90053-4] [Medline: 8437031]
31. Subar AF, Kirkpatrick SI, Mittl B, Zimmerman TP, Thompson FE, Bingley C, et al. The Automated Self-Administered 24-hour dietary recall (ASA24): a resource for researchers, clinicians, and educators from the National Cancer Institute. J Acad Nutr Diet 2012 Aug;112(8):1134-1137 [FREE Full text] [doi: 10.1016/j.jand.2012.04.016] [Medline: 22704899]
32. Colby S, Zhou W, Allison C, Mathews AE, Olfert MD, Morrell JS, et al. Development and validation of the short healthy eating index survey with a college population to assess dietary quality and intake. Nutrients 2020 Aug 27;12(9):2611 [FREE Full text] [doi: 10.3390/nu12092611] [Medline: 32867172]
33. Stunkard AJ, Messick S. The three-factor eating questionnaire to measure dietary restraint, disinhibition and hunger. J Psychosom Res 1985;29(1):71-83. [doi: 10.1016/0022-3999(85)90010-8] [Medline: 3981480]
34. Welsh EM, Jeffery RW, Levy RL, Langer SL, Flood AP, Jaeb MA, et al. Measuring perceived barriers to healthful eating in obese, treatment-seeking adults. J Nutr Educ Behav 2012;44(6):507-512 [FREE Full text] [doi: 10.1016/j.jneb.2010.06.005] [Medline: 21665549]
35. Blumberg SJ, Bialostosky K, Hamilton WL, Briefel RR. The effectiveness of a short form of the household food security scale. Am J Public Health 1999 Aug;89(8):1231-1234. [doi: 10.2105/ajph.89.8.1231] [Medline: 10432912]
36. Resnick B, Nahm ES. Reliability and validity testing of the revised 12-item short-form health survey in older adults. J Nurs Meas 2001;9(2):151-161. [Medline: 11696939]
37. Higgins-Biddle JC, Babor TF. A review of the Alcohol Use Disorders Identification Test (AUDIT), AUDIT-C, and USAUDIT for screening in the United States: past issues and future directions. Am J Drug Alcohol Abuse 2018 May 03;44(6):578-586 [FREE Full text] [doi: 10.1080/00952990.2018.1456545] [Medline: 29723083]
38. Bastien CH, Vallières A, Morin CM. Validation of the Insomnia Severity Index as an outcome measure for insomnia research. Sleep Med 2001 Jul;2(4):297-307. [doi: 10.1016/s1389-9457(00)00065-4] [Medline: 11438246]
39. Lewinsohn PM, Seeley JR, Roberts RE, Allen NB. Center for Epidemiologic Studies Depression Scale (CES-D) as a screening instrument for depression among community-residing older adults. Psychol Aging 1997 Jun;12(2):277-287. [doi: 10.1037//0882-7974.12.2.277] [Medline: 9189988]
40. Breland JY, Donalson R, Dinh JV, Maguen S. Trauma exposure and disordered eating: a qualitative study. Women Health 2018 Feb;58(2):160-174 [FREE Full text] [doi: 10.1080/03630242.2017.1282398] [Medline: 28095133]
41. Patel V, Chowdhary N, Rahman A, Verdeli H. Improving access to psychological treatments: lessons from developing countries. Behav Res Ther 2011 Sep;49(9):523-528 [FREE Full text] [doi: 10.1016/j.brat.2011.06.012] [Medline: 21788012]
42. Buman MP, Giacobbi PR, Dzierzewski JM, Aiken Morgan A, McCrae CS, Roberts BL, et al. Peer volunteers improve long-term maintenance of physical activity with older adults: a randomized controlled trial. J Phys Act Health 2011 Sep;8 Suppl 2:S257-S266 [FREE Full text] [Medline: 21918240]
43. Matz-Costa C, Howard EP, Castaneda-Sceppa C, Diaz-Valdes Iriarte A, Lachman ME. Peer-based strategies to support physical activity interventions for older adults: a typology, conceptual framework, and practice guidelines. Gerontologist 2019 Nov 16;59(6):1007-1016 [FREE Full text] [doi: 10.1093/geront/gny092] [Medline: 30085074]
44. Kritz M, Thøgersen-Ntoumani C, Mullan B, McVeigh J, Ntoumanis N. Effective peer leader attributes for the promotion of walking in older adults. Gerontologist 2020 Aug 14;60(6):1137-1148. [doi: 10.1093/geront/gnaa014] [Medline: 32275315]
45. Shepherd JA, Ng BK, Sommer MJ, Heymsfield SB. Body composition by DXA. Bone 2017 Nov;104:101-105 [FREE Full text] [doi: 10.1016/j.bone.2017.06.010] [Medline: 28625918]

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46. Kuriyan R. Body composition techniques. Indian J Med Res 2018 Nov;148(5):648-658 [FREE Full text] [doi: 10.4103/ijmr.IJMR_1777_18] [Medline: 30666990]
47. Kallioinen N, Hill A, Horswill MS, Ward HE, Watson MO. Sources of inaccuracy in the measurement of adult patients' resting blood pressure in clinical settings: a systematic review. J Hypertens 2017 Mar;35(3):421-441 [FREE Full text] [doi: 10.1097/HJH.0000000000001197] [Medline: 27977471]
48. Enright PL. The six-minute walk test. Respir Care 2003 Aug;48(8):783-785 [FREE Full text] [Medline: 12890299]
49. Steffen TM, Hacker TA, Mollinger L. Phys Ther 2002 Feb;82(2):128-137. [doi: 10.1093/ptj/82.2.128] [Medline: 11856064]
50. Jones CJ, Rikli RE, Beam WC. A 30-s chair-stand test as a measure of lower body strength in community-residing older adults. Res Q Exerc Sport 1999 Jun;70(2):113-119. [doi: 10.1080/02701367.1999.10608028] [Medline: 10380242]
51. Perera S, Mody SH, Woodman RC, Studenski SA. Meaningful change and responsiveness in common physical performance measures in older adults. J Am Geriatr Soc 2006 May;54(5):743-749. [doi: 10.1111/j.1532-5415.2006.00701.x] [Medline: 16696738]
52. Dite W, Temple VA. A clinical test of stepping and change of direction to identify multiple falling older adults. Arch Phys Med Rehabil 2002 Nov;83(11):1566-1571. [doi: 10.1053/apmr.2002.35469] [Medline: 12422327]
53. Bohannon RW. Muscle strength: clinical and prognostic value of hand-grip dynamometry. Curr Opin Clin Nutr Metab Care 2015 Sep;18(5):465-470. [doi: 10.1097/MCO.0000000000000202] [Medline: 26147527]
54. Feely M, Seay KD, Lanier P, Auslander W, Kohl PL. Measuring fidelity in research studies: a field guide to developing a comprehensive fidelity measurement system. Child Adolesc Soc Work J 2017 Aug 16;35(2):139-152. [doi: 10.1007/s10560-017-0512-6]
55. Gaglio B, Shoup JA, Glasgow RE. The RE-AIM framework: a systematic review of use over time. Am J Public Health 2013 Jun;103(6):e38-e46. [doi: 10.2105/AJPH.2013.301299] [Medline: 23597377]
56. Briesch AM, Chafouleas SM, Neugebauer SR, Riley-Tillman TC. Assessing influences on intervention implementation: revision of the usage rating profile-intervention. J Sch Psychol 2013 Feb;51(1):81-96. [doi: 10.1016/j.jsp.2012.08.006] [Medline: 23375174]
57. Radiation sources and doses. United States Environmental Protection Agency. URL: https://www.epa.gov/radiation/radiation-sources-and-doses [accessed 2022-04-03]
58. Exempt human subjects research. UT Health. URL: https://www.uthscsa.edu/vpr/services/approval/human-exempt-research [accessed 2022-06-21]
59. Investigator Manual. University of Maryland. URL: https://www.umaryland.edu/media/umb/oaa/hrp/documents/investigator-manual/HRP-103---Investigator-Manual.pdf [accessed 2022-05-06]
60. Coonrod BA, Betschart J, Harris MI. Frequency and determinants of diabetes patient education among adults in the U.S. population. Diabetes Care 1994 Aug;17(8):852-858. [doi: 10.2337/diacare.17.8.852] [Medline: 7956630]
61. Fitzgerald JT, Anderson RM, Funnell MM, Arnold MS, Davis WK, Aman LC, et al. Differences in the impact of dietary restrictions on African Americans and Caucasians with NIDDM. Diabetes Educ 1997;23(1):41-47. [doi: 10.1177/014572179702300104] [Medline: 9052053]
62. Raymond NR, D'Eramo-Melkus G. Non-insulin-dependent diabetes and obesity in the Black and Hispanic population: culturally sensitive management. Diabetes Educ 1993;19(4):313-317. [doi: 10.1177/014572179301900411] [Medline: 8370335]
63. Sansom G, Hannibal B. Disparate access to nutritional food; place, race and equity in the United States. BMC Nutr 2021 Jun 29;7(1):29 [FREE Full text] [doi: 10.1186/s40795-021-00434-2] [Medline: 34183071]
64. Choudhury S, Brophy S, Fareedi MA, Zaman B, Ahmed P, Williams DR. Intervention, recruitment and evaluation challenges in the Bangladeshi community: experience from a peer lead educational course. BMC Med Res Methodol 2008 Oct 09;8:64 [FREE Full text] [doi: 10.1186/1471-2288-8-64] [Medline: 18844992]
65. Layne JE, Sampson SE, Mallio CJ, Hibberd PL, Griffith JL, Das SK, et al. Successful dissemination of a community-based strength training program for older adults by peer and professional leaders: the people exercising program. J Am Geriatr Soc 2008 Dec;56(12):2323-2329. [doi: 10.1111/j.1532-5415.2008.02010.x] [Medline: 19112654]
66. Thøgersen-Ntoumani C, Quested E, Biddle SJ, Kritz M, Olson J, Burton E, et al. Trial feasibility and process evaluation of a motivationally-embellished group peer led walking intervention in retirement villages using the RE-AIM framework: the residents in action trial (RiAT). Health Psychol Behav Med 2019 Jun 17;7(1):202-233 [FREE Full text] [doi: 10.1080/21642850.2019.1629934] [Medline: 34040848]
67. Ginis KA, Nigg CR, Smith AL. Peer-delivered physical activity interventions: an overlooked opportunity for physical activity promotion. Transl Behav Med 2013 Dec;3(4):434-443 [FREE Full text] [doi: 10.1007/s13142-013-0215-2] [Medline: 24294332]
68. Dorgo S, King GA, Brickey GD. The application of peer mentoring to improve fitness in older adults. J Aging Phys Act 2009 Jul;17(3):344-361. [doi: 10.1123/japa.17.3.344] [Medline: 19799104]

Abbreviations

ACSM: American College of Sports Medicine

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CONSORT: Consolidated Standards of Reporting Trials
HIPAA: Health Insurance Portability and Accountability Act
IRB: institutional review board
RE-AIM: Reach, Effectiveness, Adoption, Implementation, Maintenance
SPIRIT: Standard Protocol Items: Recommendations for Interventional Trials
VA: Veterans Affairs
VAMC: Veterans Administration Medical Center

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Protocol

Adding Mobile Elements to Online Physical Activity Interventions Targeted at Adults Aged 50 Years and Older: Protocol for a Systematic Design

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Abstract

Background: Physical activity (PA) can increase mental and physical health in adults aged 50 years and older. However, it has been shown that PA guidelines are often not met within this population. Therefore, our research group developed 2 computer-tailored intervention programs in the last decade to stimulate PA: Active Plus and I Move. Although these programs were proven effective, positive effects diminished over time and attrition rates were relatively high. To respond to this, we will integrate 3 interactive mobile elements into the existing programs: activity tracker, ecological momentary intervention program, and virtual coach app.

Objective: The goal of the research is to define systematic and evidence-based steps for extending our online computer-based PA intervention programs with 3 interactive mobile elements.

Methods: Components often included in other (eHealth) design models were identified as key components and served as a base for the definition of systematic steps: exploration of context, involvement of the target population, prototype and intervention testing, and implementation. Based on these key components, 10 systematic steps were defined. The initial step is a literature search, with the results serving as a base for development of the low-fidelity prototypes in step 2. The pilot phase comprises the 3rd to 6th steps and includes semistructured interviews, pilot tests, and adaptations of the prototypes with intensive involvement of the target population of adults aged 50 years and older, where particular attention will be paid to lower educated persons. The 7th step is an effect evaluation in the form of a randomized controlled trial. During the 8th step, the most effective intervention programs will be selected and reinforced. These reinforced intervention programs will be used during the design of an implementation plan in the 9th step and the subsequent field study in the 10th step.

Results: The project will be executed from December 2019 to December 2023. During this period, the systematic approach presented will be practically executed according to the methodological procedures described.

Conclusions: Based on the 4 identified key components, we were able to design an evidence-based systematic design approach for separately adding 3 mobile elements to our existing online PA intervention programs. The 10 steps are presented as a useful approach to guide future eHealth design studies.

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KEYWORDS

mHealth; eHealth; physical activity; older adults; design protocol

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Introduction

Stimulation of physical activity (PA) in adults aged over 50 years can result in health benefits, improved mood, an increase in self-esteem, and improved quality of life [1]. Furthermore, sufficient PA in adults aged over 50 years has been shown to help maintain physical and cognitive function thereby reducing the risk of falls and dementia, both major obstacles for retaining independence [2]. The World Health Organization recommends that adults engage in PA of moderate intensity for at least 150 minutes every week, spread over several days. In addition, bone and muscle strengthening activities are recommended at least 2 times per week, with older adults supplementing the regimen with balance exercises [3]. Globally, the trend is that older adults meet these guidelines less often since they engage in less PA than younger adults and this gap increases with age [4]. In addition, taking into account that the older population is growing faster than the total population in most regions of the world [5,6], it is clear that stimulation of PA among people aged over 50 years is of major relevance.

In the last decade, eHealth interventions, also known as digital health interventions, are emerging as a cost-effective and accessible method for PA promotion. It has been shown that such interventions are promising in increasing PA levels, especially when they are based on solid theory and use behavior change techniques that are evidence-based [7-9]. In recent years, our research group has developed several effective theory-based eHealth intervention programs for a variety of populations [10-14]. Relevant for this study are Active Plus and I Move. Active Plus is a web-based computer-tailored intervention program to promote PA among people aged older than 50 years [11,15]. Preceded by a questionnaire comprising questions on factors such as current PA levels and perceived PA beliefs and barriers, a computer-tailoring program generates and sends personalized advice, tips, and exercises based on these responses. Participants receive this tailored advice 3 times, where the information is based on the participant's motivational stage of change, their motives and beliefs about being physically active, their self-efficacy levels, and the influence of their social environment [16]. The Active Plus intervention program is further based on the theory of planned behavior [17], social cognitive theory [18], and the health belief model [11,19]. On the contrary, I Move [10,20] is a more interactive and autonomy-supporting eHealth intervention program for adults based on the self-determination theory [21] and motivational interviewing [10,22]. I Move entails 4 automated text- and video-based sessions during which participants answer several questions. Since they receive directly tailored feedback messages based on the answers of these questions, a motivational dialogue is simulated between the intervention program and the participant [10]. Participants are recommended to follow Active Plus and I Move via a computer, laptop, or tablet, as it is not suitable to be used on a smartphone. Both these intervention programs were systematically developed using the intervention mapping (IM) protocol [23].

Although Active Plus and I Move have been proven effective in increasing levels of PA in the short term [15,20], these positive intervention effects decreased when follow-up time increased, which is in line with conclusions of meta-analyses [24,25]. However, maintenance of behavioral intervention effects is of major importance to achieve an impact on public health [26]. One possible explanation for the decrease in effectiveness can be found in the high attrition rates often seen in studies investigating the effects of eHealth interventions [27].

Besides computer-based eHealth interventions, mobile technologies known as mHealth have recently emerged as another promising method for stimulation of PA. Several studies have already proved the effectiveness of mobile technologies in stimulating PA in a variety of populations [28-33]. These positive effects can be explained by the increasing use of smartphones among all populations and, as a result, a more pronounced just-in-time and interactive nature of mobile technologies compared to the less flexible and in-time computer-based technologies. Although PA intervention programs including both computer and mobile technologies are emerging in recent years, they are still less common compared to intervention programs where only one of the technologies is used. Based on earlier research, it can be expected that eHealth and mHealth technologies reinforce each other when they are combined within one PA intervention program [34]. As a result, both short-term and long-term intervention effects and user engagement are expected to increase when compared to an intervention where only one of the methods is used. The mHealth technologies have several advantages such as just-in-time information, interactivity, and adaptiveness [35].

One promising mHealth technology is an activity tracker, which incorporates elements for self-monitoring, goal-setting, and feedback and have been shown to be an effective tool for increasing PA [32,36]. Effectiveness is further increased when combined with a mobile app, giving more detailed readily available feedback on a larger screen compared with the screen of the tracker [36]. Advantages of these trackers are that they enable objective measurements of PA behavior, passive data gathering without the need of active input of the participant, and the possibility to provide just-in-time tailored feedback on PA (eg, on the number of steps taken that day) [37,38]. Importantly, earlier research has shown that older adults are willing to use this technology [39-41].

Second, ecological momentary interventions (EMI) have emerged in recent years to stimulate PA. Within an EMI program, short questionnaires are send to a participant during the day to investigate their personal situation at that moment. Based on the answers, a tailored PA message that takes into account the current personal situation of a participant can be delivered. The benefit of such programs is that they can deliver just-in-time tailored messages to create self-awareness and provide strategies for being physically active. As a result, they can deliver feedback when a difficult situation occurs and give tips to overcome barriers or avoid risks related to PA [42,43]. In contrast to the passive data collection of activity trackers, EMI demands a more active contribution from a participant to get insight in relevant situations or moods that may relate to PA behavior, since they are asked to complete short questionnaires several times per day. The delivery of these questionnaires is known as ecological momentary assessment. To our knowledge, not much research has been done regarding the use and

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acceptance of smartphone-based EMI programs for PA promotion in the population of adults aged over 50 years. However, the study by King et al [44] showed promising results regarding the use and acceptance of handheld computers to promote PA in underactive older adults.

Furthermore, interactive virtual coach apps (using chatbots) are promising technologies to improve PA behavior [45]. A chatbot delivers persuasive tailored PA chat messages via a smartphone app to participants throughout the day. Message selection can be based on variables like step count measured via an app and machine learning algorithms [45,46]. These algorithms adaptively learn which message will be the most persuasive, given the specific context and preferences of an individual and taking into account previous responses to the messages. A possible benefit of this app compared with activity trackers and EMI is the ability to calculate and deliver the most effective, adaptive, tailored, and persuasive messages in an unobtrusive and familiar way at specific time points throughout the day without any active input from the user.

During this study, our existing computer-based intervention programs Active Plus and I Move will be enriched with 1 of 3 previously mentioned mobile-based elements, either an activity tracker, EMI program, or virtual coach app (using a chatbot). This will result in 3 new versions of both Active Plus and I Move. The use of a systematic approach for the renewal of the intervention programs is considered essential since this contributes to the preservation of the proven effectiveness of the Active Plus [15] and I Move [20] intervention programs. In recent years, several systematic design models applicable to eHealth and mHealth intervention development were presented in the literature [23,47,48]. In particular, intervention mapping, used in the development of Active Plus and I Move, is frequently applied [23]. The aim of our study is to add the mobile elements separately on top of the existing, retained, and IM-based Active Plus and I Move intervention programs. As a result, we are building on the previous IM results during the integration of mobile elements with the existing online PA intervention programs. To retain the effectiveness of the existing programs, the use of a systematic design approach was considered essential. Therefore, the aim of this study was to define systematic and evidence-based steps for integrating the 3 mobile elements with the computer-based Active Plus and I Move intervention programs based on the combined insights of earlier presented design models and protocols. The aim of this paper is to present the defined systematic design steps and the associated methodological procedures.

Methods

Defining the Steps of the Systematic Approach

Identification of Key Components

To define the design steps of our systematic approach, we used several existing models and protocols as a base. Examples are the more general IM protocol as well as models specifically for the development of eHealth and mHealth interventions, such as the spiral technology action research model, the CeHRes (Center for eHealth Research and Disease Management) roadmap [37], and the behavioral intervention technology model [49,50].

Although these models differ regarding the number of steps included and specific objective, key components recur in several models and can be identified. These key components served as a base for the subsequent definition of the systematic design steps for integration of the mobile elements with the existing online intervention programs within this study.

Exploration of Context

Exploration of context, where relevant information related to the topic is collected, was identified as an important initial step for a design process prior to starting the development of the first prototypes [23,37,51]. eHealth design studies often refer to a preparatory phase where a literature study is performed, the expertise of professionals is used, and the preferences of the target population are assessed [52,53]. Although these elements are mainly included during a preparatory phase, it is important to keep up with published evidence throughout the process, since it can alert developers to issues that might impact continuation of the development process [54]. This might lead to different (intervention) strategies.

Involvement of the Target Population

Involvement of the target population, also known as participation [23,55], is considered the key component for eHealth design and is therefore included in the design approach presented here. Research shows that when beneficiaries are involved in the design and dissemination of online health interventions and elements, the outcomes are more likely to be successful [56,57]. Additionally, it has been shown that older adults interact differently with information technology compared to younger people [58,59]. Therefore, interviews, focus groups, and pilot tests among the target population could be valuable to include in a design process. With our initial eHealth intervention programs, we are aiming to reach all people aged 50 years and older, regardless of gender, level of education, socioeconomic status, and activity level. Since it has been shown that digital interventions are less often used by vulnerable older adults with low education and low eHealth literacy [60], the focus should be on the preferences of this population to improve accessibility. By involving the target population (especially laggards in the use of digital apps) in the design process, higher rates of usability are expected, defined as “the extent to which a user can use a product to achieve specific goals with effectiveness, efficiency, and satisfaction” [61].

Prototype and Intervention Testing

Another important component during an eHealth design process is intervention testing [51]. First, iterative cycles of pilot testing of prototypes contribute to the improvement of the intervention. Additionally, low-fidelity prototypes could be tested during interviews and focus groups among the target population to provide visualization of the ideas, elicit preferences and requirements, and support the creative process [52]. Finally, the effects of the developed interventions should be evaluated in a large-scale [23] randomized controlled trial (RCT) [51,62].

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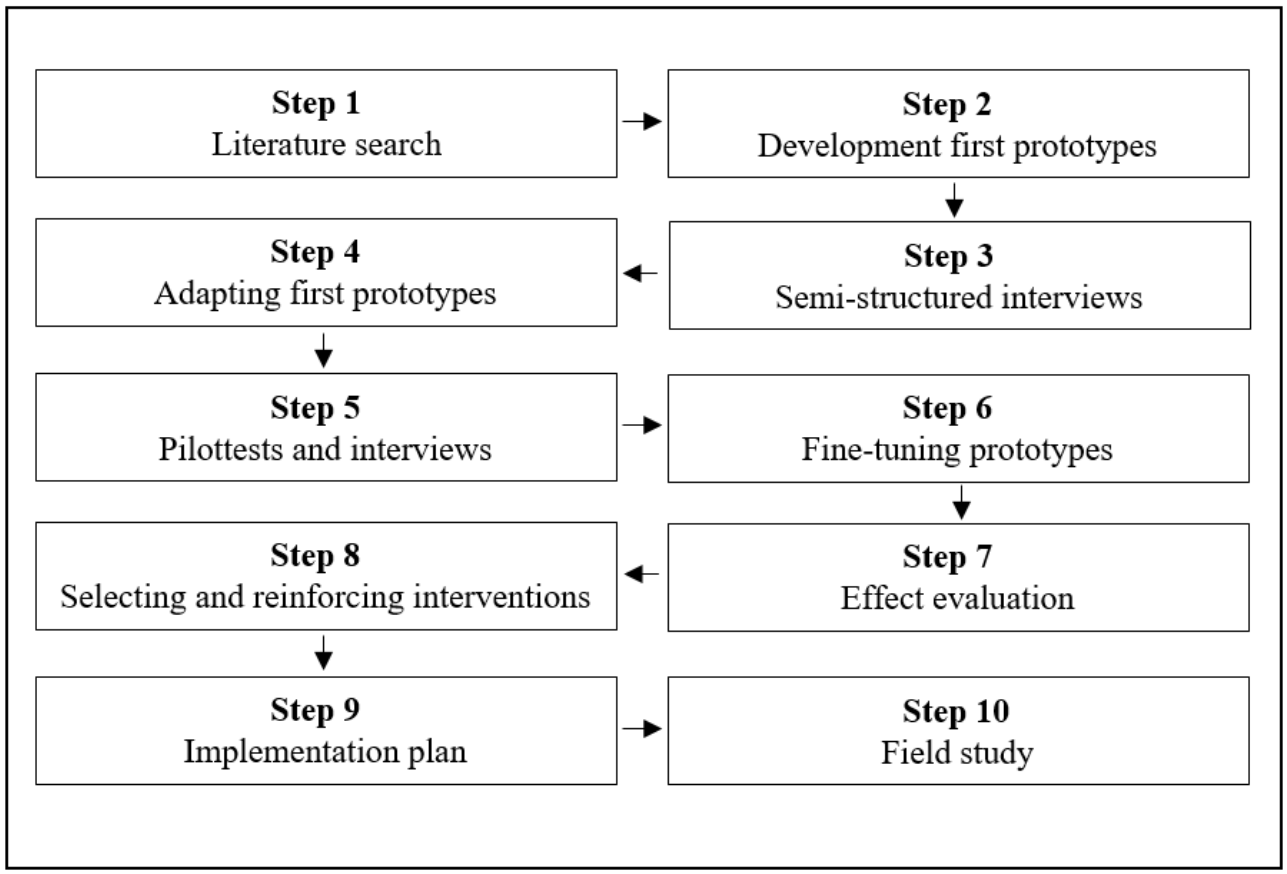
Implementation

Evaluation of a new intervention in a research setting is not the end point of a development process. After showing the effectiveness of an experiment, it is important that the intervention is implemented in practice [54]. A detailed plan summarizing the factors that facilitate or impede implementation is needed to embed the new intervention in practice and overcome the research-practice gap. During development of this implementation plan, the use of validated tools, such as the IM protocol [23], eHealth implementation toolkit [63], readiness for implementation model [64], and NASSS framework [65], could be considered to increase the odds of success.

Steps in the Systematic Approach

The 4 key components were used as a base for defining the steps of our systematic approach: (1) exploration of context, (2) involvement of the target population, (3) prototype and intervention testing, and (4) implementation. Based on these key components, in combination with the more traditional steps in systematic intervention development, 10 evidence-based steps for extending our online PA intervention programs with mobile elements were defined. Figure 1 provides a schematic overview of the design steps.

Figure 1. Overview of design steps.



Step 1: Literature Search

Literature searches will be performed per additional mobile element. For all 3 elements, the existing literature on attitude, usefulness, and ease of use regarding the mobile element within our target population of adults aged over 50 years will be searched. Additionally, for the activity tracker, we will investigate whether specific design features and preferences need to be taken into account for this population during selection of an appropriate tracker. This will be complemented with a commercial market study to select appropriate devices that match the earlier identified design features and preferences. For the EMI element, the existing literature regarding barriers and motivators for adults aged over 50 years to participate in PA will be searched to serve as a base for development of the ecological momentary assessment questionnaire and the EMI messages. Additionally, earlier published studies related to EMI interventions will be investigated on relevant design guidelines for the development of our own program. For the chatbot element, an already existing app originally developed for the Supreme Nudge project [45] will be used as a starting point. This chatbot consists of 2 apps, a step count app and a chat app to deliver the persuasive messages. Literature regarding this project will be thoroughly searched and a more general literature search on chatbots in relation to PA will be conducted. Last, a literature search will be conducted to acquire more knowledge on particular design guidelines to reach adults aged over 50 years with lower levels of education and low eHealth literacy or digital skills.

Step 2: Development of First Prototypes

Based on the results of the literature search, the additional mobile elements will be designed and subsequently integrated with both Active Plus and I Move. To secure the privacy of

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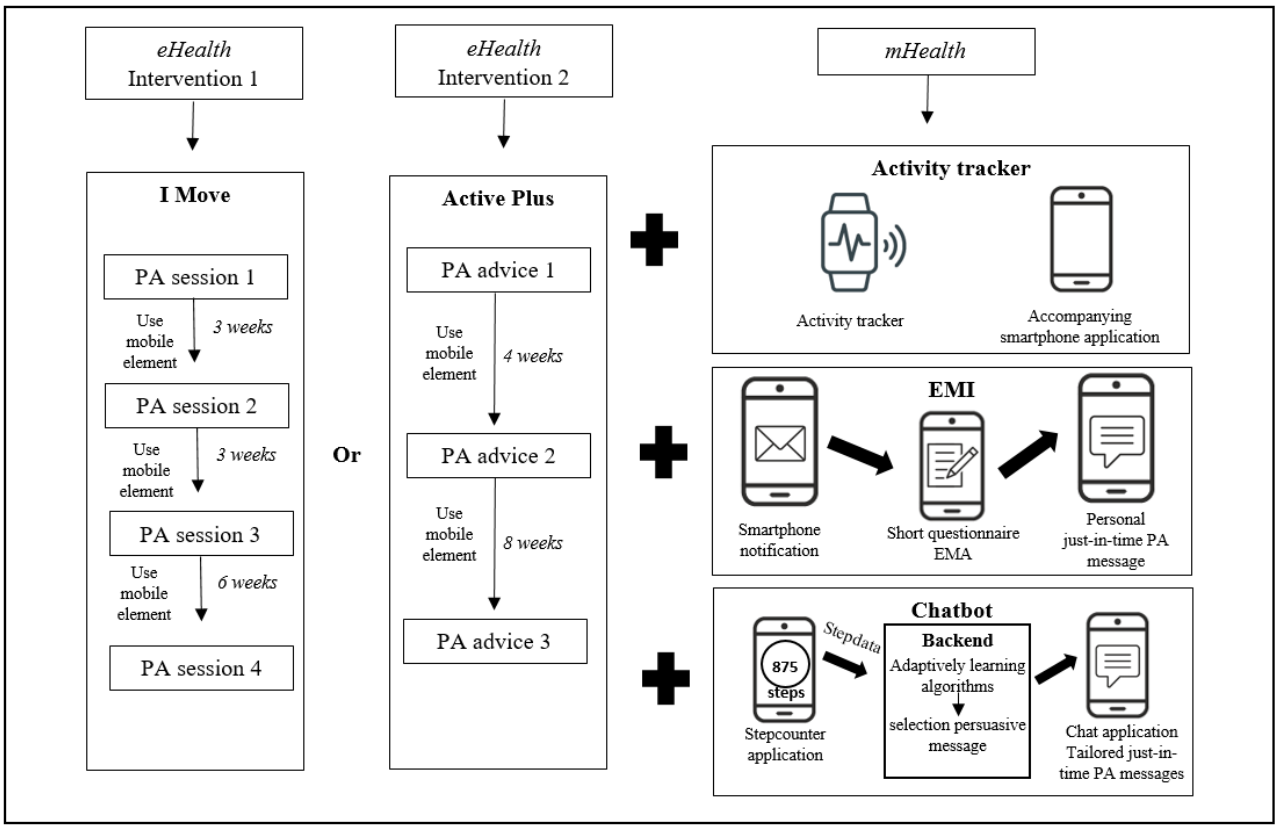
users, a detailed data management plan based on the General Data Protection Regulation was prepared prior to the start of our study and will be followed during the complete practical execution of the design approach.

For the activity tracker, the literature search comprises among other things the selection of an appropriate tracker; costs will be considered due to attainable future implementation. The results of the literature search regarding EMI will be used to choose an appropriate technical format and protocol to deliver the prompts, develop an assessment questionnaire, and identify relevant topics for the advisory intervention messages. An already existing chatbot comprising step count and chat apps [45] will be adapted to fit into the current online PA intervention programs. Messages related to manually mapped GPS locations will, for example, be replaced by location-based weather messages in order to enable a recruitment procedure at a national level at later stages of the study.

For all elements, linked components between the mobile element and the existing online PA intervention programs will be designed to improve the degree of interplay. An example of this interplay is the addition of advice related to the mobile element within the intervention programs. Furthermore, information and instruction manuals will be developed based on the guidelines for lower-literate users resulting from the literature search. In addition to the results of the literature search, software capabilities and privacy guidelines will be considered during the development of the prototypes. In the end, this will result in 3 extended low-fidelity prototype versions per eHealth intervention program: (1) Active Plus or I Move including activity tracker, (2) Active Plus or I Move including EMI, and (3) Active Plus or I Move including chatbot. An overview of the different mobile elements and online intervention programs is shown in Figure 2.

Figure 2. Overview of interventions. EMA: ecological momentary assessment; EMI: ecological momentary intervention; mHealth: mobile health; PA: physical activity.



Steps 3 and 4: Semistructured Interviews and Adapting First Prototypes

The next step is the organization of interviews among adults aged over 50 years. Thus, from this step on, the target population will be intensively involved in the design process. The aim is to include a sample of adults aged over 50 years that varies by characteristics such as level of education, age, gender, PA levels, and digital skills. The purpose of the interviews is to improve usability and acceptability of the low-fidelity prototypes for the target population. Participants will test parts of the prototypes and answer questions based on a semistructured interview protocol. Topics such as usability, ease of use, attitude, (privacy related) concerns, preferences, capabilities and needs regarding the mobile elements, and the combination with Active Plus and I Move will be covered. During development of the semistructured interview protocol, validated tools such as the System Usability Scale [66] and theoretical models such as the technology acceptance model [67] will be used as guidelines. The results of the interviews will be used to further refine the set of core components based on the needs of the target population and improve the low-fidelity prototypes of the updated versions of Active Plus and I Move.

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Steps 5 and 6: Pilot Tests, Interviews, and Fine-tuned Prototypes

The adapted prototypes of the 3 new versions each of Active Plus and I Move will be pilot-tested among the target population of adults aged over 50 years. Participants will be recruited via social media advertisements and after registration equally divided among the following research groups (n=10 per group): (1) Active Plus including activity tracker, (2) Active Plus including EMI, (3) Active Plus including chatbot, (4) I Move including activity tracker, (5) I Move including EMI, and (6) I Move including chatbot. The original intervention programs have a duration of 12 weeks, but for the pilot test, a shortened 2-week version with a focus on the interplay between the online PA intervention program and the mobile element will be used.

After registration, participants will receive an information package comprising an information letter, instructions for the mobile element, and a daily testing diary. Additionally, participants allocated to the activity tracker groups will receive a tracker with the information package. No additional materials beyond the instruction manuals are needed for the EMI or chatbot element. Participants will complete the computer-based baseline questionnaire (T0). Participants will then gain access to the first online advice session of either Active Plus or I Move. During the advice session, they will receive information and instructions regarding the added mobile element. They will then use the assigned element for 2 weeks and complete a daily entry in the testing diary (Multimedia Appendix 1). After the 2 weeks, participants will be invited via email to complete the second online advice session. This advice includes advisory texts focused on the mobile element they received. For example, for the activity tracker and chatbot groups, additional information on step count will be provided, since both elements are able to measure this. After the second advice session, participants will complete a more extensive questionnaire investigating effects, usability, and acceptability of the intervention program and the added mobile element (Multimedia Appendix 2). This questionnaire will be composed based on validated tools such as the System Usability Scale [66] and theoretical models such as the technology acceptance model [67]. After the pilot tests, a sample of participants (who provided consent) will be invited for an interview to gather qualitative in-depth information regarding their experiences. For these interviews, semistructured discussion guides will be developed specifically for the assigned mobile element.

Step 7: Effect Evaluation

During the seventh step of the design process, the effects and usability of the extended intervention programs will be evaluated by means of an RCT. The trial consists of 3 experimental conditions and one waitlist control group. According to our sample calculation (effect size=0.3; β=0.8) and taking into account a commonly reported attrition rate of 40% within eHealth studies [15,20], 200 participants will be included per arm. The following experimental conditions will be tested: (1) online PA intervention program including activity tracker, (2) online PA intervention program including EMI, and (3) online PA intervention program including chatbot. Within these conditions, there are 2 subconditions: Active Plus (n=100) and I Move (n=100). Eligible participants are 50 years or older; able to use a computer, laptop, or tablet; and have a smartphone. The aim is to have a varied research group in terms of gender, age, level of education, etc. In order to reach a varied sample of participants, a detailed recruitment plan will be made prior to the trial.

Interested people who meet the inclusion criteria can register via a website where they sign an online informed consent and enter some personal details. Subsequently, automatic randomization will take place within the software of the online PA intervention programs. First, an accelerometer (GT3X-BT, ActiGraph LLC) with instructions and a return envelope will be sent to participants to gain insight in their current PA behavior. Participants are instructed to wear the accelerometer for 7 days. Around the seventh and last day of wearing the accelerometer, participants will receive an information package via post that includes for all groups a more specific information letter and credentials for Active Plus or I Move. Additionally for the experimental groups, materials needed for the assigned mobile element are included. Participants are instructed to complete the baseline questionnaire T0 after finishing the 7-day accelerometer wear period. This questionnaire can be accessed by logging in with the credentials for either Active Plus or I Move. Subsequently, participants in the experimental conditions will follow the intervention programs, which have a total duration of 12 weeks. All research groups will complete follow-up questionnaires 3 months (T1) and 6 months (T2) after baseline. The week before questionnaire T2, participants will again receive an accelerometer via post with instructions to wear it again during a preset period of 7 days. The waitlist control group will receive the Active Plus advice combined in 1 advice after completion of the last measurement (T2).

The primary outcome will be PA behavior, which will be subjectively assessed via the validated Short Questionnaire to Assess Health-Enhancing Physical Activity (SQUASH) [68] at T0, T1, and T2 and objectively measured with an accelerometer at T0 and T2. Secondary outcomes, measured at T0, T1, and T2, will be intention to be physically active, commitment toward being physically active, and self-efficacy related to PA. Additionally, factors such as usability of and engagement with the interventions and specifically the mobile elements will be tested in the experimental conditions using evaluation questionnaires during T1 and T2 (Multimedia Appendix 3). Examples of questions are “I would like to continue using the activity tracker/EMI/chatbot” (5-point scale: 1=completely disagree to 5=completely agree), “What improvements can be made to the program you have followed?” (open question), and “How much fun did you have using the activity tracker/EMI/chatbot?” (1-10 rating). Last, use of the interventions and dropout of participants will be assessed based on process evaluation data. An overview of the research design of the RCT is shown in Figure 3.

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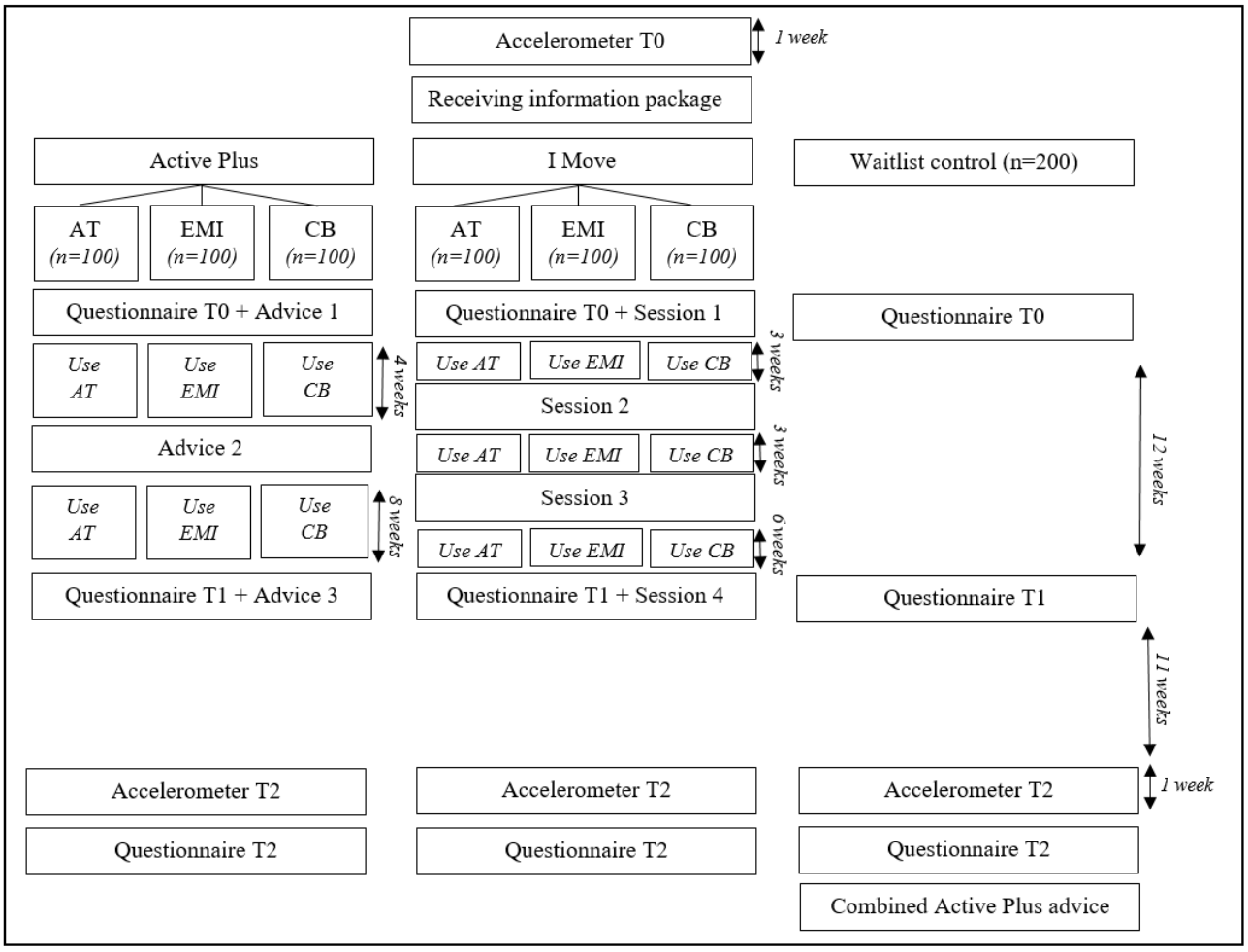
Figure 3. Schedule of procedures. AT: activity tracker; CB: chatbot; EMI: ecological momentary intervention



Step 8: Selecting and Reinforcing the Interventions

During a data science–oriented parallel study of the project, the most effective components of previous online PA interventions (eg, Active Plus and I Move) without the added mobile elements are identified by using Bayesian network analyses. For these analyses, 8 large-scale existing data sets from 5 proven effective online interventions to stimulate PA (N>5000), developed and conducted by our research group, will be merged into an integrated data set and analyzed [15,20,69-71]. This will provide knowledge on which relevant demographic factors (eg, age, gender, education), determinants of PA, and behavior change techniques are most relevant to increase intervention use and PA among adults and older adults to enhance both effect sizes and effectiveness of online computer-tailored PA intervention programs. More detailed information regarding these data analyses and preliminary results is published elsewhere [72]. The most suitable mobile element resulting from the effect evaluation of step 7 will then be added to the strengthened intervention programs. These reinforced intervention programs will be pilot-tested for effects, usability, and acceptability (n=30).

Step 9: Implementation Plan

In the ninth step, a detailed implementation and dissemination plan will be written for using the reinforced intervention programs in practice. This is a preparatory phase for the field study in the tenth step. Several steps are included during the development of this implementation plan according to the implementation mapping protocol [73] and the NASSS (nonadoption, abandonment, scale-up, spread, sustainability) framework [65]. Program adopters and implementers are already identified since they are part of our consortium. In cooperation with these already identified adopters and implementers, more potentially relevant stakeholders will be identified. Their needs and perceived barriers and facilitators regarding the implementation will then be assessed via interviews and group sessions. Based on the insights gained, appropriate previously proven effective implementation strategies will be selected [74] and a detailed implementation plan will be developed. As a result, it is expected that as the feasibility in practice improves, the facilitators of adoption are better embedded for use of the intervention programs in practice [75,76], and the research-practice gap diminishes.

Step 10: Field Study

The 2 reinforced intervention programs will be tested and implemented in practice according to the implementation plan created in step 9. Both interventions will be tested (n=200 per intervention) with main assessments in the form of questionnaires at baseline (T0), 3 months postbaseline (T1), and 6 months postbaseline (T2). Factors such as PA (SQUASH [68]), intention to participate in PA, and PA-related self-efficacy will be assessed. The aim is to provide insight into whether the

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adaptations result in a practical setting in increased use of the interventions, PA levels, and maintenance of PA levels and in decreased dropout compared to the original online interventions without mHealth apps. Since the main focus is on implementation in the field, no control groups will be included during this phase. The results will be compared with the already available detailed data on use of the original Active Plus and I Move intervention programs and effects and effect sizes of previous versions of the intervention programs. As a result, studying whether use and effects have improved and whether dropout has decreased is still possible. Again, a strong focus will be on vulnerable populations such as the lower educated and those with low eHealth skills during this field study.

Additionally, attention will be paid to factors such as data infrastructure and data management in relation to implementation in practice and whether additional instruction or training for intermediaries or end users is needed. At the end of the field study, a short process and dissemination evaluation will take place based on the data of this quantitative study combined with interviews with stakeholders and end users. The aim of this part of the evaluation is to gain insight into ways to sustain the reinforced intervention programs in practice with an emphasis on the facilitating and impeding factors for broadscale implementation.

Ethics Approval

All aforementioned procedures of steps 1 to 10 of the systematic approach will be approved by the central ethical review committee of the Open Universiteit. Additionally, all data will be obtained and stored according to the composed data management plan and following the general data protection regulation.

Results

Funding for this study was provided by grant 546003005 (ZonMW) from The Netherlands Organization for Health Research and Development. The project will be executed from December 2019 to December 2023. During this period, the systematic approach presented here will be practically executed according to the described methodological procedures.

Discussion

Aim of the Study

The aim of this study was to define a systematic and evidence-based approach for separately integrating 3 mobile elements with the computer-based Active Plus and I Move intervention programs based on the combined insights of design models and protocols presented earlier. Based on 4 identified key components, which resulted from an analysis of existing eHealth design models in combination with the more traditional intervention design models, we were able to compose 10 systematic design steps to guide the development process.

Strengths and Limitations

Use of these systematic steps for extending our online PA intervention programs with mobile elements is considered a strength of this study and essential for various reasons. First, it is important to retain the already proven effectiveness [15,20] of the original computer-based PA intervention programs Active Plus and I Move. Second, optimal and iterative involvement of the target population during the design process is effectuated since attention is paid to this repeatedly at each step. Last, results from a previous step are often used as input for the next step. As a result, data analysis takes place more gradually during the design process instead of only after finishing the development of the new intervention elements and the complete design study. Therefore, interim (prototype) intervention adjustments are possible which will contribute to a better end product. Following the design steps presented in this study might be useful for future eHealth and mHealth design studies since it is an evidence-based systematic development and evaluation approach.

Although, it is clear that the use of a systematic design approach is essential for successful intervention development, clear and thorough descriptions of the prior development process of online and mobile health interventions are often lacking. This impedes research and intervention development, as eHealth developers often start from scratch when creating or adapting an online intervention or mobile element. Therefore, more publications extensively describing the followed design process leading to a new eHealth intervention or mHealth element are warranted. By describing the followed steps for the separate integration of 3 mobile elements with our existing online PA intervention programs in this study, we aimed to contribute to this.

A possible limitation of this study is that the systematic design approach will only be executed once in practice. The design approach could be lifted to a higher level by applying iterative cycles and processes according to the CeHRes model [48]. For example after fine-tuning the prototypes in step 6, there is an option to return to step 5 and perform a second pilot test with the fine-tuned prototype. Increasing the number of iterative cycles may result in higher levels of usability, satisfaction, and acceptability of the interventions [77].

By separately integrating an activity tracker, EMI program, and chatbot with our already effective proven online intervention programs according to the designed systematic approach, the positive short-term effects on PA may be further enhanced and may be better maintained in the longer term. Additionally, engagement with the intervention programs may increase and attrition may decrease. A potential strength of adding mobile elements to our existing online PA intervention programs is that participants are expected to be more actively involved on a daily basis with the intervention [78], so levels of boredom may decrease and attention may increase [79]. Furthermore, by following a systematic design approach with involvement of the target population, levels of usability and acceptability of the renewed interventions will possibly increase [56,57], which might be a predictor for engagement [80]. However, the results of the RCT will provide insight whether the addition of mobile elements to our online PA intervention programs indeed increase the effectiveness of and engagement with our interventions, whether attrition rates decrease, and which mobile element scores best on factors such as usability and practical applicability. Based on these results, decisions will be made regarding the intervention programs that will be used in practice during the implementation phase of the study. Extensive results

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of the practical execution of the systematic design steps will be described in separate articles.

Conclusion

In conclusion, based on the 4 key components identified, we were able to design an evidence-based systematic approach for separately adding 3 mobile elements to our existing online PA intervention programs. The 10 systematic design steps of this approach and the associated methodological procedures are presented in this paper. The systematic steps are presented as a useful approach to guide future eHealth and mHealth design studies.

Acknowledgments

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Conflicts of Interest

Non declared.

Multimedia Appendix 1
Example day 1 questionnaire testing diary Activity Tracker pilot test.
[PDF File (Adobe PDF File), 269 KB - resprot_v11i7e31677_app1.pdf]

Multimedia Appendix 2
T1 questionnaire pilot test with the Active Plus including Chatbot version used as an example.
[PDF File (Adobe PDF File), 210 KB - resprot_v11i7e31677_app2.pdf]

Multimedia Appendix 3
T1 questionnaire regarding mobile element and T2 questionnaire regarding combination intervention program and mobile element randomized controlled trial with the I Move including Activity Tracker version used as an example.
[PDF File (Adobe PDF File), 202 KB - resprot_v11i7e31677_app3.pdf]

References

1. Rejeski W, Mihalko S. Physical activity and quality of life in older adults. J Gerontol A Biol Sci Med Sci 2001 Oct;56 Spec No 2:23-35. [doi: 10.1093/gerona/56.suppl_2.23] [Medline: 11730235]
2. Active S. Start active, stay active: a report on physical activity from the four home countries' Chief Medical Officers. 2011. URL: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/830943/withdrawn_dh_128210.pdf [accessed 2022-06-15]
3. Global recommendations on physical activity for health. Geneva: World Health Organization; 2010. URL: https://apps.who.int/iris/rest/bitstreams/52834/retrieve [accessed 2022-06-15]
4. Hallal PC, Andersen LB, Bull FC, Guthold R, Haskell W, Ekelund U, Lancet Physical Activity Series Working Group. Global physical activity levels: surveillance progress, pitfalls, and prospects. Lancet 2012 Jul 21;380(9838):247-257. [doi: 10.1016/S0140-6736(12)60646-1] [Medline: 22818937]
5. Bongaarts J. World Population Ageing 2009. JSTOR. 2011. URL: https://www.algec.org/biblioteca/WPA2009_WorkingPaper.pdf [accessed 2022-06-15]
6. McNicoll G. World population ageing 1950-2050. Pop Devel Rev 2002;28(4):814-816.
7. Greaves CJ, Sheppard KE, Abraham C, Hardeman W, Roden M, Evans PH, IMAGE Study Group. Systematic review of reviews of intervention components associated with increased effectiveness in dietary and physical activity interventions. BMC Public Health 2011 Feb 18;11(1):119 [FREE Full text] [doi: 10.1186/1471-2458-11-119] [Medline: 21333011]
8. Michie S, Abraham C, Whittington C, McAteer J, Gupta S. Effective techniques in healthy eating and physical activity interventions: a meta-regression. Health Psychol 2009 Nov;28(6):690-701. [doi: 10.1037/a0016136] [Medline: 19916637]
9. Vandelanotte C, Müller A, Short CE, Hingle M, Nathan N, Williams SL, et al. Past, present, and future of eHealth and mHealth research to improve physical activity and dietary behaviors. J Nutr Educ Behav 2016 Mar;48(3):219-228. [doi: 10.1016/j.jneb.2015.12.006] [Medline: 26965100]
10. Friederichs S, Oenema A, Bolman C, Guyaux J, van Keulen H, Lechner L. I Move: systematic development of a web-based computer tailored physical activity intervention, based on motivational interviewing and self-determination theory. BMC Public Health 2014 Feb 28;14:212 [FREE Full text] [doi: 10.1186/1471-2458-14-212] [Medline: 24580802]
11. Peels DA, van Stralen MM, Bolman C, Golsteijn RH, de Vries H, Mudde AN, et al. Development of web-based computer-tailored advice to promote physical activity among people older than 50 years. J Med Internet Res 2012 Mar 02;14(2):e39 [FREE Full text] [doi: 10.2196/jmir.1742] [Medline: 22390878]

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12. Boekhout J, Peels D, Berendsen B, Bolman C, Lechner L. An eHealth intervention to promote physical activity and social network of single, chronically impaired older adults: adaptation of an existing intervention using intervention mapping. JMIR Res Protoc 2017 Nov 23;6(11):e230 [FREE Full text] [doi: 10.2196/resprot.8093] [Medline: 29170146]
13. Golsteijn R, Bolman C, Volders E, Peels D, de Vries H, Lechner L. Development of a computer-tailored physical activity intervention for prostate and colorectal cancer patients and survivors: OncoActive. BMC Cancer 2017 Jun 26;17(1):446 [FREE Full text] [doi: 10.1186/s12885-017-3397-z] [Medline: 28651586]
14. Willems R, Bolman C, Mesters I, Kanera I, Beaulen A, Lechner L. The Kanker Nazorg Wijzer (Cancer Aftercare Guide) protocol: the systematic development of a web-based computer tailored intervention providing psychosocial and lifestyle support for cancer survivors. BMC Cancer 2015 Aug 11;15:580 [FREE Full text] [doi: 10.1186/s12885-015-1588-z] [Medline: 26260318]
15. Peels D, Bolman C, Golsteijn RHJ, de Vries H, Mudde A, van Stralen M, et al. Long-term efficacy of a printed or a Web-based tailored physical activity intervention among older adults. Int J Behav Nutr Phys Act 2013 Sep 02;10(1):104 [FREE Full text] [doi: 10.1186/1479-5868-10-104] [Medline: 24228862]
16. Prochaska JO, Velicer WF. The transtheoretical model of health behavior change. Am J Health Promot 1997 Aug 26;12(1):38-48. [doi: 10.4278/0890-1171-12.1.38] [Medline: 10170434]
17. Ajzen I. From intentions to actions: a theory of planned behavior. In: Kuhl J, Beckmann J, editors. Action Control. Heidelberg: Springer; 1985:11-39.
18. Bandura A. Social cognitive theory of self-regulation. Org Behav Human Decis Proc 1991 Dec;50(2):248-287. [doi: 10.1016/0749-5978(91)90022-l]
19. Champion V, Skinner C. The health belief model. In: Glanz K, Rimer B, Viswanath K, editors. Health Behavior and Health Education: Theory, Research, and Practice 4th Edition. San Francisco: Jossey-Bass; 2008:45-65.
20. Friederichs S, Oenema A, Bolman C, Lechner L. Long term effects of self-determination theory and motivational interviewing in a web-based physical activity intervention: randomized controlled trial. Int J Behav Nutr Phys Act 2015 Aug 18;12:101-113 [FREE Full text] [doi: 10.1186/s12966-015-0262-9] [Medline: 26283094]
21. Deci E, Ryan R. Self-determination theory: when mind mediates behavior. J Mind Behav 1980:33-43 [FREE Full text]
22. Hettema J, Steele J, Miller WR. Motivational interviewing. Annu Rev Clin Psychol 2005 Apr 01;1(1):91-111. [doi: 10.1146/annurev.clinpsy.1.102803.143833] [Medline: 17716083]
23. Bartholomew EL, Markham C, Ruiter R, Fernandez M, Kok G, Parcel G. Planning Health Promotion Programs: An Intervention Mapping Approach, 4th Edition. Hoboken: Wiley; 2016.
24. Davies CA, Spence JC, Vandelanotte C, Caperchione CM, Mummery W. Meta-analysis of internet-delivered interventions to increase physical activity levels. Int J Behav Nutr Phys Act 2012 Apr 30;9(1):52 [FREE Full text] [doi: 10.1186/1479-5868-9-52] [Medline: 22546283]
25. Krebs P, Prochaska JO, Rossi JS. A meta-analysis of computer-tailored interventions for health behavior change. Prev Med 2010 Sep;51(3-4):214-221 [FREE Full text] [doi: 10.1016/j.ypmed.2010.06.004] [Medline: 20558196]
26. Glasgow R, Vogt T, Boles S. Evaluating the public health impact of health promotion interventions: the RE-AIM framework. Am J Public Health 1999 Sep;89(9):1322-1327. [doi: 10.2105/ajph.89.9.1322] [Medline: 10474547]
27. Eysenbach G. The law of attrition. J Med Internet Res 2005 Mar 31;7(1):e11 [FREE Full text] [doi: 10.2196/jmir.7.1.e11] [Medline: 15829473]
28. Martin S, Feldman D, Blumenthal R, Jones S, Post W, McKibben R, et al. mActive: a randomized clinical trial of an automated mhealth intervention for physical activity promotion. J Am Heart Assoc 2015 Nov 09;4(11):e002239 [FREE Full text] [doi: 10.1161/JAHA.115.002239] [Medline: 26553211]
29. Duscha B, Piner L, Patel M, Craig K, Brady M, McGarrah IR, et al. Effects of a 12-week mHealth program on peak VO and physical activity patterns after completing cardiac rehabilitation: a randomized controlled trial. Am Heart J 2018 May;199:105-114. [doi: 10.1016/j.ahj.2018.02.001] [Medline: 29754647]
30. Antoine Parker C, Ellis R. Effect of electronic messaging on physical activity participation among older adults. J Aging Res 2016;2016:6171028 [FREE Full text] [doi: 10.1155/2016/6171028] [Medline: 27293891]
31. Kwan R, Salihu D, Lee P, Tse M, Cheung D, Roopsawang I, et al. The effect of e-health interventions promoting physical activity in older people: a systematic review and meta-analysis. Eur Rev Aging Phys Act 2020:7-17 [FREE Full text] [doi: 10.1186/s11556-020-00239-5] [Medline: 32336996]
32. Franssen WMA, Franssen GHLM, Spaas J, Solmi F, Eijnde BO. Can consumer wearable activity tracker-based interventions improve physical activity and cardiometabolic health in patients with chronic diseases? A systematic review and meta-analysis of randomised controlled trials. Int J Behav Nutr Phys Act 2020 May 11;17(1):57 [FREE Full text] [doi: 10.1186/s12966-020-00955-2] [Medline: 32393357]
33. Sohaib Aslam A, van Luenen S, Aslam S, van Bodegom D, Chavannes N. A systematic review on the use of mHealth to increase physical activity in older people. Clin eHealth 2020;3:31-39 [FREE Full text] [doi: 10.1016/j.ceh.2020.04.002]
34. Lentferink A, Oldenhuis H, de Groot M, Polstra L, Velthuijsen H, van Gemert-Pijnen J. Key components in eHealth interventions combining self-tracking and persuasive ecoaching to promote a healthier lifestyle: a scoping review. J Med Internet Res 2017 Aug 01;19(8):e277 [FREE Full text] [doi: 10.2196/jmir.7288] [Medline: 28765103]

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35. Riley W, Rivera D, Atienza A, Nilsen W, Allison S, Mermelstein R. Health behavior models in the age of mobile interventions: are our theories up to the task? Transl Behav Med 2011 Mar;1(1):53-71 [FREE Full text] [doi: 10.1007/s13142-011-0021-7] [Medline: 21796270]
36. van der Weegen S, Verwey R, Spreeuwenberg M, Tange H, van der Weijden T, de Witte L. The development of a mobile monitoring and feedback tool to stimulate physical activity of people with a chronic disease in primary care: a user-centered design. JMIR Mhealth Uhealth 2013 Jul 02;1(2):e8 [FREE Full text] [doi: 10.2196/mhealth.2526] [Medline: 25099556]
37. van Gemert-Pijnen J, Nijland N, van Limburg M, Ossebaard H, Kelders S, Eysenbach G, et al. A holistic framework to improve the uptake and impact of eHealth technologies. J Med Internet Res 2011 Dec 05;13(4):e111 [FREE Full text] [doi: 10.2196/jmir.1672] [Medline: 22155738]
38. Kelders S, Kok R, Ossebaard H, Van Gemert-Pijnen J. Persuasive system design does matter: a systematic review of adherence to web-based interventions. J Med Internet Res 2012 Nov 14;14(6):e152 [FREE Full text] [doi: 10.2196/jmir.2104] [Medline: 23151820]
39. Puri A, Kim B, Nguyen O, Stolee P, Tung J, Lee J. User acceptance of wrist-worn activity trackers among community-dwelling older adults: mixed method study. JMIR Mhealth Uhealth 2017 Nov 15;5(11):e173 [FREE Full text] [doi: 10.2196/mhealth.8211] [Medline: 29141837]
40. O'Brien T, Troutman-Jordan M, Hathaway D, Armstrong S, Moore M. Acceptability of wristband activity trackers among community dwelling older adults. Geriatr Nurs 2015 Mar;36(2 Suppl):S21-525. [doi: 10.1016/j.gerinurse.2015.02.019] [Medline: 25771957]
41. Abouzahra M, Ghasemaghaei M. Effective use of information technologies by seniors: the case of wearable device use. Eur J Inform Syst 2021 Jan 29;31(2):241-255. [doi: 10.1080/0960085x.2021.1876534]
42. Brannon E, Cushing C, Crick C, Mitchell T. The promise of wearable sensors and ecological momentary assessment measures for dynamical systems modeling in adolescents: a feasibility and acceptability study. Transl Behav Med 2016 Dec;6(4):558-565 [FREE Full text] [doi: 10.1007/s13142-016-0442-4] [Medline: 27678501]
43. Boh B, Lemmens LHJM, Jansen A, Nederkoorn C, Kerkhofs V, Spanakis G, et al. An Ecological Momentary Intervention for weight loss and healthy eating via smartphone and Internet: study protocol for a randomised controlled trial. Trials 2016 Mar 22;17(1):154 [FREE Full text] [doi: 10.1186/s13063-016-1280-x] [Medline: 27000058]
44. King A, Ahn D, Oliveira B, Atienza A, Castro C, Gardner C. Promoting physical activity through hand-held computer technology. Am J Prev Med 2008 Feb;34(2):138-142 [FREE Full text] [doi: 10.1016/j.amepre.2007.09.025] [Medline: 18201644]
45. Lakerveld J, Mackenbach J, de Boer F, Brandhorst B, Broerse J, de Bruijn G, et al. Improving cardiometabolic health through nudging dietary behaviours and physical activity in low SES adults: design of the Supreme Nudge project. BMC Public Health 2018 Jul 20;18(1):899 [FREE Full text] [doi: 10.1186/s12889-018-5839-1] [Medline: 30029600]
46. Zhou M, Fukuoka Y, Mintz Y, Goldberg K, Kaminsky P, Flowers E, et al. Evaluating machine learning-based automated personalized daily step goals delivered through a mobile phone app: randomized controlled trial. JMIR Mhealth Uhealth 2018 Jan 25;6(1):e28 [FREE Full text] [doi: 10.2196/mhealth.9117] [Medline: 29371177]
47. Van Velsen L, Wentzel J, Van Gemert-Pijnen J. Designing eHealth that matters via a multidisciplinary requirements development approach. JMIR Res Protoc 2013 Jun 24;2(1):e21 [FREE Full text] [doi: 10.2196/resprot.2547] [Medline: 23796508]
48. Kip H, van Gemert-Pijnen GL. Holistic development of eHealth technology. In: eHealth Research, Theory and Development: A Multi-Disciplinary Approach. London: Routledge; 2018:151-186.
49. Skinner H, Maley O, Norman C. Developing internet-based eHealth promotion programs: the Spiral Technology Action Research (STAR) model. Health Promot Pract 2006 Oct;7(4):406-417. [doi: 10.1177/1524839905278889] [Medline: 16840770]
50. Mohr D, Schueller S, Montague E, Burns M, Rashidi P. The behavioral intervention technology model: an integrated conceptual and technological framework for eHealth and mHealth interventions. J Med Internet Res 2014 Jun 05;16(6):e146 [FREE Full text] [doi: 10.2196/jmir.3077] [Medline: 24905070]
51. Craig P, Dieppe P, Macintyre S, Michie S, Nazareth I, Petticrew M, Medical Research Council Guidance. Developing and evaluating complex interventions: the new Medical Research Council guidance. BMJ 2008 Sep 29;337:a1655 [FREE Full text] [doi: 10.1136/bmj.a1655] [Medline: 18824488]
52. Hochstenbach LM, Courtens AM, Zwakhalen SM, Vermeulen J, van Kleef M, de Witte LP. Co-creative development of an eHealth nursing intervention: self-management support for outpatients with cancer pain. Appl Nurs Res 2017 Aug;36:1-8. [doi: 10.1016/j.apnr.2017.03.004] [Medline: 28720227]
53. Direito A, Walsh D, Hinbarji M, Albatal R, Tooley M, Whittaker R, et al. Using the intervention mapping and behavioral intervention technology frameworks: development of an mhealth intervention for physical activity and sedentary behavior change. Health Educ Behav 2018 Jun;45(3):331-348. [doi: 10.1177/1090198117742438] [Medline: 29216765]
54. O'Cathain A, Croot L, Duncan E, Rousseau N, Sworn K, Turner KM, et al. Guidance on how to develop complex interventions to improve health and healthcare. BMJ Open 2019 Aug 15;9(8):e029954 [FREE Full text] [doi: 10.1136/bmjopen-2019-029954] [Medline: 31420394]

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55. Kok G, Schaalma H, Ruiter R, van Empelen P, Brug J. Intervention mapping: protocol for applying health psychology theory to prevention programmes. J Health Psychol 2004 Jan;9(1):85-98. [doi: 10.1177/1359105304038379] [Medline: 14683571]
56. Neuhauser L. Participatory design for better interactive health communication: a statewide model in the USA. Electr J Commun 2001;11(3):1.
57. Hesse BW, Shneiderman B. eHealth research from the user's perspective. Am J Prev Med 2007 May;32(5 Suppl):S97-S103 [FREE Full text] [doi: 10.1016/j.amepre.2007.01.019] [Medline: 17466825]
58. Liao C, Groff L, Chaparro A, Chaparro B, Stumpfhauser L. A Comparison of Website Usage between Young Adults and the Elderly. Proc Human Factors Ergonom Soc Ann Mtg 2016 Nov 06;44(24):4-101. [doi: 10.1177/154193120004402432]
59. Selvidge P. The Effects of End-User Attributes on Tolerance for World Wide Web Delays [Dissertation]. Wichita: Wichita State University; 2003.
60. Arsenijevic J, Tummers L, Bosma N. Adherence to electronic health tools among vulnerable groups: systematic literature review and meta-analysis. J Med Internet Res 2020 Feb 06;22(2):e11613 [FREE Full text] [doi: 10.2196/11613] [Medline: 32027311]
61. Bevana N, Kirakowskib J, Maissela J. What is usability? 1991 Presented at: Proceedings of the 4th International Conference on HCI; 1991; Stuttgart.
62. Hariton E, Locascio J. Randomised controlled trials—the gold standard for effectiveness research: study design: randomised controlled trials. BJOG 2018 Dec;125(13):1716 [FREE Full text] [doi: 10.1111/1471-0528.15199] [Medline: 29916205]
63. MacFarlane A, Clerkin P, Murray E, Heaney D, Wakeling M, Pesola U, et al. The e-Health Implementation Toolkit: qualitative evaluation across four European countries. Implement Sci 2011 Nov 19;6:122 [FREE Full text] [doi: 10.1186/1748-5908-6-122] [Medline: 22098945]
64. Wen K, Gustafson D, Hawkins R, Brennan P, Dinauer S, Johnson P, et al. Developing and validating a model to predict the success of an IHCS implementation: the Readiness for Implementation Model. J Am Med Inform Assoc 2010;17(6):707-713 [FREE Full text] [doi: 10.1136/jamia.2010.005546] [Medline: 20962135]
65. Greenhalgh T, Wherton J, Papoutsi C, Lynch J, Hughes G, A'Court C, et al. Beyond adoption: a new framework for theorizing and evaluating nonadoption, abandonment, and challenges to the scale-up, spread, and sustainability of health and care technologies. J Med Internet Res 2017 Nov 01;19(11):e367 [FREE Full text] [doi: 10.2196/jmir.8775] [Medline: 29092808]
66. Brooke J. SUS—a quick and dirty usability scale. In: Usabil Eval Industr. Boca Raton: CRC Press; 1996:4-7.
67. Davis FD. Perceived usefulness, perceived ease of use, and user acceptance of information technology. MIS Quarterly 1989;13(3):319-340. [doi: 10.2307/249008]
68. Wendel-Vos G, Schuit A, Saris W, Kromhout D. Reproducibility and relative validity of the short questionnaire to assess health-enhancing physical activity. J Clin Epidemiol 2003 Dec;56(12):1163-1169. [doi: 10.1016/s0895-4356(03)00220-8] [Medline: 14680666]
69. van Stralen M, de Vries H, Mudde A, Bolman C, Lechner L. The long-term efficacy of two computer-tailored physical activity interventions for older adults: main effects and mediators. Health Psychol 2011 Jul;30(4):442-452. [doi: 10.1037/a0023579] [Medline: 21639638]
70. Boekhout JM, Berendsen BAJ, Peels DA, Bolman CAW, Lechner L. Evaluation of a computer-tailored healthy ageing intervention to promote physical activity among single older adults with a chronic disease. Int J Environ Res Public Health 2018 Feb 15;15(2):346 [FREE Full text] [doi: 10.3390/ijerph15020346] [Medline: 29462862]
71. Golsteijn R, Bolman C, Volders E, Peels D, de Vries H, Lechner L. Short-term efficacy of a computer-tailored physical activity intervention for prostate and colorectal cancer patients and survivors: a randomized controlled trial. Int J Behav Nutr Phys Act 2018 Oct 30;15(1):106 [FREE Full text] [doi: 10.1186/s12966-018-0734-9] [Medline: 30376857]
72. Tummers S, Hommersom A, Lechner L, Bolman C, Bemelmans R. Gaining insight into determinants of physical activity using bayesian network learning. In: Baratchi M, Cao L, Kosters W, editors. Artificial Intelligence and Machine Learning. Cham: Springer; 2020.
73. Fernandez M, Ten Hoor G, van Lieshout S, Rodriguez S, Beidas R, Parcel G, et al. Implementation mapping: using intervention mapping to develop implementation strategies. Front Public Health 2019;7:158 [FREE Full text] [doi: 10.3389/fpubh.2019.00158] [Medline: 31275915]
74. Powell B, Waltz T, Chinman M, Damschroder L, Smith J, Matthieu M, et al. A refined compilation of implementation strategies: results from the Expert Recommendations for Implementing Change (ERIC) project. Implement Sci 2015 Feb 12;10:21-14 [FREE Full text] [doi: 10.1186/s13012-015-0209-1] [Medline: 25889199]
75. Ross J, Stevenson F, Lau R, Murray E. Factors that influence the implementation of e-health: a systematic review of systematic reviews (an update). Implement Sci 2016 Oct 26;11(1):146 [FREE Full text] [doi: 10.1186/s13012-016-0510-7] [Medline: 27782832]
76. Lluch M. Healthcare professionals' organisational barriers to health information technologies: a literature review. Int J Med Inform 2011 Dec;80(12):849-862. [doi: 10.1016/j.ijmedinf.2011.09.005] [Medline: 22000677]
77. Martin A, Caon M, Adorni F, Andreoni G, Ascolese A, Atkinson S, et al. A mobile phone intervention to improve obesity-related health behaviors of adolescents across europe: iterative co-design and feasibility study. JMIR Mhealth Uhealth 2020 Mar 02;8(3):e14118 [FREE Full text] [doi: 10.2196/14118] [Medline: 32130179]

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78. Kelders S. Involvement as a working mechanism for persuasive technology. In: MacTavish T, Basapur S, editors. Persuasive Technology. Cham: Springer; 2015:3-14.
79. Perski O, Blandford A, West R, Michie S. Conceptualising engagement with digital behaviour change interventions: a systematic review using principles from critical interpretive synthesis. Transl Behav Med 2017 Jun;7(2):254-267 [FREE Full text] [doi: 10.1007/s13142-016-0453-1] [Medline: 27966189]
80. Yeager CM, Benight CC. If we build it, will they come? Issues of engagement with digital health interventions for trauma recovery. Mhealth 2018 Sep;4:37 [FREE Full text] [doi: 10.21037/mhealth.2018.08.04] [Medline: 30363749]

Abbreviations

CeHRes: Center for eHealth Research and Disease Management
EMI: ecological momentary intervention
IM: intervention mapping
mHealth: mobile health technologies
NASSS: nonadoption, abandonment, scale-up, spread, sustainability
PA: physical activity
RCT: randomized controlled trial
SQUASH: short questionnaire to assess health-enhancing physical activity

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Protocol

Sociocultural Adjustment and Well-being Among Third Culture Kids and Their Families: Protocol for a Longitudinal Study

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Abstract

Background: Increasing globalization has led to more families with children being relocated each year, highlighting the importance of issues, such as adjustment and psychological well-being, in this population. These children, commonly known as third culture kids, often spend a significant part of their developmental years in countries and cultures foreign to them.

Objective: Our longitudinal study aims to examine the roles of cognitive, psychological, sociocultural, and family factors in the longitudinal trajectories of the well-being and sociocultural adjustment of third culture kids and their families over time.

Methods: This study adopts both quantitative and qualitative procedures. Data from both procedures will be collected at baseline and at a 1-year follow-up. We aim to recruit 150 to 200 participants between 7 and 17 years old and one of their primary caregivers. After providing informed consent, participants will complete an online survey. Outcome measures include validated questionnaires on well-being and sociocultural adjustment. Predictor measures include validated questionnaires on negative self-thoughts, emotion regulation, resilience, psychological attributes, self-esteem, stress, acculturative stress, cultural intelligence, couple satisfaction, and family functioning. A multiple regression model will be used to analyze quantitative data. In addition, 15 to 20 families who participate in the online survey will be randomly selected to take part in a family interview focusing on questions related to well-being, relocation experiences, cultural issues, and challenges. A concurrent triangulation mixed methods design will be used to analyze and interpret data from both quantitative and qualitative methods.

Results: As of March 15, 2022, a total of 138 children and 126 parents have completed the baseline online survey. In addition, 44 children and 48 parents have completed the 1-year follow-up online survey. A total of 8 families have completed the baseline family interview, while 4 families have completed the 1-year follow-up interview. Data analyses, transcription of the interview, and preparation for publication are on-going.

Conclusions: Findings from this study would enable us to understand the adjustment processes, and risk and protective factors associated with the well-being and sociocultural adjustment of third culture kids and their families in Switzerland, which could have implications on the development of intervention programs for individuals and families to address acculturation and adjustment issues.

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KEYWORDS

family functioning; resilience; sociocultural adjustment; stress; third culture kids; well-being

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Introduction

Increased globalization and the expansion of multinational corporations across nations have made international assignments more common in recent years. A recent survey showed that 73% of expatriates, referred to as individuals who relocate to a new host country for a job and have a limited time frame on their assignments [1], were accompanied by a partner/spouse and 52% of expatriates had children with them [2]. Children who relocate with their expatriate parents often spend a large part of their growing up years in countries or cultures other than those of their parents [3], and are commonly known as third culture kids. Frequently, third culture kids are confronted with new challenges, such as establishing self-identity, finding a sense of belonging, adapting to a new school, and making new friends [4]. However, by living in different cultures, third culture kids have the opportunity to develop skills to manage and adapt to changes, and to experience and be more open to different cultures [5]. The ability to successfully adjust to this new environment can enrich third culture kids' lives [6], while failure to manage these challenges can result in negative consequences for psychological well-being [7].

Unfortunately, up to 70% of relocations fail due to family reasons, such as the inability or unwillingness of family members to adapt to the foreign environment [8-10], resulting in high costs for organizations, ranging from US $250,000 to US $1 million, depending on various factors [11]. Failure of relocation is often defined as the premature return of an expatriate [8]. Research suggests that the key to successful international assignments of expatriates is understanding factors that influence their family's well-being and sociocultural adjustment processes [11,12]. Well-being is defined as the subjective emotional state associated with positive feelings and an overall satisfaction with one's life [13]. Studies have shown that relocation can negatively impact one's subjective well-being, such as causing emotional and social problems, and in more severe cases, it could lead to psychological disorders, such as depression and eating disorders [14]. On the other hand, sociocultural adjustment refers to the individual's ability to cope with daily problems in the new environment, the degree of fit and familiarity to the new host culture, and the redefinition of personal and social roles within the host environment [4,15].

Previous studies have identified various factors that promote well-being and sociocultural adjustment of third culture kids and their families. Studies involving only third culture kids found that secure attachment, open mindedness, emotional stability, and a high level of social initiative were associated with better adjustment [16]. In addition, family characteristics, such as family adaptability, family cohesion, and family communication, have been found to predict higher levels of sociocultural adjustment, with family cohesion being the strongest influence of both sociocultural adjustment and quality of life of third culture kids [16].

Similarly, studies that examined expatriate families as a whole and involved all family members as informants found that a supportive climate, good family communication, and positive feelings about the international assignment were associated with better adjustment [17]. Healthy relationships between spouses/partners were also found to be important for successful adjustment among expatriate families [9].

A 2018 review by Sterle et al [4] revealed several limitations within the current literature. First, most studies consist of cross-sectional surveys, case studies, or narratives to describe third culture kids' well-being and adjustment. Findings from such studies do not examine well-being and sociocultural adjustment as a long-term process and do not provide any directional conclusions of the relationships between the various variables under study [4]. Second, there are limited studies that combine both quantitative and qualitative approaches, as well as the multi-informant approach. While both quantitative and qualitative approaches offer interesting findings, the use of mixed methods may enhance the credibility and confirmability of findings related to third culture kids' well-being and adjustment [18]. On the other hand, the multi-informant approach may provide a more detailed picture of third culture kids' functioning, which has important implications for subsequent interventions [19,20]. Finally, there are limited longitudinal studies that focus on the family as a unit and all family members. As research has indicated that the success of an expatriate assignment is dependent on the family, there is a need to examine the well-being and adjustment of all family members. As such, this study aims to address the limitations of the existing literature by using a longitudinal design that combines both quantitative and qualitative approaches. In addition, we will adopt a multi-informant approach by recruiting a child and a parent in the quantitative study and all family members in the qualitative study. We will also include a variety of measures that examine psychological, cultural, and family factors.

The term expatriate is often defined as a person who is relocated to another country by a multinational company for a temporary work assignment [21]. However, the terms expatriates and migrants are sometimes used interchangeably to refer to people who move outside their home countries for work [22]. Berry and Bell [21] highlighted several differences between expatriates and migrants in terms of their occupation, skills, compensation, etc. For instance, expatriates are often characterized as workers at executive, managerial, or professional positions, who have high skills, high compensation, and organizational benefits, while migrants are often characterized as skilled or unskilled laborers, who have low wages and no organizational benefits [21,23]. Based on these differences in definitions, we chose to use the term expatriates to define our study population. The focus on expatriates is largely driven by our study team's clinical expertise and interests. In the last 5 years, our psychotherapy center has seen an increase in requests for psychological services among expatriate families. However, there is still a lack of evidence on how relocation and sociocultural adjustment impact the onset and maintenance of psychological disorders, as well as limited evidence-based interventions to support this population [4]. In addition, Switzerland, with an estimate of 25% foreign nationals, has been consistently rated as one of the most desirable destinations for expatriates due to its high quality of life and salaries, but at the same time, it has also been rated as one of the most difficult places to settle into [24], highlighting

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potential adjustment difficulties. Therefore, understanding factors that influence well-being and adjustment among expatriate families in Switzerland is an important and relevant topic.

Our first research question examines the roles of emotion regulation, self-esteem, resilience, and negative self-thoughts for well-being and adjustment among third culture kids over time. Previous research has demonstrated that emotion regulation [25,26], negative self-thoughts [27-29], resilience [30,31], and stress [32] are important psychological processes for healthy development, such as establishing relationships and adjusting to stressful situations [33], in nonthird culture kid populations. Hence, we expect that better emotion regulation skills, self-esteem, and resilience; fewer negative cognitions; and lower stress will enhance third culture kids' well-being and sociocultural adjustment. The first hypothesis (hypothesis 1) is as follows: Increased levels of emotion regulation, self-esteem, and resilience, and decreased levels of negative self-thoughts and stress can significantly predict increased levels of well-being and adjustment among third culture kids over time.

Our second research question examines the roles of cultural intelligence and acculturative stress on well-being and adjustment among third culture kids over time. Cultural intelligence is defined as "an individual's capability to function and manage effectively in culturally diverse settings" [34], and has been widely explored as a factor of success in the relocation of adult expatriates [35-37] and in the adjustment and well-being of migrant populations [38]. On the other hand, acculturative stress (eg, difficulties assimilating to the beliefs, values, and norms of a host culture) has been found to be a strong predictor of depressive symptoms and suicidal ideation among migrant families [39]. As such, we expect to find that higher cultural intelligence and lower acculturative stress are associated with higher levels of well-being and sociocultural adjustment among third culture kids. The second hypothesis (hypothesis 2) is as follows: Increased levels of cultural intelligence and decreased levels of acculturative stress significantly predict increased levels of well-being and adjustment among third culture kids over time.

Our third research question examines the roles of family functioning, couple satisfaction, and parental stress in well-being and adjustment among third culture kids over time. As the place of residence remains unstable, the family constitutes the stable part in a third culture kid's life during relocation. Thus, the family serves as an important source of social and emotional support during the relocation experience [4,40]. Previous research has demonstrated the impact of family functioning, parental stress, and couple satisfaction on child well-being [41-45]. Hence, we expect to find higher levels of family functioning and couple satisfaction, and lower levels of parental stress to be associated with higher levels of well-being and sociocultural adjustment among third culture kids. The third hypothesis (hypothesis 3) is as follows: Increased levels of family functioning and couple satisfaction, and decreased levels of parental stress significantly predict increased levels of well-being and adjustment among third culture kids over time.

Our fourth research question aims to obtain a detailed understanding of the transition process and adjustment to Switzerland from a family perspective. In addition, it aims to further understand the factors that influence sociocultural adjustment and well-being.

Methods

Study Design

This is a longitudinal study that adopts both quantitative and qualitative procedures. Data from both procedures will be collected at baseline and at a 1-year follow-up. To answer research questions 1 to 3, a quantitative procedure using an online questionnaire will be used to obtain information from the participants. To answer research question 4 on the process of transitioning and adjustment in Switzerland, a concurrent triangulation mixed methods design will be used. This design includes concurrent but separate data collection from both quantitative and qualitative procedures, data analysis, and data interpretation [18]. Equal priority will be given to data obtained from both qualitative and quantitative procedures.

Participants and Study Procedures

We aim to recruit 150 to 200 child/adolescent participants and one of their parents. Potential participants will be contacted through various sources, such as social media, expat associations, international schools, and multinational companies. The inclusion criteria are as follows: age between 7 and 17 years for children, employment of a parent being the primary reason for the family's relocation to Switzerland, medium to high household income levels (greater than CHF 100,000 [US $100,000]), and ability to understand and speak English. As highlighted in the literature [21], the inclusion criterion of a high income level in our study is meant to include those defined as expatriates and exclude those characterized as laborers and domestic workers.

The exclusion criteria are as follows: a Swiss parent, refugee status, foreign exchange student status, and insufficient comprehension of English to complete questionnaires or interviews. Parents who are interested in participating in the study will contact the study team by email/phone. We will then send the study information and informed consent documents by email/post. Following that, informed consent will be obtained either in person at the Division of Clinical Psychology and Psychotherapy or online via phone/Skype/Zoom with a member of the study team. Once they agree to participate in the study, parents and adolescents will have to sign the informed consent form. Children (aged 10-13 years) will have to write their names in bold on the informed consent form. For children below 10 years, oral consent will be obtained in the presence of a parent. Parents will have to return the signed informed consent forms to the study team via post or email. Once written informed consent has been received by the study team, we will proceed with the following study procedures. Participants will be reimbursed CHF 30 (US $30) upon completion of the online survey. Those who participate in the family interviews will be provided cinema vouchers (CHF 40 [US $40]). Similar procedures will be conducted at the 1-year follow-up. Figure 1 provides an overview of the study procedures.

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Figure 1. Overview of the study procedures.

	Study period		
	Prestudy (Time 0)	Baseline (Time 1)	One-year follow-up (Time 2)
Informed consent	✓		
Confirmation of the eligibility criteria	✓		
Online survey		✓	✓
Reimbursement of CHF 30		✓	✓
Family interviews		✓	✓
Reimbursement of cinema vouchers		✓	✓

Quantitative Procedure

Each participant and one of their parents will receive a pseudoanonymous unique code in order to access the online survey. They will be asked to complete the online questionnaire that will last for about 10-15 minutes at their own convenience. Upon completion of the online questionnaire, parents will receive reports on their well-being and their child's well-being if they have provided consent. For the parent, a score below 13 on the 5-item World Health Organization Well-Being Index (WHO-5) [46] indicates poor well-being and is an indication for further evaluation. For the child/adolescent, a score of 15 or above for Total Difficulties or a score of 1 or above for Impact Score on the Strengths and Difficulties Questionnaire (SDQ) [47] is an indication for further evaluation. In such cases, parents who have consented to receive this information will be contacted for a recommendation for further assessment at the Center for Psychotherapy, University of Basel. This initial evaluation will be conducted free of charge, but the cost of subsequent assessments/treatment will be borne by the participants. Participants and their families who have consented to be contacted for the 1-year follow-up study will be invited to complete the same online questionnaire again. They will need to provide informed consent again should they want to participate in the follow-up study.

Measures

Quantitative data will be collected using an online questionnaire hosted on the university's website. The following sociodemographic information will be collected: age, ethnicity, nationality, marital status, employment status, relationship with the child, spoken languages, number of previous international relocations, countries lived in before Switzerland, education, school type, and reasons and length of relocation. In addition, measures as listed in Textbox 1 will also be used.

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Textbox 1. List of measures.

Predictor measures

Psychological

- Emotion regulation: Emotion Regulation Questionnaire for Children and Adolescents [48]
- Negative self-thoughts: Social Threat Subscale of the Children's Automatic Thoughts Scale [49]
- Psychological attributes: Strengths and Difficulties Questionnaire [47]
- Perceived stress: Perceived Stress Scale for Children [50]
- Resilience: Child and Youth Resilience Measure-12 [51]
- Self-esteem: Rosenberg Self-Esteem Scale [52] or Behavioral Rating Scale of Presented Self-Esteem in Young Children [53]

Cultural

- Acculturation stress: Acculturative Stress Inventory for Children [54]
- Cultural intelligence: Short-Form Cultural Intelligence Scale [55]

Family

- Family functioning: McMaster Family Assessment Device [56]
- Parent's resilience: Adult Resilience Measure [51]
- Parental stress: Perceived Stress Scale [57]
- Quality of couple relationship: Couples Satisfaction Index-4 [58]

Outcome measures

Well-being

- KIDSCREEN-10 Index [59]
- 5-item World Health Organization Well-Being Index [46]

Sociocultural adjustment

- Social Cultural Adaptation Scale–Child [60]
- Social Cultural Adaptation Scale–Revised [61]

Outcome Measures

Our outcome measures include well-being and sociocultural adjustment.

Well-being

Third culture kids' well-being will be assessed using KIDSCREEN-10 [59]. Children and adolescents will be asked to rate each item based on a Likert-type scale ranging from 1 (not at all) to 5 (extremely). Items are summed to provide a total score, with higher scores indicating higher levels of well-being. Parents' well-being will be assessed using the WHO-5 [46]. Parents will be asked to rate each item based on a Likert-type scale ranging from 0 (at no time) to 5 (all of the time). Items are summed to provide a total score, with higher scores indicating higher levels of well-being.

Sociocultural Adjustment

Third culture kids' sociocultural adjustment will be assessed using the 20-item child version of the Social Cultural Adaptation Scale–Child [60]. For children below 12 years old, parents will be asked to fill out the Social Cultural Adaptation Scale–Child on their behalf. Parents' sociocultural adjustment will be assessed using the 11-item Social Cultural Adaptation Scale–Revised [61]. For both measures, items are rated based on a Likert-type scale ranging from 1 (no difficulty) to 5 (extreme difficulty). Items are summed to provide a total score. Higher scores indicate more difficulties in the new sociocultural environment, suggesting poorer adjustment.

Predictor Measures

Our predictor measures include psychological, cultural, and family factors.

Psychological Factors

Psychological factors will be evaluated using different assessments as presented below.

Emotion Regulation

Children and adolescents will be asked to complete the 10-item Emotion Regulation Questionnaire for Children and Adolescents [48] based on a 5-point Likert scale ranging from 1 (strongly disagree) to 5 (strongly agree). Items are summed to provide a total score, with higher scores indicating greater use of emotion regulation strategies.

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Negative Self-thoughts

Children and adolescents will be asked to complete the 10-item Children's Automatic Thoughts Scale [49]. Each item is rated on a 5-point Likert scale ranging from 0 (not at all) to 4 (all the time). Items are summed to provide a total score, with higher scores indicating a higher frequency of negative automatic thoughts related to social situations.

Resilience

Children and adolescents will be asked to complete the Child and Youth Resilience Measure-12 [51] based on a 3-point Likert scale ranging from 1 (no) to 3 (yes). Items are summed to provide a total score, with higher scores indicating higher levels of resilience.

Psychological Attributes

Third culture kids' psychological positive and negative attributes will be assessed using the 25-item SDQ [47]. These 25 items are divided between the following 5 subscales: emotional symptoms (5 items), conduct problems (5 items), hyperactivity/inattention (5 items), peer relationship problems (5 items), and prosocial behavior (5 items). Parents will be asked to rate their child/adolescent based on a Likert-type scale ranging from 0 (not true) to 2 (certainly true). The total difficulties score is summed using the emotional symptoms, conduct problems, hyperactivity/inattention, and peer relationship problems subscales. Higher total scores indicate more difficulties. Higher scores on the prosocial behavior subscale indicate better prosocial behaviors.

Stress

Children and adolescents will be asked to complete the 13-item Perceived Stress Scale for Children [50] based on a Likert-type scale ranging from 0 (never) to 3 (a lot). Items 2, 5, 6, 9, 10, 12, and 13 are reverse scored, and all items are then summed to provide a total score. Higher scores indicate higher levels of stress.

Self-esteem

Adolescents will be asked to complete the 10-item Rosenberg Self-Esteem Scale [52] that measures global self-worth based on a 4-point Likert scale ranging from "strongly agree" to "strongly disagree." Items 2, 5, 6, 8, and 9 are reverse scored, and all items are then summed to provide a total score. For children aged 12 years or below, parents will be asked to complete the 15-item Behavioral Rating Scale of Presented Self-Esteem in Young Children [53]. Parents will be asked to rate descriptions that best describe their child based on scores of 1 to 4. Items are summed, and a mean score is calculated. For both measures, higher scores indicate higher self-esteem.

Cultural Factors

Cultural factors will be evaluated using different assessments as presented below.

Acculturative Stress

Acculturative stress will be assessed using the 4-item Acculturative Stress Inventory for Children [54]. All participants will be asked to rate each item based on a Likert-type scale ranging from 0 (does not apply) to 5 (bothers me a lot). Items are summed to provide a total score, with higher scores indicating higher levels of acculturative stress.

Cultural Intelligence

Parents will be asked to complete the 10-item Short-Form Cultural Intelligence Scale [55] that assesses their experiences when interacting with people from other cultures. Each item is rated on a 5-point Likert scale ranging from 1 (not at all) to 5 (extremely well). Items are summed to provide a total score, with higher scores indicating higher levels of cultural intelligence.

Family Factors

Family factors will be evaluated using different assessments as presented below.

Family Functioning

Parents will be asked to complete the 12-item family functioning subscale of the McMaster Family Assessment Device [56] based on a Likert-type scale ranging from 1 (strongly agree) to 4 (strongly disagree). Odd items are reverse scored, and all items are summed to provide a total score. Higher scores indicate poorer family functioning.

Parental Stress

Parents will be asked to complete the 10-item Perceived Stress Scale [57] based on a Likert-type scale ranging from 0 (never) to 4 (very often). Items 4, 5, 7, and 8 are reverse scored, and all items are then summed to provide a total score. Higher scores indicate higher levels of stress.

Parental Resilience

Resilience in parents will be assessed using the Adult Resilience Measure [51]. Parents will be asked to rate each item on a Likert-type scale ranging from 1 (not at all) to 5 (a lot). Items are summed to provide a total score, with higher scores indicating higher levels of resilience.

Qualitative Procedure

A random sample of participants and their families from the quantitative study, who have given their consent to be contacted for the family interview, will be invited for a face-to-face interview. Participant recruitment will end when saturation occurs. Based on previous studies [62], we expect the sample size to be between 15 and 20 families. They will need to complete the informed consent again prior to the interview. Each family will be interviewed together for about 40-50 minutes. The interview will be conducted either at the Center for Psychotherapy or at venues where the participants are recruited. However, in view of COVID-19 pandemic measures, the family interview may be conducted online via Zoom. Subsequently, participants and their families, who have consented to be contacted again for the 1-year follow-up, will be invited for the interview again. They will need to provide informed consent again should they want to participate in the interview. Qualitative data consisting of family interviews will be video recorded. Questions related to their well-being, relocation experiences, cultural issues, and challenges and difficulties living in Switzerland will be asked. See Textbox 2 for a list of the interview questions.

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Textbox 2. List of interview questions.

Questions for the entire family

Experience:

1. What has been the experience of moving to Switzerland for...
   - the family?
   - each individual?
2. What have been the positive things about moving? What have been the negative things about moving? How has it changed the family?

Cultural issues:

1. Have you moved before?
2. If yes, what are the specifics about moving to Switzerland compared with your previous moves?
3. If no, how does Switzerland compare with your hometown?
4. What have you perceived about being in Switzerland, what do you notice about the Swiss culture, and what is your experience of locals?

Needs:

1. What advice would you give another family who is moving here?

Questions for parents

Challenges/difficulties:

1. How has it challenged the family? How did you cope with that?
2. How has your family changed since the move?
3. How do members of your family support each other? (how have you supported one another during this time?)
4. Is there anything I have not asked you about living in Switzerland that might be important for me to know?

Questions for children

1. How happy are you to live in Switzerland?
2. What has been easy/difficult? How has it changed the family?
3. What did you miss most?
4. Is there anything I have not asked you about living in Switzerland that might be important for me to know?

Ethics Approval

The study has been approved by the Ethics Committee within the Faculty of Psychology, University of Basel, Switzerland (study number 047-18-4). Written informed consent and assent in accordance with the Declaration of Helsinki will be obtained from participants and their parents prior to any study-related procedures. In order to ensure confidentiality, all data will be pseudocoded without personal identifiers. Participants may withdraw from the study at any time without any consequences.

Data Analysis

Research Questions 1 to 3

Research questions 1 to 3 involve the roles of emotion regulation, self-esteem, resilience, negative self-thoughts, cultural intelligence, acculturative stress, family functioning, parents' stress, and couple satisfaction in changes to third culture kids' well-being and sociocultural adjustment over time.

Based on a multiple linear regression model with 5 predictors, whereby the focus is on the increase in the variance accounted for by a specific predictor, our planned sample size would be sufficiently powered at 0.80 for a small to medium effect size based on Cohen f^2 of 0.04-0.05, given α=.05 [63]. To answer research questions 1 to 3, multiple regression analyses will be conducted, with well-being or sociocultural adjustment at the 1-year follow-up as an outcome and the respective psychological, cultural, and family factors as predictors, thereby controlling for the baseline values of the respective outcome variables and for sociodemographics (eg, age, gender, family composition, number of previous international relocations, years lived in Switzerland, and school type). As dropouts are frequently encountered in longitudinal studies, we will use multiple imputation to deal with the problem of missing values. Multiple imputation is superior to traditional approaches, such as completer analysis, if missing values follow the "missing at random" pattern, which we consider a more realistic scenario than the "missing completely at random" pattern.

Research Question 4

Research question 4 involves a family's perspective of the process of transitioning and adjusting to another country and culture.

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Content analysis will be chosen to analyze the family interviews, as it is deemed suitable for mixed methods studies [64]. Data will first be transcribed by trained research assistants and imported to MAXQDA Analytics Pro (VERBI GmbH) for coding. A codebook will be developed to guide the coding process. Each transcribed interview will be coded independently by a study team member and a trained research assistant. Discrepancies will be discussed and resolved together by another study team member. Intercoder reliability will be calculated using the MAXQDA intercoder agreement function. Data will be later triangulated to examine the relationships between the study variables and to identify the similarities and differences in the findings from both qualitative and quantitative procedures [64].

Results

Data collection started on August 25, 2019, and will end on July 1, 2022. As of March 15, 2022, a total of 138 children and 126 parents have completed the baseline online survey. In addition, 44 children and 48 parents have completed the 1-year follow-up online survey. A total of 8 families have completed the baseline family interview, while 4 families have completed the 1-year follow-up interview. Transcription of the interviews is on-going. Results from this study will be presented at various conferences and are expected to be published in peer-reviewed journals from late 2022 onwards.

Discussion

Expected Principal Findings

Our longitudinal study aims to examine the roles of psychological, cultural, and family factors for third culture kids' well-being and sociocultural adjustment over time, and gain in-depth insights into the family's perspective of the process of transitioning and adjustment in Switzerland. Specifically, we hypothesize that higher levels of emotion regulation, self-esteem, and resilience, and lower levels of negative self-thoughts and stress will significantly predict higher levels of well-being and adjustment among third culture kids. In addition, we hypothesize that higher levels of self-esteem, resilience, cultural intelligence, couple satisfaction, and family functioning, and lower levels of stress will significantly predict higher levels of well-being and adjustment among the parents of third culture kids. Therefore, understanding the relationships between these factors would provide a better understanding of the well-being and adjustment among the third culture kid population in Switzerland. Furthermore, by examining a wide variety of psychological, cultural, and family factors, we will gain insights into critical resources that help to promote well-being and adjustment among third culture kids and their families. For instance, given that third culture kids and their families are likely to experience significant periods of stress when they relocate, it is extremely important to consider how they manage this and what skills might be helpful in dealing with relocation and adjustment in a healthy way. The identification of difficulties in these specific areas would enable early intervention and prevention of more severe problems associated with relocation stress.

Other important aspects include knowledge and skills to deal with acculturative stress and boost cultural intelligence. However, evidence is mixed for the potential preventive effect of premove preparation programs, including cultural pretraining, as cross-cultural training has measurable effects on knowledge about the host country [65], but is not proven to be efficient for stress reduction or adaptation [66]. It is possible that previous approaches for supporting expatriates have not been as successful as expected, as they only worked on one of these areas and did not take into account the interactions between psychological, cultural, and family factors. In summary, findings from our study will provide a foundation for the development of an evidence-based multi-level intervention program addressing the various psychological, cultural, and family factors, which may help to promote positive well-being and adjustment among third culture kids and their families. Specifically, the program will provide support in developing psychological skills, improving family and couple functioning, and developing cultural intelligence in 3 levels. Level 1 will consist of a combination of cultural training and psychoeducation regarding adjustment, acculturation, stress, and common challenges of relocation. Level 2 will consist of a parent or child group program aimed at building skills in stress management, emotion regulation, resilience, managing negative cognitions, boosting self-esteem, and improving family functioning. Level 3 will consist of an individualized program based on the specific needs of the family.

Strengths

The strengths of this study include the longitudinal design, as it addresses the scarcity of methodologically strong studies in this area [4]. The longitudinal approach is particularly appropriate for this area of research as it enables us to understand the progression of well-being and adjustment of third culture kids and their families over a period of 1 year. Another strength is that the use of a mixed methods concurrent triangulation design addresses the existing gap in the literature of limited studies that adopt both approaches for understanding third culture kids' well-being and adjustment. In addition, adopting a family-focused and multi-informant approach enables us to gain a more holistic perspective.

Limitations and Future Directions

The limitations include a lack of manipulation checks to detect the attention of study participants while completing the online survey. We assume that all participants will answer the online survey with full attention. To account for this issue, we will examine the response time of each participant in order to identify those who have answered the survey too quickly, and these outliers may be excluded. In addition, only one of the parents is being recruited for the online survey. It is possible that our findings may differ depending on which parent is recruited. Finally, our sample will only consist of third culture kids and their families living in Switzerland. Hence, findings from this study may have limited generalizability to third culture kids living in other countries.

With these limitations, more research is clearly needed to further understand the factors that may influence well-being and sociocultural adjustment among third culture kids and their

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families. First, future research should consider including each family member to provide a more holistic perspective of the relocation experience and adjustment. Second, it would be interesting to extend the research sample to those living in countries beyond Switzerland. Finally, additional factors beyond those examined in this study, such as coping styles, parenting, and self-care behaviors, should be considered.

Conclusions

This study addresses an emerging issue of globalization. Relocation failure results in high costs for organizations, while unhappy and unsettled expatriate families may be at risk for psychosocial problems and may be a burden for other members of the community. Findings from our study may provide further understanding of the risk and protective factors associated with the well-being of third culture kids and their families, and could therefore be helpful in developing a tailored multi-modal and multi-level program to promote positive well-being and adjustment during their stay abroad.

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Authors' Contributions

YPO, MR, EMJ, and JG contributed to the conception of the study. YPO, MR, and EMJ were responsible for writing the study protocol. AHM provided expertise in sample size calculation and the statistical analysis plan. All authors provided feedback to refine the manuscript and approved the final manuscript.

Conflicts of Interest

None declared.

References

1. McNulty Y, Brewster C. Theorizing the meaning(s) of 'expatriate': establishing boundary conditions for business expatriates. The International Journal of Human Resource Management 2016 Oct 31;28(1):27-61. [doi: 10.1080/09585192.2016.1243567]
2. 2016 Global Mobility Trends Survey. Brookfield Global Relocation Services. URL: http://globalmobilitytrends.bgrs.com/#/download [accessed 2018-10-17]
3. Pollock DC, Van Reken RE. Third Culture Kids: Growing Up Among Worlds. Boston, MA: Hachette Book Group; 2009.
4. Sterle MF, Fontaine JRJ, De Mol J, Verhofstadt LL. Expatriate family adjustment: An overview of empirical evidence on challenges and resources. Front Psychol 2018 Jul 23;9:1207 [FREE Full text] [doi: 10.3389/fpsyg.2018.01207] [Medline: 30083117]
5. Van Reken RE, Pollock MV, Pollock DC. Third Culture Kids 3rd Edition: Growing Up Among Worlds. London, United Kingdom: Nicholas Brealey Publishing; 2017.
6. Kempen R, Pangert B, Hattrup K, Mueller K, Joens I. Beyond conflict: the role of life-domain enrichment for expatriates. The International Journal of Human Resource Management 2014 May 29;26(1):1-22. [doi: 10.1080/09585192.2014.919954]
7. Brown RJ. Dominant stressors on expatriate couples during international assignments. The International Journal of Human Resource Management 2008 Jun;19(6):1018-1034. [doi: 10.1080/09585190802051303]
8. Haslberger A, Brewster C. The expatriate family: an international perspective. Journal of Managerial Psychology 2008;23(3):324-346. [doi: 10.1108/02683940810861400]
9. Lazarova M, McNulty Y, Semeniuk M. Expatriate Family Narratives on International Mobility: Key Characteristics of the Successful Moveable Family. In: Mäkelä L, Suutari V, editors. Work and Family Interface in the International Career Context. Cham: Springer; 2015:29-51.
10. Rushing K, Kleiner B. New developments in executive relocation practices. Management Research News 2003;26:12-19. [doi: 10.1108/01409170310783745]
11. McNulty Y, Selmer J. Research Handbook of Expatriates. Cheltenham, England: Edward Elgar Publishing; 2017.
12. Yeaton K, Hall N. Expatriates: Reducing failure rates. J. Corp. Acct. Fin 2008 Mar;19(3):75-78. [doi: 10.1002/jcaf.20388]
13. Brodsky S. The Psychology of Adjustment and Well-Being. San Diego, CA: Harcourt College Publishers; 1988.
14. Melles EA, Frey LL. "Here, everybody moves": Using relational cultural therapy with adult third-culture kids. Int J Adv Counselling 2014 Jun 1;36(3):348-358. [doi: 10.1007/s10447-014-9211-6]
15. Haslberger A, Brewster C. Capital gains: expatriate adjustment and the psychological contract in international careers. Hum. Resour. Manage 2009 May;48(3):379-397. [doi: 10.1002/hrm.20286]
16. Van Der Zee KI, Ali AJ, Haaksma I. Determinants of effective coping with cultural transition among expatriate children and adolescents. Anxiety Stress Coping 2007 Mar 16;20(1):25-45. [doi: 10.1080/10615800601032781] [Medline: 17999213]

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17. Caligiuri PM, Hyland MM, Joshi A, Bross AS. Testing a theoretical model for examining the relationship between family adjustment and expatriates' work adjustment. J Appl Psychol 1998 Aug;83(4):598-614. [doi: 10.1037/0021-9010.83.4.598] [Medline: 9729928]
18. Creswell J. Research Design: Qualitative, Quantitative, and Mixed Methods Approaches. Thousand Oaks, CA: SAGE Publications; 2018.
19. De Los Reyes A, Kazdin AE. Informant discrepancies in the assessment of childhood psychopathology: a critical review, theoretical framework, and recommendations for further study. Psychol Bull 2005 Jul;131(4):483-509. [doi: 10.1037/0033-2909.131.4.483] [Medline: 16060799]
20. Karver MS, Handelsman JB, Fields S, Bickman L. Meta-analysis of therapeutic relationship variables in youth and family therapy: the evidence for different relationship variables in the child and adolescent treatment outcome literature. Clin Psychol Rev 2006 Jan;26(1):50-65. [doi: 10.1016/j.cpr.2005.09.001] [Medline: 16271815]
21. Berry D, Bell M. 'Expatriates': Gender race and class distinctions in international management. Gender, Work and Organization 2012;19:10-28. [doi: 10.1111/j.1468-0432.2011.00577.x]
22. Andresen M, Bergdolt F, Margenfeld J, Dickmann M. Addressing international mobility confusion – developing definitions and differentiations for self-initiated and assigned expatriates as well as migrants. The International Journal of Human Resource Management 2014 Jan 14;25(16):2295-2318. [doi: 10.1080/09585192.2013.877058]
23. Shaffer MA, Harrison DA, Gregersen H, Black JS, Ferzandi LA. You can take it with you: individual differences and expatriate effectiveness. J Appl Psychol 2006 Jan;91(1):109-125. [doi: 10.1037/0021-9010.91.1.109] [Medline: 16435942]
24. Expat City Ranking 2021. InterNations. 2021. URL: https://cms-internationsgmbh.netdna-ssl.com/cdn/file/cms-media/public/2021-11/Expat-Insider_City-Ranking-Report-2021_1.pdf [accessed 2022-03-29]
25. Southam-Gerow MA, Kendall PC. Emotion regulation and understanding: implications for child psychopathology and therapy. Clinical Psychology Review 2002 Mar;22(2):189-222. [doi: 10.1016/s0272-7358(01)00087-3]
26. Zalewski M, Lengua L, Wilson A, Trancik A, Bazinet A. Emotion regulation profiles, temperament, and adjustment problems in preadolescents. Child Dev 2011;82(3):951-966. [doi: 10.1111/j.1467-8624.2011.01575.x] [Medline: 21413935]
27. Beck AT. The current state of cognitive therapy: a 40-year retrospective. Arch Gen Psychiatry 2005 Sep 01;62(9):953-959. [doi: 10.1001/archpsyc.62.9.953] [Medline: 16143727]
28. Kendall PC, Chansky TE. Considering cognition in anxiety-disordered children. Journal of Anxiety Disorders 1991 Jan;5(2):167-185. [doi: 10.1016/0887-6185(91)90027-q]
29. Maric M, Heyne DA, van Widenfelt BM, Westenberg PM. Distorted cognitive processing in youth: The structure of negative cognitive errors and their associations with anxiety. Cognit Ther Res 2011 Feb;35(1):11-20 [FREE Full text] [doi: 10.1007/s10608-009-9285-3] [Medline: 21461039]
30. Egeland B, Carlson E, Sroufe LA. Resilience as process. Dev Psychopathol 2009 Sep 09;5(4):517-528. [doi: 10.1017/s0954579400006131]
31. Suedfeld P. Invulnerability, coping, salutogenesis, integration: four phases of space psychology. Aviat Space Environ Med 2005 Jun;76(6 Suppl):B61-B66. [Medline: 15943196]
32. Hilsman R, Garber J. A test of the cognitive diathesis-stress model of depression in children: Academic stressors, attributional style, perceived competence, and control. Journal of Personality and Social Psychology 1995;69(2):370-380. [doi: 10.1037/0022-3514.69.2.370]
33. Compas BE, Jaser SS, Bettis AH, Watson KH, Gruhn MA, Dunbar JP, et al. Coping, emotion regulation, and psychopathology in childhood and adolescence: A meta-analysis and narrative review. Psychol Bull 2017 Sep;143(9):939-991. [doi: 10.1037/bul0000110] [Medline: 28616996]
34. Ang S, Van Dyne L, Koh C, Ng KY, Templer KJ, Tay C, et al. Cultural intelligence: Its measurement and effects on cultural judgment and decision making, cultural adaptation and task performance. Manag. Organ. Rev 2015 Feb 02;3(3):335-371. [doi: 10.1111/j.1740-8784.2007.00082.x]
35. Huff KC, Song P, Gresch EB. Cultural intelligence, personality, and cross-cultural adjustment: A study of expatriates in Japan. International Journal of Intercultural Relations 2014 Jan;38:151-157. [doi: 10.1016/j.ijintrel.2013.08.005]
36. Lin Y, Chen AS, Song Y. Does your intelligence help to survive in a foreign jungle? The effects of cultural intelligence and emotional intelligence on cross-cultural adjustment. International Journal of Intercultural Relations 2012 Jul;36(4):541-552. [doi: 10.1016/j.ijintrel.2012.03.001]
37. Abdul Malek M, Budhwar P. Cultural intelligence as a predictor of expatriate adjustment and performance in Malaysia. Journal of World Business 2013 Apr;48(2):222-231. [doi: 10.1016/j.jwb.2012.07.006]
38. Lorenzo-Blanco EI, Meca A, Unger JB, Romero A, Szapocznik J, Piña-Watson B, et al. Longitudinal effects of latino parent cultural stress, depressive symptoms, and family functioning on youth emotional well-being and health risk behaviors. Fam Process 2017 Dec 23;56(4):981-996. [doi: 10.1111/famp.12258] [Medline: 27774629]
39. Hovey JD. Acculturative stress, depression, and suicidal ideation in Mexican immigrants. Cultur Divers Ethnic Minor Psychol 2000 May;6(2):134-151. [doi: 10.1037/1099-9809.6.2.134] [Medline: 10910528]
40. Rosenbusch K, Cseh M. The cross-cultural adjustment process of expatriate families in a multinational organization: a family system theory perspective. Human Resource Development International 2012 Feb;15(1):61-77. [doi: 10.1080/13678868.2011.646895]

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41. Liliana B, Nicoleta TM. Personality, family correlates and emotion regulation as wellbeing predictors. Procedia - Social and Behavioral Sciences 2014 Dec;159:142-146. [doi: 10.1016/j.sbspro.2014.12.346]
42. McFarlane AH, Bellissimo A, Norman GR. Family structure, family functioning and adolescent well-being: the transcendent influence of parental style. J Child Psychol Psychiatry 1995 Jul;36(5):847-864. [doi: 10.1111/j.1469-7610.1995.tb01333.x] [Medline: 7559849]
43. Pollard E, Lee P. Child well-being: a systematic review of the literature. Social Indicators Research 2003;61:59-78. [doi: 10.1023/A:1021284215801]
44. Luo L, Cooper CL. Stress of job relocation: Progress and prospect. Work & Stress 2007 Sep 27;4(2):121-128. [doi: 10.1080/02678379008256974]
45. Munton AG, Forster N. Job relocation: Stress and the role of the family. Work & Stress 1990 Jan;4(1):75-81. [doi: 10.1080/02678379008256967]
46. Wellbeing measures in primary health care/The Depcare Project. World Health Organization. 1998. URL: https://www.euro.who.int/__data/assets/pdf_file/0016/130750/E60246.pdf [accessed 2018-10-03]
47. Goodman R. The strengths and difficulties questionnaire: A research note. J Child Psychol Psychiatry 1997 Jul;38(5):581-586. [doi: 10.1111/j.1469-7610.1997.tb01545.x] [Medline: 9255702]
48. Gullone E, Taffe J. The Emotion Regulation Questionnaire for Children and Adolescents (ERQ-CA): a psychometric evaluation. Psychol Assess 2012 Jun;24(2):409-417. [doi: 10.1037/a0025777] [Medline: 22023559]
49. Schniering CA, Lyneham HJ. The Children's Automatic Thoughts Scale in a clinical sample: psychometric properties and clinical utility. Behav Res Ther 2007 Aug;45(8):1931-1940. [doi: 10.1016/j.brat.2006.09.009] [Medline: 17078927]
50. White BP. The perceived stress scale for children: A pilot study in a sample of 153 children. Int. J. Pediatr. Child Health 2014 Dec 31;2(2):45-52. [doi: 10.12974/2311-8687.2014.02.02.4]
51. Resilience Research. Halifax; 2019. URL: https://cyrm.resilienceresearch.org/files/CYRM_&_ARM-User_Manual.pdf [accessed 2022-06-15]
52. Rosenberg M. Society and the Adolescent Self-Image. Princeton, NJ: Princeton University Press; 2016.
53. Haltiwanger J, Harter S. The behavioral rating scale of presented self-esteem for young children. J Psychiatry Behav Sci 2019;2(1):1021 [FREE Full text] [doi: 10.1080/00221325.1996.9914858]
54. Suarez-Morales L, Dillon FR, Szapocznik J. Validation of the acculturative stress inventory for children. Cultur Divers Ethnic Minor Psychol 2007 Jul;13(3):216-224. [doi: 10.1037/1099-9809.13.3.216] [Medline: 17638478]
55. Thomas DC, Liao Y, Aycan Z, Cerdin J, Pekerti AA, Ravlin EC, et al. Cultural intelligence: A theory-based, short form measure. J Int Bus Stud 2015 Jan 29;46(9):1099-1118. [doi: 10.1057/jibs.2014.67]
56. Epstein N, Baldwin L, Bishop D. The McMaster family assessment device. J Marital Fam Ther 1983;9(2):171-180. [doi: 10.1111/j.1752-0606.1983.tb01497.x]
57. Cohen S, Kamarck T, Mermelstein R. A global measure of perceived stress. J Health Soc Behav 1983 Dec;24(4):385-396. [Medline: 6668417]
58. Funk JL, Rogge RD. Testing the ruler with item response theory: increasing precision of measurement for relationship satisfaction with the Couples Satisfaction Index. J Fam Psychol 2007 Dec;21(4):572-583. [doi: 10.1037/0893-3200.21.4.572] [Medline: 18179329]
59. KIDSCREEN Group Europe. The KIDSCREEN questionnaires: Quality of life questionnaires for children and adolescents. Lengerich, Germany: Pabst Science Publishers; 2006.
60. Ward C, Kennedy A. The measurement of sociocultural adaptation. International Journal of Intercultural Relations 1999 Aug;23(4):659-677. [doi: 10.1016/s0147-1767(99)00014-0]
61. Wilson J, Ward C, Fischer R. Beyond culture learning theory. Journal of Cross-Cultural Psychology 2013 Jul 15;44(6):900-927. [doi: 10.1177/0022022113492889]
62. Creswell JW, Hanson WE, Clark Plano VL, Morales A. Qualitative research designs. The Counseling Psychologist 2016 Jun 30;35(2):236-264. [doi: 10.1177/0011000006287390]
63. Cohen J. Statistical Power Analysis for the Behavioral Sciences. New York, NY: Routledge; 1998.
64. Kansteiner K, König S. The role(s) of qualitative content analysis in mixed methods research designs. Forum Qualitative Sozialforschung / Forum: Qualitative Social Research 2020;21(1):3412. [doi: 10.17169/fqs-21.1.3412]
65. Martin R. Adjusting to job relocation: Relocation preparation can reduce relocation stress. Journal of Occupational and Organizational Psychology 1999;72(2):231-235. [doi: 10.1348/096317999166626]
66. Mendenhall M, Stahl G, Ehnert I, Oddou G, Osland J, Kuhlmann T. Evaluation studies of cross-cultural training programs. In: Landis D, Bennett JM, Bennett MJ, editors. Handbook of Intercultural Training. Thousand Oaks, CA: SAGE Publications; 2004.

Abbreviations

SDQ: Strengths and Difficulties Questionnaire
WHO-5: 5-item World Health Organization Well-Being Index

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Protocol

Intravenous Infusion of Autoserum-Expanded Autologous Mesenchymal Stem Cells in Patients With Chronic Brain Injury: Protocol for a Phase 2 Trial

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Abstract

Background: Brain injuries resulting from motor vehicle accidents and falls, as well as hypoxic insults and other conditions, are one of the leading causes of disability and death in the world. Current treatments are limited but include continuous rehabilitation, especially for chronic brain injury. Recent studies have demonstrated that the intravenous infusion of mesenchymal stem cells (MSCs) has therapeutic efficacy for several neurological diseases, including stroke and spinal cord injury.

Objective: The objective of our investigator-initiated clinical trial is to assess the safety and potential efficacy of the intravenous infusion of autoserum-expanded autologous MSCs for patients with chronic brain injury.

Methods: The (phase 2) trial will be a single-arm, open-label trial with the primary objective of confirming the safety and efficacy of autoserum-expanded autologous MSCs (STR-01; produced under good manufacturing practices) when administered to patients with chronic brain injury. The estimated number of enrolled participants is 6 to 20 patients with a modified Rankin Scale grade of 3 to 5. The assessment of safety and the proportion of cases in which the modified Rankin Scale grade improves by 1 point or more at 180 days after the injection of STR-01 will be performed after MSC infusion.

Results: We received approval for our clinical trial from the Japanese Pharmaceuticals and Medical Devices Agency on December 12, 2017. The trial will be completed on June 11, 2023. The registration term is 5 years. The recruitment of the patients for this trial started on April 20, 2018, at Sapporo Medical University Hospital in Japan.

Conclusions: Our phase 2 study will aim to address the safety and efficacy of the intravenous infusion of MSCs for patients with chronic brain injury. The use of STR-01 has been performed for patients with cerebral infarction and spinal cord injury, providing encouraging results. The potential therapeutic efficacy of the systemic administration of autoserum-expanded autologous MSCs for chronic brain injury should be evaluated, given its safety and promising results for stroke and spinal cord injury.

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KEYWORDS

autologous mesenchymal stem cells; chronic brain injury; cell therapy; intravenous delivery; stem cells; rehabilitation; brain injury; brain; motor vehicle accident; falls; hypoxia

Introduction

Background

A *brain injury* is defined as an alteration in brain function or other evidence of brain pathology caused by trauma, including trauma resulting from motor vehicle accidents, falls, hypoxic insults, infections, and other conditions. Survivors—not only in severe cases but also in moderate or mild brain injury cases—experience the significant burdens of physical and neuropsychological disabilities. These disabilities disrupt the lives of patients and their families and result in substantial health care and social costs [1]. Chronic histopathological changes, such as cell death, axonal injury, vascular damage, and inflammation, have long-term persistence in brain injury survivors [2]. Thus, it is important to develop a novel approach to treating chronic brain injury.

The intravenous infusion of mesenchymal stem cells (MSCs) has shown therapeutic efficacy in experimental animal models of neurological diseases and injuries, including cerebral ischemia [3-12], spinal cord injury (SCI) [13-16], chronic epilepsy [17], and peripheral nerve injury [18-20]. The suggested therapeutic mechanisms of MSCs from animal studies include the secretion of neurotrophic factors that can provide neuroprotection [14,17,21], neovascularization [22,23], the restoration of the blood-brain barrier [13,24], the regeneration of axonal injury [13,25], remyelination [13], synaptogenesis [12,25], induced neural plasticity [12,25], and remote effects [15]. These therapeutic mechanisms may have beneficial effects on chronic brain injury as well. We also conducted clinical studies in which the intravenous infusion of autologous MSCs in patients with stroke [26,27] and SCI [28] was performed, and we showed its safety and improvements in neurologic symptoms. Thus, we hypothesize that the intravenous infusion of MSCs may have therapeutic efficacy for patients with chronic brain injury.

Objectives

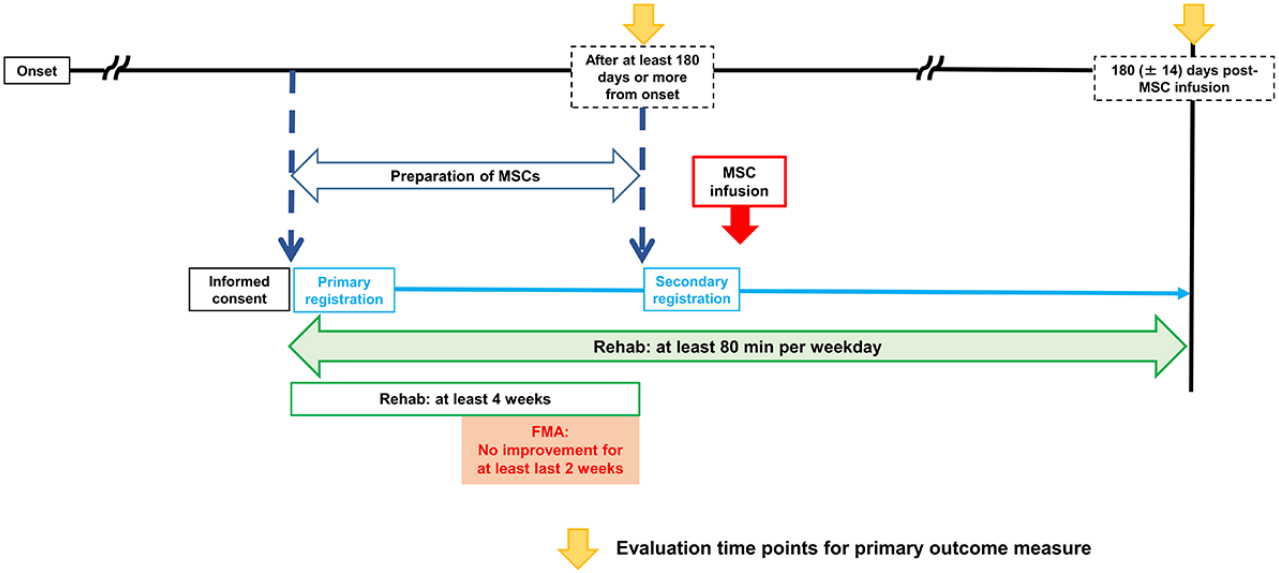
The objectives of the proposed clinical trial include evaluating the safety and efficacy of intravenously infused autologous MSCs that are expanded with autosera in patients with chronic brain injury.

Methods

Study Design

The (phase 2) trial will be a single-arm, open-label trial. The outline of the clinical protocol is shown in Figure 1. We will infuse the MSCs at least 180 days after onset. This trial will be carried out at Sapporo Medical University Hospital, Japan. The study protocol was based on advice provided by the Pharmaceuticals and Medical Devices Agency (PMDA) in Japan.

Figure 1. Clinical protocol. FMA: Fugl-Meyer assessment; MSC: mesenchymal stem cell.



We propose to provide an extensive rehabilitation protocol to all participants prior to MSC infusion in order to exclude the potential effects of rehabilitation alone and evaluate MSC-specific effects. Briefly, all patients with chronic brain injury will receive formal rehabilitation (at least 80 min/weekday for 4 weeks) and continue formal rehabilitation until they show

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no further improvements in Fugl-Meyer assessment (FMA) scores for the last 2 weeks prior to MSC infusion. Thus, we expect to evaluate the therapeutic effects of MSC infusion in addition to the effects of rehabilitation therapy. We will evaluate FMA scores approximately every week. The clinical data will be collected by at least 1 physical therapist and at least 1 Japanese board-certified neurosurgeon at Sapporo Medical University Hospital. If the patients require more than 2 weeks to reach an FMA score plateau, we will continue formal rehabilitation until they show no further improvements for the next 2 weeks.

For cell preparation, peripheral blood draws from each patient for autoserum and bone marrow collection will be performed. The autologous MSCs will be cultured in autologous sera, and the autologous human MSCs (called *STR-01*) will be manufactured in a cell processing center at Sapporo Medical University. STR-01 will be prepared under good manufacturing practice conditions by personnel, who have received formal good manufacturing practice training, within a facility with highly controlled temperature, room air, pressure, and environmental conditions and then cryopreserved at −150 °C until its use, as previously described [28]. On the day of infusion, cryopreserved units will be thawed at the bedside in a 37 °C water bath and will be administered with saline to each patient for approximately 60 minutes. The total number of cells in the STR-01 product is based on our previous study (0.5×10^8 to 2×10^8 cells per patient) [27]. Hospital treatment, including rehabilitation for a target of 80 min/weekday, will be performed for 180 (±14) post-MSC infusion days, after which final outcome measures will be evaluated.

Sample Size

We will recruit 10 people (minimum: 6; maximum: 20) with a modified Rankin Scale (mRS) grade of 3 to 5. The focus of our trial is to establish safety and potential efficacy. However, it should be noted that if the proportion of cases in which the mRS grade improves by 1 point or more exceeds 10%, the trial will provide significant clinical benefit. To detect a difference by using a *Z*-test with continuity correction, a minimum of 6 people is required. Thus, the target sample size of people with an mRS grade of 3 to 5 was determined to be 10 (minimum: 6; maximum: 10), under the consideration of dropout.

Ethics Approval

This study protocol was approved by the institutional review board (IRB) at Sapporo Medical University Hospital (approval number: 29-15). Changes to the protocol will require IRB and Japanese PMDA approval. The trial will be conducted in accordance with the ethical principles of the Declaration of Helsinki, the Japanese Pharmaceutical Affairs Law, and good clinical practice. Trial investigators will obtain written informed consent from each participant before study inclusion. If the participants do not have the ability to write, written informed consent will be obtained from a legal representative alone. Participants will be free to withdraw from the study at any time.

Consent for Publication

The results from our study will be presented in peer-reviewed publications and meetings without identifying data. Written consent for publication will be obtained from all participants in the study.

Eligibility Criteria

Since MSCs will be collected from the participants (autologous MSCs) in our study, we must start the MSC cultures after primary registration in order to initiate the collection of peripheral blood and bone marrow when the protocol therapy starts. Afterward, we must confirm that the MSC product passed the shipping standards before infusion. Thus, we must perform a secondary registration of the participants. Therefore, case registration will require 2 steps in the trial; we will register the participants before blood and bone marrow collections (first registration) and before the infusion of MSCs (second registration).

Inclusion Criteria at the Time of the First Registration

For the first registration, the inclusion criteria will be as follows: (1) a brain injury oth.er than stroke diagnosed via magnetic resonance imaging (MRI), computed tomography, 3D computed tomography angiography (3D-CTA), or angiography (including a suspected brain injury other than stroke); (2) a classification of grade 3 to 5 on the mRS; (3) patients aged 20 to 80 years; (4) patients whose rehabilitation can be performed for at least 80 minutes per weekday; and (5) written informed consent, which will be obtained as much as possible from the participants. If a participant does not have ability to write, written informed consent will be obtained from a legal representative alone.

Exclusion Criteria at the Time of the First Registration

For the first registration, the exclusion criteria will be as follows:

1. Severe disturbance of consciousness (a Japan Coma Scale score of between 200 and 300)
2. Severe contracture, deformity, or calcification of a joint
3. Diagnosed with hepatitis B, hepatitis C, or syphilis via initial screening
4. Pancytopenia (a white blood cell concentration of <2000 cells/μL, hemoglobin concentration of <10.0 g/dl, or platelet concentration of <100,000 platelets/μL)
5. MRI (or computed tomography) scan revealing a severe asymptomatic lesion or white matter lesion
6. MRI scan revealing multiple and severe instances of microbleeding or hemosiderosis in the whole brain
7. Head and neck magnetic resonance angiography (or 3D-CTA or angiography) scan revealing ≥70% stenosis of main cerebral arteries and cervical carotid arteries even after the revascularization (except for complete occlusion) or dissection of an artery
8. Head and neck magnetic resonance angiography (or 3D-CTA or angiography) scan revealing severe arteriosclerotic change or severe calcification
9. Moyamoya disease, cerebral aneurysm, and other vascular malformations with a high risk of rupture or cerebral embolism
10. Uncontrollable hypertension with therapy prior to infusion (systolic pressure: >140 mm Hg; diastolic pressure: >90 mm Hg)
11. Past history of neoplasms (except complete response); severe diseases of the blood and blood-forming organs;

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certain disorders involving the immune mechanism; severe mental and behavioral disorders; severe diseases of the nervous system; and severe congenital malformations, deformations, and chromosomal abnormalities
12. Past history of penicillin and streptomycin allergy or other severe allergy (shock or anaphylactic symptoms)
13. Poor general condition due to endocrine, nutritional, and metabolic diseases; uncontrollable mental disorders; diseases of the nervous system (refractory epilepsy), diseases of the circulatory system (uncontrollable and refractory heart failure, moderate or severe valvular heart disorder, uncontrollable and refractory atrial fibrillation, refractory atrial and ventricular thrombi, a history of ischemic heart disease with percutaneous coronary intervention within the past 12 months, and serious arrhythmia); diseases of the respiratory system; diseases of the digestive system; diseases of the musculoskeletal system and connective tissue; diseases of the genitourinary system (dialysis); injury; poisoning; and certain other consequences of external causes
14. Participation in another clinical trial related to any organ or a past history of cellular therapy
15. Pregnant or possibly pregnant women, nursing women, women who plan to be pregnant during the study period, or male patients who want their partners to get pregnant
16. Other patients who are judged by investigators holding a medical license as inappropriate for the study

Inclusion Criteria at the Time of the Second Registration

For the second registration, the inclusion criteria will be as follows: (1) ≥180 days after the onset of a brain injury other than stroke; (2) patients who, after rehabilitation for at least 80 minutes per weekday or as much as possible over the past 1 month or more, showed no improvement in FMA score over the last 2 weeks (definition of *improvement in FMA score*: improvement by 1 point or more, as shown by the total FMA score); (3) a classification of grade 3 to 5 on the mRS; and (4) patients who are ready for the infusion of STR-01 that satisfies the specifications of the acceptance criteria.

Exclusion Criteria at the Time of the Second Registration

For the second registration, the exclusion criteria will be as follows:

1. Severe disturbance of consciousness (Japan Coma Scale score of between 200 and 300)
2. Diagnosed with hepatitis B, hepatitis C, HIV, human T-lymphotropic virus 1 infection, syphilis, or human parvovirus B19 infection via detailed examination
3. More than 70% stenosis of main cerebral arteries and cervical carotid and vertebral arteries even after the revascularization (except for complete occlusion and a healed dissecting artery) or dissection of an artery
4. Severe arteriosclerotic change and calcification
5. Moyamoya disease, cerebral aneurysm, or other vascular malformations with a high risk of rupture or cerebral embolism
6. Uncontrollable hypertension with therapy prior to infusion
7. Ischemic heart disease (more than 75% stenosis of coronary arteries)
8. Cardiac shunt malformation (ventricular septal defect or arterial septal defect)
9. Possible large thrombus, as determined via laboratory examination
10. Neoplasms (except complete response); severe diseases of the blood and blood-forming organs; certain disorders involving the immune mechanism; severe mental and behavioral disorders; severe diseases of the nervous system; and severe congenital malformations, deformations, and chromosomal abnormalities
11. Penicillin and streptomycin allergy and other severe allergy (shock or anaphylactic symptoms)
12. Poor general condition due to endocrine, nutritional, and metabolic diseases; uncontrollable mental disorders; diseases of the nervous system (refractory epilepsy), diseases of the circulatory system (uncontrollable and refractory heart failure, moderate or severe valvular heart disorder, uncontrollable and refractory atrial fibrillation, refractory atrial and ventricular thrombi, a history of ischemic heart disease and percutaneous coronary intervention within the past 12 months, and serious arrhythmia); diseases of the respiratory system; diseases of the digestive system; diseases of the musculoskeletal system and connective tissue; diseases of the genitourinary system (dialysis); injury; poisoning; and certain other consequences of external causes
13. Pregnant women, nursing women, those who plan to be pregnant during the study period, or male patients who want their partners to get pregnant
14. Other patients who are judged by investigators holding a medical license as inappropriate for the study

Outcome Measures

Outcome measures will be performed by more than 2 Japanese board-certified neurosurgeons at Sapporo Medical University Hospital**.**

Primary Outcome

The primary outcome is the proportion of cases in which the mRS grade improves by 1 point or more between 180 (±14) days after the injection of STR-01 and just before injection (−14 to 0 days).

Secondary Outcomes

The following are the secondary outcomes: (1) the rate of all adverse events during the whole study period, (2) the differences in FMA scores (each item score and total score) between 180 (±14) days after the injection of STR-01 and just before injection (−14 to 0 days), (3) the differences in National Institutes of Health Stroke Scale scores (each item score and total score) between 180 (±14) days after the injection of STR-01 and just before injection (−14 to 0 days), and (4) the differences in Functional Independence Measure scores (each item score and total score) between 180 (±14) days after the injection of STR-01 and just before injection (−14 to 0 days).

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Statistical Analysis

The plan of analysis for study data will be performed by a biomedical statistician (YMI), and statistical analyses will be performed by using JMP 11.1 for Windows (SAS Institute Inc). The details are described in our statistical analysis plan and are described briefly in the following subsections.

Primary Outcome Measure

The valid target population is patients with an mRS grade of 3 to 5 before MSC infusion. We assume that the proportion of cases without MSC infusion in which the mRS grade improves by 1 point or more will be 0.1%. We will perform a Z-test with continuity correction at 180 (±14) days after MSC infusion.

Secondary Outcome Measure

We will estimate the proportion of cases with at least 1 level of improvement in mRS grade and the 95% CI by using the scoring method at 180 (±14) days after MSC infusion. We will also estimate the mean changes in FMA, National Institutes of Health Stroke Scale, and Functional Independence Measure scores from immediately before (−14 to 0 days) MSC infusion to 180 (±14) days after MSC infusion and the 95% CIs by using the Wald method.

Provisions for Posttrial Care

The participants of the trial will follow standard clinical procedures during the study; thus, there will be no specific posttrial care. As the participants are the patients within Japan's National Health Insurance system, postcare will be provided through the National Health Insurance schemes, if necessary. Clinical research insurance for studies will also be covered.

Access to Data

All investigators will have access to the trial data.

Data Management

All participant trial data will be entered into the electronic data capture system hosted at the Translational Research Center for Medical Innovation (Kobe, Japan). The data collected will be deidentified by using unique study code numbers. To maintain the privacy of the participants, any reports of individual data will only consist of clinical data without any names, addresses, or identifying information. This complies with the university's IRB guidelines. All patient-related information and data that are generated will be maintained on a secure server. Data monitoring will comply with the university's policies, its guidelines, and the data management plan that was approved for the study. Data will be audited at an appropriate period by the EPS Corporation (Tokyo, Japan). At the completion of the study, the results will be submitted for publication in a peer-reviewed journal and presented at national and international conferences.

Results

We received approval for our clinical trial from the Japanese PMDA on December 12, 2017. The trial will be completed on June 11, 2023. The registration term is 5 years. The recruitment of the patients for this trial started on April 20, 2018, at Sapporo Medical University Hospital in Japan.

Discussion

The specific objective of our trial is to evaluate the safety and potential therapeutic efficacy of the intravenous infusion of autoserum-expanded autologous MSCs for patients with chronic brain injury. The patients who enrolled in our study with chronic brain injury and decreased neural function due mainly to brain trauma will receive an intravenous infusion of autologous MSCs that are expanded in autosera. A brain injury presents serious health and socioeconomic burdens that the development of an effective therapy could alleviate.

Various treatments have been developed that focus mainly on the acute phase, including neurorestorative, anti-inflammatory, and neuroprotective agents. However, no established medical therapies that promote effective therapeutic efficacy have been made, especially for the chronic phase. Therefore, a novel therapy that promotes recovery from brain damage after a chronic brain injury should be developed [29].

We previously reported on the safety, feasibility, and potential therapeutic efficacy of the intravenous infusion of autoserum-expanded autologous MSCs for patients with cerebral infarction [27] and subacute SCI [28]. The intravenous infusion of MSCs derived from bone marrow improves functional outcomes in experimental animal models of stroke [4-7,9-11], SCI [13,14,16,24,30,31], neonatal hypoxic ischemia [12], chronic epilepsy [17], cerebral small vessel disease [8,32], amyotrophic lateral sclerosis [33,34], and peripheral nerve injury [18,21]. Although the mechanisms underlying these beneficial effects have not been fully elucidated, potential mechanisms include neuroprotection and immunomodulation [14], the induction of axonal sprouting [13], remyelination [13], the restoration of the blood-brain and blood–spinal cord barriers [13,24], and the enhancement of remote gene expression responses [15].

We reported that infused MSCs facilitate neural plasticity in experimental models of neonatal [12] and adult [4,5] cerebral ischemia. Since brain injuries in the chronic phase are heterogenous injuries that are underpinned by numerous complex and interrelated pathophysiological conditions [35], it is conceivable that the enhanced neural plasticity resulting from MSC injection promotes structural rewiring, which might contribute to functional improvement in chronic state of neural diseases. In addition, there are other multimodal and orchestrated mechanisms, as shown in previous studies [3-13,15-18,25,28,32-34,36-38]. Given these considerations of the potential therapeutic effects of MSCs in a number of neurological disorders, we planned a clinical trial for chronic brain injury.

The purpose of our study is to address the safety and potential therapeutic efficacy of the intravenous infusion of autologous MSCs based on the primary outcome measures. If the intravenous infusion of autologous MSCs shows possible therapeutic efficacy and is shown to be safe without any major adverse effects, this approach could be successfully translated to a larger controlled and blinded clinical study in the future. The data from our study will be used to develop a new clinical protocol for any future, larger, definitive evaluation trials.

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In conclusion, due to the promising therapeutic effects of autoserum-expanded autologous MSCs for stroke [27] and SCI [28], this approach should be evaluated for chronic brain injury, which shares many of the histopathological conditions that have been seen in patients with stroke and SCI. We thus believe that this cell therapy approach for patients chronic brain injury could have a significant impact and warrants evaluation in the near future [39].

Acknowledgments

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Authors' Contributions

OH is responsible for the processing of the trial. RO and OH wrote and reviewed all protocol versions. SO, MS, RU, MT, TY, YKS, JDK, and OH reviewed all protocol versions. SO, TY, MS, RU, MT, TY, YKS, YMI, SK, YI, and OH participated in the conduction of the trial. All authors read and approved the final manuscript.

Conflicts of Interest

The Department of Advanced Regenerative Therapeutics at Sapporo Medical University has been partnered with the Nipro Corporation since February 1, 2014. Sapporo Medical University and Nipro Corporation entered into a joint research and development agreement on April 1, 2014, which provides research support to the department, including support for the work carried out by some of the coauthors (SO, MS, YKS, and OH). JDK receives research support through Yale University from the Nipro Corporation for associated research on preclinical studies of rodent mesenchymal stem cells. YT, RU, MT, TY, RO, YMI, SK, and YI report no competing interests.

References

1. Maas AIR, Menon DK, Adelson PD, Andelic N, Bell MJ, Belli A, InTBIR Participants and Investigators. Traumatic brain injury: integrated approaches to improve prevention, clinical care, and research. Lancet Neurol 2017 Dec;16(12):987-1048. [doi: 10.1016/S1474-4422(17)30371-X] [Medline: 29122524]
2. Osier ND, Carlson SW, DeSana A, Dixon CE. Chronic histopathological and behavioral outcomes of experimental traumatic brain injury in adult male animals. J Neurotrauma 2015 Dec 01;32(23):1861-1882 [FREE Full text] [doi: 10.1089/neu.2014.3680] [Medline: 25490251]
3. Nakazaki M, Sasaki M, Kataoka-Sasaki Y, Oka S, Namioka T, Namioka A, et al. Intravenous infusion of mesenchymal stem cells inhibits intracranial hemorrhage after recombinant tissue plasminogen activator therapy for transient middle cerebral artery occlusion in rats. J Neurosurg 2017 Oct;127(4):917-926. [doi: 10.3171/2016.8.JNS16240] [Medline: 28059661]
4. Sasaki Y, Sasaki M, Kataoka-Sasaki Y, Nakazaki M, Nagahama H, Suzuki J, et al. Synergic effects of rehabilitation and intravenous infusion of mesenchymal stem cells after stroke in rats. Phys Ther 2016 Nov;96(11):1791-1798. [doi: 10.2522/ptj.20150504] [Medline: 27174259]
5. Suzuki J, Sasaki M, Harada K, Bando M, Kataoka Y, Onodera R, et al. Bilateral cortical hyperactivity detected by fMRI associates with improved motor function following intravenous infusion of mesenchymal stem cells in a rat stroke model. Brain Res 2013 Feb 25;1497:15-22. [doi: 10.1016/j.brainres.2012.12.028] [Medline: 23274536]
6. Namioka A, Namioka T, Sasaki M, Kocsis JD, Honmou O. Focal brainstem infarction in the adult rat. Lab Anim (NY) 2021 Apr;50(4):97-107. [doi: 10.1038/s41684-021-00722-1] [Medline: 33564191]
7. Kiyose R, Sasaki M, Kataoka-Sasaki Y, Nakazaki M, Nagahama H, Magota H, et al. Intravenous infusion of mesenchymal stem cells enhances therapeutic efficacy of reperfusion therapy in cerebral ischemia. World Neurosurg 2021 May;149:e160-e169. [doi: 10.1016/j.wneu.2021.02.056] [Medline: 33618048]
8. Nakazaki M, Sasaki M, Kataoka-Sasaki Y, Oka S, Suzuki J, Sasaki Y, et al. Intravenous infusion of mesenchymal stem cells improves impaired cognitive function in a cerebral small vessel disease model. Neuroscience 2019 Jun 01;408:361-377. [doi: 10.1016/j.neuroscience.2019.04.018] [Medline: 30999031]
9. Nakamura H, Sasaki Y, Sasaki M, Kataoka-Sasaki Y, Oka S, Nakazaki M, et al. Elevated brain derived neurotrophic factor levels in plasma reflect in vivo functional viability of infused mesenchymal stem cells for stroke in rats. J Neurosurg Sci 2019 Feb;63(1):42-49. [doi: 10.23736/S0390-5616.17.03989-3] [Medline: 28181779]

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10. Namioka T, Namioka A, Sasaki M, Kataoka-Sasaki Y, Oka S, Nakazaki M, et al. Intravenous infusion of mesenchymal stem cells promotes functional recovery in a rat model of chronic cerebral infarction. J Neurosurg 2018 Oct 01:1-8. [doi: 10.3171/2018.5.JNS18140] [Medline: 30485210]
11. Namioka A, Namioka T, Sasaki M, Kataoka-Sasaki Y, Oka S, Nakazaki M, et al. Intravenous infusion of mesenchymal stem cells for protection against brainstem infarction in a persistent basilar artery occlusion model in the adult rat. J Neurosurg 2018 Oct 01:1-9. [doi: 10.3171/2018.4.JNS173121] [Medline: 30485204]
12. Sakai T, Sasaki M, Kataoka-Sasaki Y, Oka S, Nakazaki M, Fukumura S, et al. Functional recovery after the systemic administration of mesenchymal stem cells in a rat model of neonatal hypoxia-ischemia. J Neurosurg Pediatr 2018 Nov 01;22(5):513-522. [doi: 10.3171/2018.5.PEDS1845] [Medline: 30074448]
13. Morita T, Sasaki M, Kataoka-Sasaki Y, Nakazaki M, Nagahama H, Oka S, et al. Intravenous infusion of mesenchymal stem cells promotes functional recovery in a model of chronic spinal cord injury. Neuroscience 2016 Oct 29;335:221-231. [doi: 10.1016/j.neuroscience.2016.08.037] [Medline: 27586052]
14. Osaka M, Honmou O, Murakami T, Nonaka T, Houkin K, Hamada H, et al. Intravenous administration of mesenchymal stem cells derived from bone marrow after contusive spinal cord injury improves functional outcome. Brain Res 2010 Jul 09;1343:226-235. [doi: 10.1016/j.brainres.2010.05.011] [Medline: 20470759]
15. Oshigiri T, Sasaki T, Sasaki M, Kataoka-Sasaki Y, Nakazaki M, Oka S, et al. Intravenous infusion of mesenchymal stem cells alters motor cortex gene expression in a rat model of acute spinal cord injury. J Neurotrauma 2019 Feb 01;36(3):411-420 [FREE Full text] [doi: 10.1089/neu.2018.5793] [Medline: 29901416]
16. Hirota R, Sasaki M, Kataoka-Sasaki Y, Oshigiri T, Kurihara K, Fukushi R, et al. Enhanced network in corticospinal tracts after infused mesenchymal stem cells in spinal cord injury. J Neurotrauma. Epub ahead of print 2022 May 25. [doi: 10.1089/neu.2022.0106] [Medline: 35611987]
17. Fukumura S, Sasaki M, Kataoka-Sasaki Y, Oka S, Nakazaki M, Nagahama H, et al. Intravenous infusion of mesenchymal stem cells reduces epileptogenesis in a rat model of status epilepticus. Epilepsy Res 2018 Mar;141:56-63. [doi: 10.1016/j.eplepsyres.2018.02.008] [Medline: 29475054]
18. Takayanagi A, Sasaki M, Kataoka-Sasaki Y, Kobayashi K, Matsuda Y, Oka S, et al. Intravenous preload of mesenchymal stem cells rescues erectile function in a rat model of cavernous nerve injury. J Sex Med 2015 Aug;12(8):1713-1721. [doi: 10.1111/jsm.12957] [Medline: 26211660]
19. Lerner MZ, Matsushita T, Lankford KL, Radtke C, Kocsis JD, Young NO. Intravenous mesenchymal stem cell therapy after recurrent laryngeal nerve injury: a preliminary study. Laryngoscope 2014 Nov;124(11):2555-2560. [doi: 10.1002/lary.24798] [Medline: 25043703]
20. Matthes SM, Reimers K, Janssen I, Liebsch C, Kocsis JD, Vogt PM, et al. Intravenous transplantation of mesenchymal stromal cells to enhance peripheral nerve regeneration. Biomed Res Int 2013;2013:573169 [FREE Full text] [doi: 10.1155/2013/573169] [Medline: 24459671]
21. Matsuda Y, Sasaki M, Kataoka-Sasaki Y, Takayanagi A, Kobayashi K, Oka S, et al. Intravenous infusion of bone marrow-derived mesenchymal stem cells reduces erectile dysfunction following cavernous nerve injury in rats. Sex Med 2018 Mar;6(1):49-57 [FREE Full text] [doi: 10.1016/j.esxm.2017.10.005] [Medline: 29275062]
22. Kocsis JD, Honmou O. Bone marrow stem cells in experimental stroke. Prog Brain Res 2012;201:79-98. [doi: 10.1016/B978-0-444-59544-7.00005-6] [Medline: 23186711]
23. Liu H, Honmou O, Harada K, Nakamura K, Houkin K, Hamada H, et al. Neuroprotection by PlGF gene-modified human mesenchymal stem cells after cerebral ischaemia. Brain 2006 Oct;129(Pt 10):2734-2745 [FREE Full text] [doi: 10.1093/brain/awl207] [Medline: 16901914]
24. Matsushita T, Lankford KL, Arroyo EJ, Sasaki M, Neyazi M, Radtke C, et al. Diffuse and persistent blood-spinal cord barrier disruption after contusive spinal cord injury rapidly recovers following intravenous infusion of bone marrow mesenchymal stem cells. Exp Neurol 2015 May;267:152-164. [doi: 10.1016/j.expneurol.2015.03.001] [Medline: 25771801]
25. Nagahama H, Nakazaki M, Sasaki M, Kataoka-Sasaki Y, Namioka T, Namioka A, et al. Preservation of interhemispheric cortical connections through corpus callosum following intravenous infusion of mesenchymal stem cells in a rat model of cerebral infarction. Brain Res 2018 Sep 15;1695:37-44. [doi: 10.1016/j.brainres.2018.05.033] [Medline: 29802840]
26. Honmou O, Onodera R, Sasaki M, Waxman SG, Kocsis JD. Mesenchymal stem cells: therapeutic outlook for stroke. Trends Mol Med 2012 May;18(5):292-297. [doi: 10.1016/j.molmed.2012.02.003] [Medline: 22459358]
27. Honmou O, Houkin K, Matsunaga T, Niitsu Y, Ishiai S, Onodera R, et al. Intravenous administration of auto serum-expanded autologous mesenchymal stem cells in stroke. Brain 2011 Jun;134(Pt 6):1790-1807 [FREE Full text] [doi: 10.1093/brain/awr063] [Medline: 21493695]
28. Honmou O, Yamashita T, Morita T, Oshigiri T, Hirota R, Iyama S, et al. Intravenous infusion of auto serum-expanded autologous mesenchymal stem cells in spinal cord injury patients: 13 case series. Clin Neurol Neurosurg 2021 Apr;203:106565 [FREE Full text] [doi: 10.1016/j.clineuro.2021.106565] [Medline: 33667953]
29. Thapa K, Khan H, Singh TG, Kaur A. Traumatic brain injury: Mechanistic insight on pathophysiology and potential therapeutic targets. J Mol Neurosci 2021 Sep;71(9):1725-1742. [doi: 10.1007/s12031-021-01841-7] [Medline: 33956297]

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30. Quertainmont R, Cantinieaux D, Botman O, Sid S, Schoenen J, Franzen R. Mesenchymal stem cell graft improves recovery after spinal cord injury in adult rats through neurotrophic and pro-angiogenic actions. PLoS One 2012;7(6):e39500. [doi: 10.1371/journal.pone.0039500] [Medline: 22745769]
31. Cízková D, Rosocha J, Vanický I, Jergová S, Cízek M. Transplants of human mesenchymal stem cells improve functional recovery after spinal cord injury in the rat. Cell Mol Neurobiol 2006;26(7-8):1167-1180. [doi: 10.1007/s10571-006-9093-1] [Medline: 16897366]
32. Nakazaki M, Oka S, Sasaki M, Kataoka-Sasaki Y, Nagahama H, Hashi K, et al. Prolonged lifespan in a spontaneously hypertensive rat (stroke prone) model following intravenous infusion of mesenchymal stem cells. Heliyon 2020 Dec 25;6(12):e05833 [FREE Full text] [doi: 10.1016/j.heliyon.2020.e05833] [Medline: 33392407]
33. Magota H, Sasaki M, Kataoka-Sasaki Y, Oka S, Ukai R, Kiyose R, et al. Intravenous infusion of mesenchymal stem cells delays disease progression in the SOD1G93A transgenic amyotrophic lateral sclerosis rat model. Brain Res 2021 Apr 15;1757:147296. [doi: 10.1016/j.brainres.2021.147296] [Medline: 33516815]
34. Magota H, Sasaki M, Kataoka-Sasaki Y, Oka S, Ukai R, Kiyose R, et al. Repeated infusion of mesenchymal stem cells maintain the condition to inhibit deteriorated motor function, leading to an extended lifespan in the SOD1G93A rat model of amyotrophic lateral sclerosis. Mol Brain 2021 May 07;14(1):76 [FREE Full text] [doi: 10.1186/s13041-021-00787-6] [Medline: 33962678]
35. Gozt A, Hellewell S, Ward PGD, Bynevelt M, Fitzgerald M. Emerging applications for quantitative susceptibility mapping in the detection of traumatic brain injury pathology. Neuroscience 2021 Jul 15;467:218-236. [doi: 10.1016/j.neuroscience.2021.05.030] [Medline: 34087394]
36. Sasaki M, Oka S, Kataoka-Sasaki Y, Kocsis JD, Honmou O. "Chronic" state in neural diseases as the target of cellular therapy with mesenchymal stem cells. World Neurosurg 2020 Mar;135:375-376. [doi: 10.1016/j.wneu.2019.12.137] [Medline: 32143241]
37. Yasuda N, Sasaki M, Kataoka-Sasaki Y, Nagahama H, Kocsis JD, Kawaharada N, et al. Intravenous delivery of mesenchymal stem cells protects both white and gray matter in spinal cord ischemia. Brain Res 2020 Nov 15;1747:147040. [doi: 10.1016/j.brainres.2020.147040] [Medline: 32771405]
38. Nakazaki M, Oka S, Sasaki M, Kataoka-Sasaki Y, Onodera R, Komatsu K, et al. Prevention of neointimal hyperplasia induced by an endovascular stent via intravenous infusion of mesenchymal stem cells. J Neurosurg 2019 Oct 04:1-13. [doi: 10.3171/2019.7.JNS19575] [Medline: 31585431]
39. Kawabori M, Weintraub AH, Imai H, Zinkevych L, McAllister P, Steinberg GK, et al. Cell therapy for chronic TBI: Interim analysis of the randomized controlled STEMTRA trial. Neurology 2021 Jan 04;96(8):e1202-e1214 [FREE Full text] [doi: 10.1212/WNL.0000000000011450] [Medline: 33397772]

Abbreviations

3D-CTA: 3D computed tomography angiography
FMA: Fugl-Meyer assessment
IRB: institutional review board
MRI: magnetic resonance imaging
mRS: modified Rankin Scale
MSC: mesenchymal stem cell
PMDA: Pharmaceuticals and Medical Devices Agency
SCI: spinal cord injury

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Protocol

Strengthening Interpersonal Relationships in Maternal and Child Health Care in Rural Tanzania: Protocol for a Human-Centered Design Intervention

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Abstract

Background: Evidence indicates that clients' dissatisfaction with providers' competencies within maternal and child health (MCH) continues to impact trust in formal health care systems, service uptake, continuity with care, and MCH outcomes. A major problem with existing interventions is the failure to address all the complexities of provider-client relationships necessitating targeted, contextualized, innovative solutions that place providers and clients at the forefront as agents of change in optimizing intervention design and implementation. To improve the provider-client relationship, the Aga Khan University is piloting a human-centered design (HCD) intervention where MCH nurses and clients are invited to partner with researchers in the intervention design and evaluation process.

Objective: The objective of this research is to co-design an intervention package (prototype) for improving nurse-client relationships in the rural Shinyanga region of Tanzania using a series of iterative HCD steps, involving key stakeholders to tailor solutions for complex problems impacting provider-client interactions in MCH care.

Methods: The following 5-step HCD approach will be implemented: (1) community-driven discovery through qualitative descriptive research methods using focus group discussions and key informant interviews; (2) co-design of an intervention package through consultative ideation and cocreation meetings with nurses, clients, and other stakeholders; (3) prototype validation through qualitative insight gathering using focus group discussions; (4) refinement and adaptation meeting; and (5) documentation and sharing of lessons learned before the final prototype is tested and validated in a broader community.

Results: A prototype characterized by a package of interventions for improving nurse-client relationships in MCH care in rural contexts is expected to be developed from the co-design process.

Conclusions: An HCD approach provides a novel entry point for strengthening provider-client relationships, where clients are invited to partner with providers in the design of acceptable and feasible interventions.

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KEYWORDS

human-centered design; user-centred design; human-centred design; provider-patient relationship; nurse-client relationship; nurse; nursing; maternal and child health; maternal; maternity; mother; child; primary health care; primary care; rural; Tanzania; Africa; community-based; focus group; co-design; prototype; validation; nurse-patient; provider-client

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Introduction

Nurses and midwives form a critical component of maternal and child health (MCH) services globally. They play a vital role in the delivery of primary health care services related to pregnancy monitoring, delivery, and postnatal care for women and newborns around the world [1-4]. In sub-Saharan Africa, nurses and midwives are often respected members of the community and provide advice and evidence-based information on a range of health issues, including care of newborns and young children [2-4]. With sufficient, well-supported, and competent nurses and midwives, 83% of maternal deaths, stillbirths, and neonatal deaths could be prevented [5-7]. Competent nurses and midwives have the potential to increase client service uptake and continuity, and consequently improve health outcomes, such as increased breastfeeding initiation and duration, and reductions in cesarean sections, maternal infections, postpartum hemorrhage, and preterm births [8]. Literature suggests that investing in nurses and midwives has the potential to yield a 16-fold return on investments resulting from improved MCH outcomes [9].

Despite the critical role of nurses and midwives, there has been increasing client dissatisfaction with the interpersonal and perceived technical competencies of nurses and midwives within MCH care in recent years [10-19]. Perceived technical incompetence associated with skills, reliability, assurance, confidentiality, and patient engagement; behavioral incompetence involving demeanor, attitudes, and empathy; communication skills and language; and violation of client rights and respect continue to obscure the positive value of nurses and midwives in the delivery of MCH interventions in Tanzania and other settings [10-21]. Recent studies indicate that clients' dissatisfaction with nurses' interpersonal and technical aspects of care continues to erode client trust in the formal health care system, service uptake, continuity, and MCH outcomes [19-23].

To address clients' dissatisfaction, health care service governance instruments including policies, client service charters, health facility governance committees, complaints mechanisms, and professional bodies have been emphasized in both high- and low-income settings; however, their effectiveness is not well established. Consequently, political interventions such as employment termination and labeling of nurses as "bad, lazy, and incompetent" are the current actions taken for addressing this complex problem, creating tension between clients and nurses as well as contributing to the poor morale of providers [24,25]. Competence-based interventions focusing on provider communication skills, patient-centered care, patient literacy, information seeking, participation, and questioning skills are often implemented erratically, yielding unsatisfactory results. A major challenge with existing interventions documented in the literature is the failure to address all the complexities of nurse-client relationships along the continuum of MCH care. Patients' socioeconomic fragility, literacy, and behaviors coupled with providers' poor interpersonal skills and health system challenges add to the complexity of nurse-client relationships. This complexity necessitates targeted contextualized and innovative solutions that place nurses and clients at the forefront as agents of change in optimizing the design and implementation of interventions [26].

Rather than replicating existing interventions that may not be contextually applicable, new and innovative interventions to improve the provision of high-quality and satisfactory care are needed within resource-constrained settings such as rural Tanzania [26-32]. If embraced, a stepwise incremental process from intervention design to evaluation of effectiveness could offer flexibility in problem-solving while using a standardized process that has the potential to be applied in diverse settings. It is within this context that the Aga Khan University (AKU) is piloting a human-centered design (HCD) intervention in rural Tanzania, where nurses and MCH clients are invited to partner in the intervention design and evaluation process to deepen understanding of and address the identified challenges. Abookire et al [31] consider HCD as "an innovative approach to problem-solving that leverages insights from the end users of new products, services, and experiences to develop best-fit solutions that are rapidly prototyped and iteratively refined." HCD is considered to facilitate improvements in client, provider, and community satisfaction, as well as increased efficiency and collaboration in public health intervention development and implementation process [30-32]. Furthermore, HCD may result in more successful and sustainable interventions compared to traditional problem-solving approaches in health care and public health [31]. Melles et al [30] recently proposed that the implementation of HCD in health care needs to focus on developing an understanding of the people facing a particular barrier and their needs and engaging them as stakeholders throughout the design process. The HCD approach also embraces a system-wide outlook by considering interactions of factors at different levels and harmonizing individual interests to form collective interests when developing solutions. Therefore, we aim to co-design an intervention package (prototype) for improving nurse-client relationships in the Shinyanga region of rural Tanzania. We will use a series of iterative HCD steps involving key stakeholders to contextualize solutions for complex problems impacting interactions in MCH care. We hypothesize that the emerging prototype will have high potential in improving nurse-client relationships, thereby leading to increased client satisfaction, MCH service uptake, and service continuity in rural communities.

Methods

Design

A 5-step HCD approach will be employed as an investigative framework to co-design interventions for improving nurse-client relationships using qualitative descriptive design with focus group discussions (FGDs), key informant interviews (KIIs), and consultative meetings. This approach was deemed appropriate to answer two key questions: (1) What are the drivers of poor nurse-client relationships in MCH care? and (2) What is/are the best intervention codeveloped by nurses and clients for strengthening nurse-client relationships to address these drivers considering feasibility and acceptability? A qualitative descriptive approach is appropriate for this inquiry as it aims to develop understanding and describe nurse-client

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relationships without testing an existing theory [33]. This approach offers an effective way of gaining a deep and rich understanding of nurse and client perceptions and experiences in the chosen context, as this may differ from other contexts in terms of culture, expectations, and resources within health care settings. The qualitative descriptive design also allows us to acknowledge the subjectivity of nurses and clients as well as researcher experiences of nurse-client relationships and the research process to collect data in a natural setting. Furthermore, by listening to the descriptions of nurses and clients, we could learn from these experiences of MCH care and use "…this knowledge to influence interventions design" using the HCD process and generate research findings of "specific relevance to practitioners and policy makers" to improve MCH care [33].

As an investigative framework for this study, HCD is a problem-solving approach that uses a series of iterative and often nonlinear steps to tailor solutions for complex problems [26-32]. Although similar to other participatory research frameworks in their inclusion of end-user feedback throughout the research process, HCD differs in its endeavor toward empathy, a deep understanding of the motivations and desires that govern human behavior, as the inspiration and core of intervention development [26]. In the HCD approach, end users are invited to partner in the design and evaluation process to better understand, meet, and address the identified challenges. In a low-resource complex setting where the drivers of poor nurse-client relationships may differ significantly from well-resourced settings, these key principles of HCD can be leveraged to optimize intervention development and implementation.

Settings

This study will be conducted in Shinyanga, a region located in Lake Zone and predominantly inhabited by Bantus. Isangula [23] offers a detailed description of the region. Briefly, Shinyanga falls within the low-income category of the regions in Tanzania. It is administratively divided into 5 districts: Shinyanga Municipal Council (MC), Shinyanga District Council (DC), Kishapu DC, Kahama MC, and Kahama DC. The rationale for choosing Shinyanga is twofold. First, ethnically, the region is predominantly inhabited by Sukuma, who share a range of sociocultural beliefs and practices with minimal diversity. Due to its near homogeneity, the region is a perfect exemplar of many other rural regions of Tanzania. Second, despite a number of capacity-building interventions, local data indicate enormous concerns about poor nurse-client relationships in MCH care [23]. Within the Shinyanga region, Shinyanga MC was purposefully selected because patients in this district have greater access to both the formal health care system (mostly public and few private and faith-based facilities) and traditional care [23].

By focusing on the Shinyanga region, we will embrace the importance of deepening our understanding of the unique barriers to nurse-client relationships in this setting and aim to provide a context-specific intervention model that is applicable in this and similar contexts. The UK Medical Research Council's framework for the development and evaluation of complex interventions underlines the crucial role of the context in the adaptation and implementation of interventions [34]. The region, like many other parts of Tanzania and sub-Saharan Africa, has a wide range of rural and urban populations with varying socioeconomic statuses including highly marginalized populations with immense potential to positively impact population health. However, given the contextual differences within Tanzania and across Africa, the prototype generated may differ but still provide an applicable and exemplary model for feasibility testing and adaptation in diverse settings.

The concerns of poor nurse-client relationships in MCH documented in Shinyanga have been previously documented in other rural regions of Tanzania and Africa. This means the prototype developed in Shinyanga may be feasible in other rural regions of Tanzania and Africa with some minor adaptations. However, further testing and refinement of the prototype during the feasibility study may offer more insights into the feasibility of the prototype in other regions of Tanzania and beyond.

Study Population, Sample Size, Sampling, and Data Collection

The 5-step HCD process is envisaged below (Multimedia Appendix 1).

Step 1. Community-Driven Discovery Inquiry

A combination of qualitative research methodologies will be employed to explore community and individual perspectives. A minimum of 8 FGDs and 10 KIIs will be conducted with purposefully selected nurses and midwives, women attending MCH services, and administrators using a semistructured interview guide in the Swahili language. We believe this sample is adequate because recent reviews have found that most qualitative studies achieve data saturation between 9 and 17 interviews [35]. The semistructured interview guide will contain questions on the existing drivers of poor nurse-client relationships and the contextual factors, barriers, and facilitators that could impact intervention design, implementation, and sustainability. Participants will be recruited through MCH managers. All interviews will be conducted at a convenient location confirmed with the respondents in advance to enable them to identify an alternate location if required. Upon arrival, research assistants will provide detailed information on the study, obtain informed consent, and engage respondents for approximately 45 to 60 minutes in a semistructured audio-taped discussion. The findings will be used in step 2 of the HCD process.

Step 2. Consultative Co-design Meetings

In this stage, a transdisciplinary team of purposively sampled MCH nurses and midwives, clients, administrators, and other relevant stakeholders (30 members) will gather to define the challenges based on discovery findings and design an intervention package (prototype) with the highest potential to improve nurse-client relationships considering acceptability and feasibility. Invitation letters will be sent to purposively sampled participants with information on the date of the consultative meeting and preselected venue. This 3-month process will involve 3 consultative meetings: (1) a synthesis meeting to review the qualitative data gathered in step 1 and share insights, experiences, and questions to generate a deeper

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understanding of the challenges of nurse-client relationships in Shinyanga; (2) an ideation meeting to brainstorm and generate "how might we" questions that facilitate the development of potential ideas for the solution; (3) a prototype and cocreation meeting to evaluate the ideas generated considering pros, cons, and feasibility and develop the initial (rough) prototype model(s) as well as elements crucial to its testing (features, modality, responsible person, etc). Each meeting will be conducted for 4 to 6 hours and all key discussion points will be documented. The findings will inform step 3.

Step 3. Validation and Insight Gathering Inquiry

This will involve gathering insights on the rough prototype in Shinyanga MC for 3 months depending on the features of the prototype model to be tested. The aim is to gather qualitative feedback using guided FGDs (6 sessions) with purposively sampled participants to identify features appealing to both nurses and clients for strengthening their relationship to increase MCH service satisfaction, uptake, and continuity. Nurses and clients will be recruited through MCH managers and engaged in 45- to 60-minute audio-taped discussions. The findings will inform step 4.

Step 4. Refinement and Adaptation Meeting

The design team will reconvene for 1 day to evaluate the feedback and rough prototype insights as well as to refine and adapt the prototype. Representatives of the participants for rough prototype testing (insight gathering inquiry) will be selected by their peers to join the participants of co-design meetings (40 members) in the refinement and adaptation process leading to the final prototype model. The lessons learned in arriving at the final prototype model will inform step 5.

Step 5. Document and Share

The lessons will be synthesized and disseminated to local and international stakeholders. These lessons will form the basis for transitioning the intervention package (prototype) to feasibility and definitive testing.

We will recruit 3 research assistants and train them on the HCD process and techniques pertaining to this study. The discussion, interview, and consultative meeting guides will be pretested in purposefully selected settings and refined to ensure readiness for use in the actual data collection process (Multimedia Appendix 2). Close and supportive supervision of research assistants will be conducted throughout the data collection and analysis stages to ensure data quality.

Data Management and Analysis

The HCD process will generate data from FGDs, KIIs, and consultative meetings. Data transcription and translation will occur simultaneously by research assistants and verified by the research team. Interview transcripts will be deidentified, pseudonyms generated for each participant, and the data uploaded into the NVivo 12 software (QSR International) for management and deductive thematic coding. A stepwise approach will be used for a deductive thematic analysis of the interview transcripts [36]. First, the research team will examine the research questions and generate several themes based on consensus. This will result in an analytical matrix of the main themes and subthemes. Individual transcripts and phrases (codes) representing participants' responses to investigators' questions will be exported to relevant themes and related subthemes within NVivo. A consensus-based approach will then be used by the research team to decide on including codes that do not fit within the developed subthemes and themes; the codes will be excluded if do not provide critical value to the study, as confirmed by subjective and objective evaluations. The data within NVivo will then be exported to Microsoft Word (Microsoft Corporation) for interpretative analysis and report generation.

Ethics Approval

This study has received ethics clearance from the AKU Ethics Review Committee and The National Institute for Medical Research (NIMR/HQ/R.8a/Vol. IX/3906), as well as local approvals from the Regional Medical Officer of Shinyanga and the Municipal Medical Officer in Shinyanga (Multimedia Appendix 3). At the health facility level, verbal approvals will be sought from the managers of the selected facilities from where nurses and clients will be recruited after providing letters from the district medical officers and copies of ethical clearance. We will ensure responsible conduct of research by obtaining written consent from all participants before participation.

The study does not directly or indirectly expose nurses and clients to any diagnosis or treatment. As safeguards, all study responses will be kept confidential, and data analysis and reporting will be conducted at an aggregated level within the Shinyanga region. Further, all data gathered will not be used for purposes other than the present research. Due to the global COVID-19 pandemic, face masks, sanitizers, and social distancing will be used to mitigate infection transmission during fieldwork activities.

Results

Participant Demographics

We will summarize the characteristics of all participants across all stages of the HCD process. Descriptions and tables will be used to present key participant characteristics.

Findings From the Community-Driven Discovery Inquiry

We expect to generate results from a qualitative study employing FGDs with nurses and MCH clients and KIIs with MCH administrators and stakeholders conducted as part of the community-driven inquiry. The results will include participants' understanding of what nurse-client relationships mean; their experiences with good and bad nurse-client interactions; the existing drivers of poor nurse-client relationships; and the contextual factors, barriers, and facilitators that could impact intervention design, implementation, and sustainability. The findings will include analysis supported by participant quotes and will form the first set of HCD results to guide the co-design step.

Findings From Consultative Co-design Meetings

We expect to generate findings from the consultative meeting proceedings conducted as part of the co-design process. These

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findings will include the discussions with nurses, MCH clients, and key stakeholders in defining the challenges based on discovery findings (synthesis meeting), potential solutions to address the identified challenges (ideation meeting), and the intervention package (prototype and cocreation meeting) with the highest potential to improve nurse-client relationships considering acceptability and feasibility. The findings will be presented through interpretations, participant quotes, tables, and figures and will form the second set of HCD findings and guide the insight gathering/prototype validation step.

Findings From the Validation/Insight Gathering Inquiry

We expect to subject the emerging prototype to a validation process by gathering insights through FGDs with nurses and clients who were not involved in the initial HCD steps. The results of the FGDs will be analyzed to identify features appealing to both nurses and clients for strengthening their relationship to increase MCH service satisfaction, uptake, and continuity. The findings will be presented through interpretations and the proposed intervention package (prototype). These findings will form the third set of HCD results and will guide the final adaptation step.

Findings From the Prototype Refinement/Adaptation Meeting

We expect to refine and adapt the prototype based on the insights of nurses and clients who were not part of the initial HCD steps. The findings of the refinement and adaptation meeting will be presented through interpretation, participant quotes, tables, and figures. The final prototype (package of interventions) for strengthening nurse-client relationships in MCH care will also be presented. The findings will guide scholarly discussions and future interventions in a broader setting.

Dissemination Plan

A number of strategies will be employed to disseminate the results of this interventional study. First, we will employ the AKU networks by sharing a research report with the funding agency (University Research Council in this case), depositing the reports and publications in eCommons, and presenting the findings in AKU-wide forums including journal clubs and research meetings. Second, we will share the results with local nursing and health care authorities by sending summary reports to district and regional medical officers, nursing and midwifery councils, the Ministry of Health, and the National Institute for Medical Research for dissemination through government channels. This will ensure that the proposed interventions contribute to practice, policy, and strategic plan discussions at the local and national levels. We will also present the findings in local health care and scientific forums. We plan to prepare at least 3 research manuscripts to be published in reputed scholarly journals. We will also disseminate the findings at international conferences and share a media brief for the general public.

Discussion

Study Overview

The purpose of this study is to pilot an HCD approach for improving provider-client relationships in MCH care in rural Tanzania. Using this approach, the research team seeks to partner with nurses, midwives, clients, and other stakeholders to develop a prototype for addressing the complex problem of nurse-client relationships in Shinyanga.

The principal results are expected to be fourfold. First, the results of the community-driven inquiry including the existing drivers of poor nurse-client relationships and the contextual factors, barriers, and facilitators that could impact intervention design, implementation, and sustainability. These results will be discussed in comparison to previous works that have examined the factors that impact nurse-client relationships in both low- and high-income contexts [10-23]. Second, the results of the consultative meetings conducted as part of the co-design process will be used to design an interventional package (prototype) with the highest potential to improve nurse-client relationships. During this phase, ideation and cocreation meetings will be held to brainstorm and evaluate possible solutions leading to the development of a contextualized rough prototype to address poor nurse-client relationships. The rough prototype may include conventional capacity-building interventions such as training providers on interpersonal communication, the development of an interpersonal encounter algorithm for providers, community sensitization, and advocacy activities on client charters, and competitions to incentivize good provider behavior such as the “nurse of the month/year” duly informed by formative research. It is also possible that the capacity-building and community mobilization and advocacy activities will leverage technology (mobile health) using provider algorithms to remind nurses and midwives to conduct themselves in a certain way, and to develop behavior change and communication strategies for clients through SMS text messaging or audiovisual methods. The emerging rough intervention package will be discussed in view of previous interventions for strengthening nurse-client relationships [19,37-42]. Third, the results of prototype validation will be used to identify features appealing to both nurses and clients for strengthening their relationship to increase MCH service satisfaction, uptake, and continuity. We will gather feedback on the rough prototype for refining it accordingly. A preliminary theory of change map will be developed based on the stakeholder consultations. The results of the prototype validation will be discussed considering acceptable and feasible interventions that have been proposed to improve nurse-client relationships [19,37-42]. Lastly, we will evaluate the results of the refinement and adaptation meeting leading to a final prototype for strengthening nurse-client relationships. We will examine the existing body of literature in both high- and low-income countries to assess the novelty of the emerging prototype, whether it has been considered in other settings, and key considerations for implementation. We will consider the body of literature on interventions aimed at strengthening both nurse-client relationships as well as general provider-client relationships [19,23,37-42]. Intrinsic to the co-design process

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is the fact that stakeholders jointly understand a problem, act on it, and learn from working collaboratively to contest power relations and effect change [26-32].

As noted above, the strength of the HCD methodology is that it is a highly adaptive and creative approach to problem-solving [26-32] and will enable the team to deeply understand the drivers of poor client-provider relationships and ensure a collaborative approach to the design of solutions by stakeholders, yielding a final model that is highly feasible as a result. We will document the co-design process and develop the final prototype manual and associated materials to facilitate replication of the intervention in similar or other settings. Specifically, we envision applying for additional funds to test the emerging prototype within Tanzania and across the East African region to determine whether it could be applicable to a much broader African context.

Limitations

The application of HCD to develop a prototype for improving nurse-client relationships is not without limitations. The HCD intervention uses nurses as exemplars of providers to codevelop a prototype for strengthening interpersonal relationships in MCH care in a rural setting. However, patients interact with multidisciplinary teams of providers within health care settings. Conducting a similar study with other providers such as doctors and in a different setting may yield a different prototype. However, this being the first study in this context, future inquiry may extend beyond the nursing profession and rural context.

Comparison With Prior Work

Discussion of the emerging findings will be contextualized based on previous studies and interventions on strengthening provider-client relationships in Tanzania and beyond [17-25,37-41]. In particular, the results will be discussed taking stock of a previous study in a similar setting conducted by the principal investigator that proposed the need for novel approaches to address the complexity of patient-provider relationships [23].

Conclusions and Future Directions

In conclusion, the HCD approach may provide a novel entry point for strengthening provider-client relationships where clients are invited to partner with providers in the design of highly acceptable and feasible interventions. The results of this pilot study will inform the design of interventions and policies to strengthen interpersonal relationships in health care settings more broadly. Moreover, future implementation teams and researchers can learn from the experience of this HCD intervention to guide program development.

Acknowledgments

The authors acknowledge the financial support from the University Research Council at the Aga Khan University to support this novel pilot project. We thank the National Institute for Medical Research, the regional medical officer, and the municipal medical officer in Shinyanga for approving this project.

Data Availability

The authors confirm that the data supporting the findings from the HCD intervention will be available in future publications as supplementary materials. Additional data on the HCD process that are not part of the published article will be available on request from the AKU through the corresponding author (KI). Some data may not publicly available for ethical reasons (ie, information that could compromise the privacy of research participants).

Authors' Contributions

KI and CS designed the study. KI solicited funding and developed the initial draft of the manuscript. ESP, CM, and EN-M participated in the project conception and design, critically reviewed the manuscript, and provided inputs for improvement.

Conflicts of Interest

None declared.

Multimedia Appendix 1
Human-centered design (HCD) steps, population, activities, and sample size.
[DOCX File , 14 KB - resprot_v11i7e37947_app1.docx]

Multimedia Appendix 2
Copies of data collection tools.
[PDF File (Adobe PDF File), 361 KB - resprot_v11i7e37947_app2.pdf]

Multimedia Appendix 3
Ethical clearance certificate from the National Institute for Medical Research, Tanzania.
[PDF File (Adobe PDF File), 301 KB - resprot_v11i7e37947_app3.pdf]

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References

1. Survive and Thrive: Transforming care for every small and sick newborn – Key findings. World Health Organization & United Nations Children's Fund. 2018. URL: https://apps.who.int/iris/bitstream/handle/10665/276655/WHO-FWC-MCA-18.11-eng.pdf?ua=1 [accessed 2022-01-15]
2. Investing in Midwives and Others with Midwifery Skills to Save the Lives of Mothers and Newborns and Improve Their Health. United Nations Population Fund. 2006. URL: https://www.unfpa.org/sites/default/files/pub-pdf/midwives_eng.pdf [accessed 2022-01-10]
3. Fraser S, Grant J, Mannix T. Maternal child and family health nurses: delivering a unique nursing speciality. Matern Child Health J 2016 Dec;20(12):2557-2564. [doi: 10.1007/s10995-016-2081-2] [Medline: 27406150]
4. Taft AJ, Small R, Humphreys C, Hegarty K, Walter R, Adams C, et al. Enhanced maternal and child health nurse care for women experiencing intimate partner/family violence: protocol for MOVE, a cluster randomised trial of screening and referral in primary health care. BMC Public Health 2012 Sep;12(1):811 [FREE Full text] [doi: 10.1186/1471-2458-12-811] [Medline: 22994910]
5. Homer CSE, Friberg IK, Dias MAB, ten Hoope-Bender P, Sandall J, Speciale AM, et al. The projected effect of scaling up midwifery. The Lancet 2014 Sep;384(9948):1146-1157. [doi: 10.1016/s0140-6736(14)60790-x]
6. Amiri A, Vehviläinen-Julkunen K, Solankallio-Vahteri T, Tuomi S. Impact of nurse staffing on reducing infant, neonatal and perinatal mortality rates: evidence from panel data analysis in 35 OECD countries. Int J Nurs Sci 2020 Apr;7(2):161-169 [FREE Full text] [doi: 10.1016/j.ijnss.2020.02.002] [Medline: 32685612]
7. Nove A, Friberg IK, de Bernis L, McConville F, Moran AC, Najjemba M, et al. Potential impact of midwives in preventing and reducing maternal and neonatal mortality and stillbirths: a Lives Saved Tool modelling study. Lancet Glob Health 2021 Jan;9(1):e24-e32 [FREE Full text] [doi: 10.1016/S2214-109X(20)30397-1] [Medline: 33275948]
8. Strengthening quality midwifery education for Universal Health Coverage 2030: framework for action. World Health Organization. 2019. URL: https://apps.who.int/iris/bitstream/handle/10665/324738/9789241515849-eng.pdf [accessed 2022-02-05]
9. The state of the world's midwifery. United Nations Population Fund, International Confederation of Midwives, World Health Organization. 2014. URL: https://www.unfpa.org/sowmy [accessed 2022-01-25]
10. Gilson L, Alilio M, Heggenhougen K. Community satisfaction with primary health care services: an evaluation undertaken in the Morogoro region of Tanzania. Soc Sci Med 1994 Sep;39(6):767-780. [doi: 10.1016/0277-9536(94)90038-8]
11. Khamis K, Njau B. Patients' level of satisfaction on quality of health care at Mwananyamala hospital in Dar es Salaam, Tanzania. BMC Health Serv Res 2014 Sep;14(1):400 [FREE Full text] [doi: 10.1186/1472-6963-14-400] [Medline: 25230739]
12. Kumbani L, Bjune G, Chirwa E, Malata A, Odland J. Why some women fail to give birth at health facilities: a qualitative study of women's perceptions of perinatal care from rural Southern Malawi. Reprod Health 2013 Feb;10(1):9 [FREE Full text] [doi: 10.1186/1742-4755-10-9] [Medline: 23394229]
13. Bassett MT, Bijlmakers L, Sanders DM. Professionalism, patient satisfaction and quality of health care: experience during Zimbabwe's structural adjustment programme. Soc Sci Med 1997 Dec;45(12):1845-1852. [doi: 10.1016/s0277-9536(97)00122-6]
14. Bukuku D, Chontawan R, Akkadechanunt T. Nurse Caring Behaviors and Patient Satisfaction in a Tertiary Care Hospital, The United Republic of Tanzania. Nursing Journal CMU 2018;45(4):217-218 [FREE Full text]
15. Juma D, Manongi R. Users' perceptions of outpatient quality of care in Kilosa District Hospital in central Tanzania. Tanzan J Health Res 2009 Oct;11(4):196-204. [doi: 10.4314/thrb.v11i4.50176] [Medline: 20734699]
16. Ojwang BO, Ogutu EA, Matu PM. Nurses' impoliteness as an impediment to patients' rights in selected Kenyan hospitals. Health Hum Rights 2010 Dec;12(2):101-117. [Medline: 21178193]
17. Gourlay A, Wringe A, Birdthistle I, Mshana G, Michael D, Urassa M. "It Is Like That, We Didn't Understand Each Other": Exploring the influence of patient-provider interactions on prevention of mother-to-child transmission of HIV service use in rural Tanzania. PLoS ONE 2014 Sep;9(9):e106325. [doi: 10.1371/journal.pone.0106325]
18. Loghmani L, Borhani F, Abbaszadeh A. Factors affecting the nurse-patients' family communication in intensive care unit of kerman: a qualitative study. J Caring Sci 2014 Mar;3(1):67-82 [FREE Full text] [doi: 10.5681/jcs.2014.008] [Medline: 25276750]
19. Molina-Mula J, Gallo-Estrada J. Impact of nurse-patient relationship on quality of care and patient autonomy in decision-making. Int J Environ Res Public Health 2020 Jan;17(3):835 [FREE Full text] [doi: 10.3390/ijerph17030835] [Medline: 32013108]
20. Mannava P, Durrant K, Fisher J, Chersich M, Luchters S. Attitudes and behaviours of maternal health care providers in interactions with clients: a systematic review. Global Health 2015 Aug;11:36 [FREE Full text] [doi: 10.1186/s12992-015-0117-9] [Medline: 26276053]
21. Madula P, Kalembo FW, Yu H, Kaminga AC. Healthcare provider-patient communication: a qualitative study of women's perceptions during childbirth. Reprod Health 2018 Aug;15(1):135 [FREE Full text] [doi: 10.1186/s12978-018-0580-x] [Medline: 30103766]

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22. Kaur B. Interpersonal communications in nursing practice - key to quality health care. Arch Nurs Pract Care 2020 Jul;6(1):19-22. [doi: 10.17352/2581-4265.000044]
23. Isangula K. Patient trust in doctors in rural Tanzania: Meanings, factors and benefits in the context of NCDs and hypertension care (thesis). Sydney, Australia: University of New South Wales; 2018. URL: http://unsworks.unsw.edu.au/fapi/datastream/unsworks:54751/SOURCE02?view=true [accessed 2022-02-15]
24. Uganda Radio Network. Opposition demands reinstatement of sacked health workers. The Observer. 2016 Aug 05. URL: http://observer.ug/news-headlines/45765-opposition-demands-reinstatement-of-sackedhealth-workers [accessed 2022-02-15]
25. Buguzi S. Tanzania: Doctors Up in Arms Against 'Unfair' Government Officials. The Citizen. 2016 Mar 14. URL: http://allafrica.com/stories/201603140999.html [accessed 2021-11-20]
26. Leung CL, Naert M, Andama B, Dong R, Edelman D, Horowitz C, et al. Human-centered design as a guide to intervention planning for non-communicable diseases: the BIGPIC study from western Kenya. BMC Health Serv Res 2020 May;20(1):415 [FREE Full text] [doi: 10.1186/s12913-020-05199-1] [Medline: 32398131]
27. Altman M, Huang TT, Breland JY. Design thinking in health care. Prev Chronic Dis 2018 Sep;15:E117 [FREE Full text] [doi: 10.5888/pcd15.180128] [Medline: 30264690]
28. Roberts JP, Fisher TR, Trowbridge MJ, Bent C. A design thinking framework for healthcare management and innovation. Healthc (Amst) 2016 Mar;4(1):11-14. [doi: 10.1016/j.hjdsi.2015.12.002] [Medline: 27001093]
29. Bartlett R, Boyle JA, Simons Smith J, Khan N, Robinson T, Ramaswamy R. Evaluating human-centred design for public health: a case study on developing a healthcare app with refugee communities. Res Involv Engagem 2021 May;7(1):32 [FREE Full text] [doi: 10.1186/s40900-021-00273-2] [Medline: 34053451]
30. Melles M, Albayrak A, Goossens R. Innovating health care: key characteristics of human-centered design. Int J Qual Health Care 2021 Jan;33(Supplement_1):37-44 [FREE Full text] [doi: 10.1093/intqhc/mzaa127] [Medline: 33068104]
31. Abookire S, Plover C, Frasso R, Ku B. Health design thinking: an innovative approach in public health to defining problems and finding solutions. Front Public Health 2020 Aug;8:459 [FREE Full text] [doi: 10.3389/fpubh.2020.00459] [Medline: 32984247]
32. Gong Y, Zhang J. A human-centered design and evaluation framework for information search. AMIA Annu Symp Proc 2005:281-285 [FREE Full text] [Medline: 16779046]
33. Bradshaw C, Atkinson S, Doody O. Employing a qualitative description approach in health care research. Glob Qual Nurs Res 2017 Nov;4 [FREE Full text] [doi: 10.1177/2333393617742282] [Medline: 29204457]
34. Bobrow K, Farmer A, Cishe N, Nwagi N, Namane M, Brennan TP, et al. Using the Medical Research Council framework for development and evaluation of complex interventions in a low resource setting to develop a theory-based treatment support intervention delivered via SMS text message to improve blood pressure control. BMC Health Serv Res 2018 Dec;18(1):33 [FREE Full text] [doi: 10.1186/s12913-017-2808-9] [Medline: 29361934]
35. Hennink M, Kaiser BN. Sample sizes for saturation in qualitative research: a systematic review of empirical tests. Soc Sci Med 2022 Jan;292:114523 [FREE Full text] [doi: 10.1016/j.socscimed.2021.114523] [Medline: 34785096]
36. Braun V, Clarke V. Using thematic analysis in psychology. Qual Res Psychol 2006 Jan;3(2):77-101. [doi: 10.1191/1478088706qp063oa]
37. Giacomin J. What is human centred design? Design J 2014 Dec;17(4):606-623. [doi: 10.2752/175630614X14056185480186]
38. Adams A, Mannix T, Harrington A. Nurses' communication with families in the intensive care unit - a literature review. Nurs Crit Care 2017 Mar;22(2):70-80. [doi: 10.1111/nicc.12141] [Medline: 25583405]
39. Cleary M, Edwards C, Meehan T. Factors influencing nurse-patient interaction in the acute psychiatric setting: an exploratory investigation. Aust N Z J Ment Health Nurs 1999 Sep;8(3):109-116. [doi: 10.1046/j.1440-0979.1999.00141.x] [Medline: 10661080]
40. Korsah KA. Nurses' stories about their interactions with patients at the Holy Family Hospital, Techiman, Ghana. Open J Nurs 2011 Jun;1:1-9. [doi: 10.4236/ojn.2011.11001]
41. Hartley S, Raphael J, Lovell K, Berry K. Effective nurse-patient relationships in mental health care: a systematic review of interventions to improve the therapeutic alliance. Int J Nurs Stud 2020 Feb;102:103490 [FREE Full text] [doi: 10.1016/j.ijnurstu.2019.103490] [Medline: 31862531]
42. Schalk DM, Bijl ML, Halfens RJ, Hollands L, Cummings GG. Interventions aimed at improving the nursing work environment: a systematic review. Implement Sci 2010 Apr;5(1):34 [FREE Full text] [doi: 10.1186/1748-5908-5-34] [Medline: 20423492]

Abbreviations

AKU: Aga Khan University
DC: District Council
FGD: focus group discussion
HCD: human-centered design
KII: key informant interview
MC: Municipal Council

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MCH: maternal and child health

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Protocol

Psychological Effects of Aromatherapy on Smokers With Depressive Tendencies During Smoking Cessation Treatment: Protocol for a Pre-Post Single-Arm Clinical Trial

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Abstract

Background: Cessation of smoking can markedly reduce the incidence of cardiovascular disease, improve health economics, and benefit society. Aromatherapy has the potential to be a novel option as an adjuvant therapy for smoking cessation that may alleviate depressive symptoms. However, research on the efficacy of aromatherapy as an adjuvant therapy for smoking cessation is scarce.

Objective: The aim of this study was to examine the potential effects of aromatherapy on psychological states in smokers with depressive tendencies and to determine if it is reasonable to proceed to the next step (ie, a phase III trial).

Methods: This is a pre-post single-arm clinical trial. Smokers with depression will be subjected to aromatherapy during smoking cessation treatment for 12 weeks. We will evaluate changes in scores on the Zung Self-Rating Depression Scale and the Profile of Mood States from pretreatment screening to 4 weeks and 12 weeks after the start of aromatherapy. Moreover, we will compare the group treated with aromatherapy with the group that received standard treatment in our previous randomized controlled trial (ie, the control group in that study). Furthermore, we will compare successful smoking cessation rates after 12 weeks. In addition, we will conduct an exploratory analysis of the efficacy of aromatherapy. The target sample size is 100, which is the number of subjects expected to be enrolled in this study during the 2-year study period.

Results: This study was approved by the Kyoto Medical Center Institutional Review Board (IRB approval No. 19-016). Enrollment started on July 1, 2019. As of May 2022, 76 patients have been recruited. In the original plan, recruitment should have been finished on June 30, 2021. However, the number of subjects decreased due to the COVID-19 pandemic, and the study inclusion period was extended by 1 year (ie, until the end of June 2022) with the approval of the IRB on May 17, 2021. Analyses of the results will be completed subsequently.

Conclusions: This study has some limitations. This is not a rigorous validation study because it compares the same subjects who received standard treatment in a previous study. Moreover, the sample size and methods of statistical analysis were not fully set with prior consideration of statistical rigor. To address these limitations, we plan to conduct a phase III trial that will reflect the exploratory findings of this study. This is the first study to evaluate the psychological effects of aromatherapy during a smoking cessation program, and it may help improve the quality of treatment for smoking cessation in the future.

Trial Registration: UMIN Clinical Trials Registry UMIN000043102; https://tinyurl.com/tn3hvt9w

International Registered Report Identifier (IRRID): DERR1-10.2196/38626

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(JMIR Res Protoc 2022;11(7):e38626) doi:10.2196/38626

KEYWORDS

smoking cessation; aromatherapy; depression; cardiovascular risk; inhaler; complementary and alternative medicine

Introduction

Psychological Effects of Smoking

Smoking is a major risk factor for noncommunicable diseases (NCDs), such as cancer, chronic obstructive pulmonary disease, diabetes, cerebral infarction, and myocardial infarction [1]. There is an urgent need for active guidance on smoking cessation, not only to reduce the risk of developing NCDs, but also from social and health economics perspectives. Nicotine patches and varenicline are widely used as pharmacotherapies for smoking cessation, as they are known to increase the rate of successful smoking cessation by 2 to 5 times [2-4].

Smoking is known to cause or exacerbate negative emotions [5]. Moreover, the risk of developing depression is higher among smokers than among nonsmokers [6,7]. In addition, smokers with mental disorders show changes in behavior, agitation, and depressed mood after starting smoking cessation treatment, and the rate of outpatient psychiatric visits increases due to worsening of these symptoms [8]. In patients with no mental disorders at the start of smoking cessation treatment, major depression was reported to have occurred in 14.1% of the patients within 12 months of starting treatment [9]. It is well known that nicotine withdrawal can cause depressive symptoms [10], and the Standard Procedure Manual for Smoking Cessation Treatment (version 8.1) states that smoking cessation, with or without treatment, may be associated with a variety of symptoms and may exacerbate underlying mental disorders [11]. Hence, it can be argued that it is essential to adopt a comprehensive approach considering the close relationship between smoking and psychosocial stress, because smoking cessation can lead to temporal worsening of a depressive state and failure to quit smoking, even in those without a history of mental disorders.

Aromatherapy

Aromatherapy involves the use of essential oils extracted from flowers, leaves, seeds, pericarps, and resins for the treatment and prevention of diseases, physical and mental health, relaxation, and stress relief [12]. Aromatherapy includes methods such as the inhalation of aromas and massage using essential oils diluted in vegetable oils [13]. Among aromatherapy methods, inhalation of essential oils has the advantage of being simple and noninvasive [14]. Once the olfactory cells receive the aroma components of essential oils, sensory information is transmitted from the olfactory nerve to the hypothalamus, which, in turn, acts on the autonomic nervous system via the brainstem. Furthermore, by influencing emotions via the limbic system [15-17], aromatherapy has been shown to alleviate anxiety and depression [18]. This has also been shown to improve sleep quality [19], alleviate fatigue [20,21] and perceived stress [22], and improve cognitive function [23].

Existing Research on Aromatherapy for Smoking Cessation

Regarding the efficacy of aromatherapy as an adjuvant therapy for smoking cessation, it has been reported that black pepper reduces the urge to smoke [24], and peppermint has been reported to help alleviate respiratory symptoms, such as sputum and cough associated with smoking cessation [25]. Moreover, it has also been reported that various olfactory stimuli, including essential oils, can reduce the urge to smoke [26]. However, high-quality research on this topic is scarce. Furthermore, although it was not a study on treatment for smoking cessation, a systematic review of the efficacy of aromatherapy on depression concluded that it reduces the propensity for depression [18]. In a study in which aromatherapy was applied as an adjuvant therapy, lavender and rosemary were reported to have an anxiolytic effect after smoking cessation [25]. Another study suggested that lavender has anxiolytic and antidepressant-like effects, which are thought to be mediated by the modulation of the N-methyl-D-aspartate receptor and serotonin transporters [27]. Furthermore, exposure to limonene by inhalation, which is found in citrus essential oil, has been reported to increase dopamine levels in the brain [28], and a mechanism of action has been reported for peppermint, suggesting therapeutic efficacy against depression [29]. Furthermore, aromatherapy has been shown to relieve depression, and inhalation is presented as a particularly effective method [30].

Use of Inhalers as an Adjuvant Therapy for Smoking Cessation

There are various aromatherapy devices, such as aromatherapy inhalers, which are simple and cost-effective for incorporation into daily life. An aromatherapy inhaler is a portable, plastic, lipstick-like container that houses a cotton wick soaked in essential oils. The inhaler enables users to smell the aromas without getting their hands dirty or spilling the oils. Similar “aromasticks” have been used in British hospitals to control symptoms of nausea, insomnia, and anxiety, and to induce relaxation [31,32]. We assume that if aromatherapy inhalers can alleviate psychological and depressive symptoms and reduce cravings for cigarettes, they can form the basis of a novel adjuvant therapy for smoking cessation.

Hypothesis and Objective

Depression may temporarily worsen during smoking cessation treatment [11]. This study hypothesizes that aromatherapy may help improve this depressive state during treatment. This study aims to examine the effect of adding aromatherapy to standard smoking cessation treatment in patients with depressive tendencies who visited a smoking cessation clinic and to compare these to a historical control group (ie, standard treatment group).

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Methods

Study Design

This is a pre-post single-arm clinical trial conducted at the National Hospital Organization Kyoto Medical Center in Japan. Patients in this study who visited the smoking cessation clinic at the medical center to receive smoking cessation treatment were assessed using the Zung Self-Rating Depression Scale (SDS) and were classified into two groups: the healthy group (SDS score ≤38) and the depressed group (SDS score = 39-59). Patients in the depressed group are considered to have depressive tendencies. Patients who provide consent will be included in this study, with a target sample size of 100. Smokers with depression will be subjected to aromatherapy during smoking cessation treatment for 12 weeks. Changes in the SDS score and the Profile of Mood States (POMS) score from pretreatment screening to 4 and 12 weeks after the start of aromatherapy will be evaluated. This study will also compare the aromatherapy group with the standard treatment group from a previous study entitled "A Randomized, Multi-center, Double-Blind, Placebo-Controlled Trial for the Effects of Yokukansan on Depressive or Neurotic Smoking Patients during Smoking Cessation Therapy" (University Hospital Medical Information Network [UMIN] ID: 000027036); this group will act as a control group (ie, historical control group). In both studies, only smokers with SDS scores of 39 to 59 were included in the study, and the study subjects were randomly assigned to either the yokukansan group (ie, yokukansan plus standard treatment) or the control group (ie, standard treatment), with 220 subjects in each group. Changes in SDS and POMS scores from pretreatment screening to 4 and 12 weeks after the start of treatment, as well as the rate of successful smoking cessation, will be evaluated. Furthermore, an exploratory analysis on the efficacy of aromatherapy will also be conducted (eg, analyzing the correlation between essential oil preference and smoker information items at the first visit and the changes in essential oil preferences over time).

Recruitment

Inclusion Criteria

In Japan, smoking cessation treatment is covered by health insurance if it is the patient's first time undergoing the treatment or if more than 1 year has passed since the last treatment. Accordingly, this study included patients covered by health insurance [11] and who met all of the following criteria based on the diagnosis and tests before starting treatment for smoking cessation:

1. Smokers with nicotine dependence (Fagerström Test for Nicotine Dependence [FTND] score of 5 points or more) who wish to quit smoking.
2. Patients with depression with SDS scores of 39 to 59, based on the self-report questionnaire for assessing propensity to depression.
3. Patients aged 20 to 79 years at the time of the informed consent procedure.
4. Outpatients.
5. Patients whose informed consent has been obtained in writing.

This study aims to include 100 participants in the analysis.

Exclusion Criteria

Patients will be excluded from this study if it is determined that they meet any one of the following exclusion criteria based on their diagnosis or test results prior to the start of the study:

1. Patients whose condition is inappropriate for aromatherapy, that is, those suffering from shock, severe disease states, poor respiratory status, feeling of nausea, or vomiting, etc.
2. Patients who habitually practice aromatherapy.
3. Patients who are unable to smell the aromas of essential oils due to olfactory dysfunction.
4. Patients with a history of epileptic seizures.
5. Patients who are currently on medication for a psychiatric or psychosomatic condition.
6. Patients with an SDS score of 53 points or higher, which is indicative of underlying depression and need for psychiatric consult, and those prescribed medication for a psychiatric and psychosomatic condition [33].
7. Patients with current symptoms of drug allergy.
8. Patients who are pregnant, are lactating, or intend to become pregnant during the study period.
9. Other patients who are deemed to be unsuitable according to the attending physician (patients with severe dementia, poor compliance, etc).

Withdrawal Criteria

A subject will discontinue their participation in the study if any of the following occurs:

1. If a subject informs us of their withdrawal from the study or requests withdrawal of consent.
2. If the attending physician determines that it is inadvisable for the subject to continue participation in the study due to an adverse event (ie, Grade 3 or higher adverse event according to the Common Terminology Criteria for Adverse Events [CTCAE; version 4.0]) [34].
3. If the attending physician determines that continuation of participation in the study is clinically inappropriate due to the exacerbation of a comorbidity or complication.
4. Death.
5. If the attending physician determines that the subject is ineligible to continue the study.
6. If the subject is unable to visit the medical center where the study is being conducted due to relocation or other reasons.

Enrollment and Interventions

The attending physician will provide a complete written explanation and obtain written consent from patients who meet the inclusion criteria. Subsequently, the attending physician will perform subject registration after confirming that the patients meet all the inclusion criteria and none of the exclusion criteria by performing prespecified medical tests.

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Procedures

Time Point: Enrollment (4 Weeks Before the Study to the Start of the Study)

An eligibility screen will be conducted and informed consent will be provided to those who are eligible. The following assessments will be carried out: the SDS (ie, the tool that is used for tracking changes in depressive symptoms over time during the course of a study and after treatment [35]) and physical examination findings (ie, height, weight, abdominal circumference, blood pressure, and heart rate). In addition, smoking status and exhaled carbon monoxide (CO) levels will be determined, and subject background data will be collected, including age; sex; medical history; comorbidities; presence or absence of allergies; subjective symptoms; drinking patterns, regarding subjects who drink daily or 3 to 4 times a week, and alcohol consumption, which is monitored and reported in converted values; sleep duration; smoking index (ie, the number of cigarettes smoked per day × years of tobacco use); nicotine dependence, measured by the Tobacco Dependence Screener and the FTND; and the subject's first medication for smoking cessation.

Time Point: Allocation (Day of Treatment Start)

Procedures

We will commence the following standard smoking cessation and aromatherapy programs for patients who have provided informed consent. In principle, a sufficient amount of time will be allowed for briefing the subjects to facilitate a complete understanding of the content of this study. Subsequently, their informed consent will be obtained. The maximum duration of obtaining informed consent after briefing is 4 weeks. However, if it is confirmed that the subject has sufficiently understood the content of the briefing, their informed consent may be obtained on the day of the briefing. The standard smoking cessation program was administered according to the Standard Procedure Manual for Anti-Smoking Treatment, which was originally issued in March 2006 by the Japanese Circulation Society, the Japan Lung Cancer Society, and the Japanese Cancer Association. Treatment consists of pharmacotherapy with transdermal nicotine patches and oral varenicline as well as nonpharmaceutical therapy with counseling by doctors and nurses. The patients were examined on their first visit and after 2, 4, 8, and 12 weeks (ie, 3 months) while being treated with transdermal nicotine patches or oral varenicline.

Aromatherapy

The following aromatherapy program will be provided in this clinical trial. Subjects will choose from four essential oils: black pepper, lavender, peppermint, and citrus (ie, lemon and grapefruit). These essential oils have been used in previous smoking cessation studies, were reported to have antidepressant and anxiety-reducing effects, and are readily available. Black pepper has been used in previous smoking cessation studies [24], while lavender has antianxiety and antidepressant effects [27]. Moreover, peppermint also has a mechanism of action that suggests a therapeutic effect in people with depression [29]. Limonene is reported to increase dopamine levels in the brain [28], similar to how dopamine is released during smoking [36]; all the essential oils selected for this study contain limonene [37-40]. The aromatherapist will provide subjects with an inhaler filled with their chosen oil; subjects will smell these for 10 to 20 seconds 3 times a day (ie, after breakfast, lunch, and dinner) and at other personally preferred times (ie, when their urge to smoke increases or when they feel anxious). The essential oils and inhalers are produced by Mont Saint Michel, Sanritsu Corporation, Osaka, Japan.

Profile of Mood States

We will collect the POMS self-assessment sheets completed by the patients. The short version of the POMS is a tool that facilitates understanding of subjects' current moods, emotions, and changes, with little effort required from the subjects [41]. Self-assessment tests—the SDS and the POMS—will be completed by the subjects. In case of any omissions or obvious errors detected, the medical staff will ask for the information verbally.

Blood Tests

We will analyze subjects' baseline clinical data by performing blood tests (ie, blood glucose, hemoglobin A_{1c}, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, triglyceride, uric acid, sodium, potassium, creatinine, glutamic-oxaloacetic transaminase, glutamic-pyruvic transaminase, alkaline phosphatase, g-glutamyl transpeptidase, creatine phosphokinase, C-reactive protein, and complete blood count). We will determine whether or not patients are taking antihypertensive drugs, dyslipidemia drugs, oral diabetes drugs, insulin, sleep medication, or other drugs, specifically anticancer drugs, drugs for hormonal treatment, and steroids.

Time Point: 2, 4, 8, and 12 Weeks

We will check for any adverse event and list its grade according to the CTCAE (version 4.0). Aromatherapy adherence status will be rated as follows:

- Good: the aromatherapy inhaler is used nearly every day (approximately 80% of the days)
- Somewhat poor: the aromatherapy inhaler is not used on some days (approximately 60% of the days)
- Poor: the aromatherapy inhaler is not used on most days (approximately 30% of the days).

SDS scores, physical examination findings (ie, height, weight, abdominal circumference, blood pressure, and heart rate), smoking status, and exhaled CO levels will also be monitored. Further, in weeks 4 and 12, we will collect the POMS self-assessment sheets completed by the patients. At 12 weeks, we will perform the blood tests and perform a confirmation of smoking cessation. We will determine whether or not patients are taking antihypertensive drugs, dyslipidemia drugs, oral diabetes drugs, insulin, sleep medication, and other drugs, specifically anticancer drugs, drugs for hormonal treatment, and steroids. If a subject does not arrive for a scheduled visit, the reason for their absence will be discussed via a phone call. When the reason is hesitation or the unwillingness of a subject to visit the smoking cessation clinic, they will be requested by medical doctors or nurses to visit the hospital. This strategy is described in the Standard Procedure Manual for Anti-Smoking Treatment, which was originally issued in March 2006 by the Japanese

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Circulation Society, the Japan Lung Cancer Society, and the Japanese Cancer Association (Figure 1).

Figure 1. Schedule for observations and tests. "X" indicates that the study task or assessment was performed at the indicated time point. CO: carbon monoxide; POMS: Profile of Mood States; SDS: Zung Self-Rating Depression Scale.

	Study period					
	Enrollment	Allocation	Postallocation			Closeout
Time point	−4 weeks to week 0	Day of treatment start	2 weeks	4 weeks	8 weeks	12 weeks
Enrollment:						
Eligibility screen	X					
Informed consent	X					
Allocation		X				
Interventions:						
Aromatherapy		←	—	—	→	
Assessments:						
Mental state assessment (SDS)	X		X	X	X	X
Mental state assessment (POMS)		X		X		X
Adverse events and aromatherapy adherence status			X	X	X	X
Physical examination	X		X	X	X	X
Blood test		X				X
Smoking status and exhaled CO levels	X		X	X	X	X

Study Period

The observation period (ie, follow-up) will last 3 months after the enrollment of the last subject, and the total study period will amount to 2 years and 3 months; the scheduled period was expected to run from July 2019 to September 2021. Since the number of subjects decreased due to the COVID-19 pandemic, the study period was extended to 3 years and 3 months on May 17, 2021, with the approval of the Institutional Review Board (IRB); the study is now expected to run until September 2022.

Primary Outcome, Secondary Outcomes, and Procedures

Primary Outcome

The primary outcome is the change in SDS and POMS scores [35,41] (ie, depression assessment following smoking cessation), which will be evaluated for the period from the pretreatment screening to 4 weeks and 12 weeks after the start of aromatherapy.

Secondary Outcomes

The secondary outcomes are as follows:

- Successful smoking cessation rate. The percentage of subjects who stop smoking 12 weeks after aromatherapy (ie, the number of subjects who stop smoking divided by the total number of allocated subjects, as a percentage). Successful smoking cessation refers to a report of smoking cessation for the past 7 days and an exhaled CO level below 7 ppm [42].
- Changes in body weight, abdominal circumference, and glycolipid metabolism (ie, assessment of obesity following smoking cessation and dyslipidemia).
- Adverse events during the period of aromatherapy.
- Blood cell counts and biochemical tests by blood sample collection.
- Other laboratory findings or symptoms.
- Correlation between essential oil preference and smoker information items at first-time visit (ie, day of treatment start). Smoker information items include the following subject background data: age, sex, BMI, number of tobacco pieces consumed or smoked per day, FTND scores, and SDS and POMS scores. These items will be compared among different essential oil types.
- Changes in essential oil preferences over time.

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Statistical Analysis

Research on the efficacy of aromatherapy as an adjuvant therapy for smoking cessation is scarce. Further, based on our research, the size of the effects of aromatherapy on psychological tests as measured by the SDS and the POMS in smokers has never been reported. Therefore, this study was designed as a pre-post single-arm clinical trial in which the sample size has been determined by considering the feasibility of registration. We will perform a comparison of the aromatherapy group with the standard treatment group from our previous study, "A Randomized, Multi-center, Double-Blind, Placebo-Controlled Trial for the Effects of Yokukansan on Depressive or Neurotic Smoking Patients during Smoking Cessation Therapy" (UMIN ID: 000027036). Similar to this aromatherapy study, the yokukansan study targeted the population of "depressed smoking patients." For the yokukansan study, 100 patients were registered in our hospital.

Assuming that the registration number of this aromatherapy study would be comparable to that of the previous yokukansan study, this study planned to register 100 patients. The SDS scores and POMS subscale scores at baseline and at the 12-week time point will be compared using paired-samples *t* tests in the aromatherapy group of this study and in the standard treatment group of our previous study. Statistical significance was set at $P<.05$. Furthermore, concerning changes in data from baseline to the 12-week time point, a two-way analysis of variance will be used analyze the interaction between the standard treatment group and the aromatherapy group. The same will be used to compare changes in SDS and POMS scores before and after smoking cessation between the historical control group and the aromatherapy group of this study.

We will also compare the successful smoking cessation rates for a period of 12 weeks from the start of treatment between the standard treatment group and the aromatherapy group. Successful smoking cessation refers to a report of smoking cessation for the past 7 days and an exhaled CO level below 7 ppm. The successful smoking cessation rate was calculated by dividing the number of subjects who successfully stopped smoking 12 weeks after smoking cessation treatment by the total number of subjects who provided consent and received the treatment, multiplied by 100 to give the percentage. Descriptive statistics on subjects' background data will be generated. No interim analysis will be performed.

Protection of Personal Information

All parties involved in this research shall strictly protect the personal information of the subjects in accordance with the Personal Information Protection Law. Personal information will be used to identify subjects so that accurate data can be obtained for each subject, and the personal information obtained will be managed appropriately. When information obtained from the research is published by the principal investigator or others, sufficient care will be taken to ensure that subjects are not identified.

Early Discontinuation of the Study

The Data and Safety Monitoring Committee will recommend discontinuation of the study to the principal investigator if the experimental treatment is deemed unsafe based on safety information, including reports of serious adverse events and information outside of the study. If the committee reports to the principal investigator that the study needs to be discontinued due to safety issues or for other reasons, the principal investigator will deliberate the report and will promptly inform the secretariat in writing about the results of the deliberation. In addition to the head of the institution where the study is conducted and the IRB, the subjects will also be informed.

Ethics Approval

This study was approved by the Kyoto Medical Center IRB on June 17, 2019 (approval No. 19-016) and has been registered in the UMIN Clinical Trials Registry (UMIN000043102).

Results

Enrollment started on July 1, 2019. As of May 2022, 76 patients have been recruited. In the original plan, recruitment should have been finished on June 30, 2021. However, the number of subjects decreased due to the COVID-19 pandemic, and the study inclusion period was extended by 1 year (ie, until the end of June 2022) with the approval of the IRB on May 17, 2021. The observation period (ie, follow-up) will last 3 months after the enrollment of the last subject, and the study period will last for 3 years and 3 months (July 2019 to September 2022). The corresponding author will have complete access to the study data and will submit the report for publication. The results of this research will be published in international peer-reviewed journals. Both positive and negative results will be reported. In addition, the study results will be shared on the UMIN Clinical Trials Registry. Our findings will be posted on the hospital website and will be made publicly available.

Discussion

Principal Findings

This study is the first clinical trial study to examine the psychological effects of aromatherapy on smokers with depression. Hence, we believe that this study is of major significance. If aromatherapy can inhibit an increase in a transient propensity for depression, it can be expected to increase the rate of successful smoking cessation, which will not only reduce the risk of NCDs, but will also lead to a reduction in future medical expenses. Moreover, as aromatherapy has been reported to reduce insomnia [19], alleviate fatigue [20,21], and improve cognitive function [23], we believe that smoking cessation may have the secondary benefit of alleviating the adverse effects of smoking, such as insomnia [43,44], fatigue [45], and reduced ability to focus [44].

Limitations

This study was designed to confirm the efficacy and safety of aromatherapy. The control group included patients in the usual care group of a previous study. This study was a pre-post single-arm study and not a double-blind randomized controlled trial. In addition, the aromatherapy survey was based on patient self-report, which may lead to inaccuracy in the frequency of inhaler use.

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Comparison With Previous Work

Smoking can cause or exacerbate negative emotions [5] and increase the risk of developing depression [6,7]. Furthermore, it has been reported that when patients with mental disorders are unstable and quit smoking, their depressive symptoms become temporarily exacerbated [8]. We have previously reported that depressive tendencies are common among smokers without a history of mental disorders [46] and that depressive tendency is the most significant factor that prevents successful smoking cessation [47]. Although aromatherapy showed potential therapeutic efficacy against depression [18], research on the efficacy of aromatherapy as an adjuvant therapy for smoking cessation is scarce. Therefore, it is significant to examine the psychological effects of aromatherapy on smokers with depression in this study.

Conclusions

This is a pre-post single-arm study. In this study, the group treated with aromatherapy will be compared with the group that received standard treatment in a previous randomized controlled trial as the control group. If this study shows that aromatherapy has psychological benefits for patients with depression who are undergoing smoking cessation treatment, then aromatherapy could be used to improve the success rate of smoking cessation, thus reducing the risk of NCDs and lowering future medical care needs. A phase III trial is intended to be conducted to confirm the findings and correct the limitations of this study.

Data Availability

Study data will be available upon reasonable request from the corresponding author.

Authors' Contributions

KH and AH were responsible for the study conception and design. AH, KH, MK, and YT were responsible for the acquisition of data. HW and HY analyzed the data. NSA and TM interpreted the data. AH and MK drafted the manuscript, and KH was responsible for critical revision of the manuscript. All authors reviewed and approved the final manuscript.

Conflicts of Interest

None declared.

References

1. World Health Organization. Global Action Plan for the Prevention and Control of NCDs 2013-2020. Geneva, Switzerland: World Health Organization; 2013. URL: https://www.who.int/publications/i/item/9789241506236 [accessed 2022-06-15]
2. Hartmann-Boyce J, Chepkin SC, Ye W, Bullen C, Lancaster T. Nicotine replacement therapy versus control for smoking cessation. Cochrane Database Syst Rev 2018 May 31;5:CD000146 [FREE Full text] [doi: 10.1002/14651858.CD000146.pub5] [Medline: 29852054]
3. Cahill K, Lindson-Hawley N, Thomas KH, Fanshawe TR, Lancaster T. Nicotine receptor partial agonists for smoking cessation. Cochrane Database Syst Rev 2016 May 09(5):CD006103 [FREE Full text] [doi: 10.1002/14651858.CD006103.pub7] [Medline: 27158893]
4. Laniado-Laborín R. Smoking cessation intervention: An evidence-based approach. Postgrad Med 2010 Mar;122(2):74-82. [doi: 10.3810/pgm.2010.03.2124] [Medline: 20203458]
5. Hajek P, Taylor T, McRobbie H. The effect of stopping smoking on perceived stress levels. Addiction 2010 Aug;105(8):1466-1471. [doi: 10.1111/j.1360-0443.2010.02979.x] [Medline: 20528815]
6. Glassman AH. Cigarette smoking: Implications for psychiatric illness. Am J Psychiatry 1993 Apr;150(4):546-553. [doi: 10.1176/ajp.150.4.546] [Medline: 8465868]
7. Kendler KS, Neale MC, MacLean CJ, Heath AC, Eaves LJ, Kessler RC. Smoking and major depression. A causal analysis. Arch Gen Psychiatry 1993 Jan;50(1):36-43. [doi: 10.1001/archpsyc.1993.01820130038007] [Medline: 8422220]
8. Cunningham FE, Hur K, Dong D, Miller DR, Zhang R, Wei X, et al. A comparison of neuropsychiatric adverse events during early treatment with varenicline or a nicotine patch. Addiction 2016 Jul;111(7):1283-1292. [doi: 10.1111/add.13329] [Medline: 26826702]
9. Tsoh JY, Humfleet GL, Muñoz RF, Reus VI, Hartz DT, Hall SM. Development of major depression after treatment for smoking cessation. Am J Psychiatry 2000 Mar;157(3):368-374. [doi: 10.1176/appi.ajp.157.3.368] [Medline: 10698811]
10. Howes S, Hartmann-Boyce J, Livingstone-Banks J, Hong B, Lindson N. Antidepressants for smoking cessation. Cochrane Database Syst Rev 2020 Apr 22;4:CD000031 [FREE Full text] [doi: 10.1002/14651858.CD000031.pub5] [Medline: 32319681]
11. The Japanese Circulation Society, The Japan Lung Cancer Society, The Japanese Cancer Association, The Japanese Respiratory Society. Standard Procedure Manual for Smoking Cessation Treatment. Version 8.1. Kyoto, Japan: The Japanese Circulation Society; 2021. URL: https://www.j-circ.or.jp/kinen/anti_smoke_std/ [accessed 2022-06-15]
12. Sharifi-Rad J, Sureda A, Tenore GC, Daglia M, Sharifi-Rad M, Valussi M, et al. Biological activities of essential oils: From plant chemoecology to traditional healing systems. Molecules 2017 Jan 01;22(1):70 [FREE Full text] [doi: 10.3390/molecules22010070] [Medline: 28045446]

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13. Lis-Balchin M. Aromatherapy practice. In: Aromatherapy Science: A Guide for Healthcare Professionals. London, UK: Pharmaceutical Press; 2006:17-30.
14. Ndao DH, Ladas EJ, Cheng B, Sands SA, Snyder KT, Garvin JH, et al. Inhalation aromatherapy in children and adolescents undergoing stem cell infusion: Results of a placebo-controlled double-blind trial. Psychooncology 2012 Mar;21(3):247-254. [doi: 10.1002/pon.1898] [Medline: 22383266]
15. PDQ Integrative, Alternative, and Complementary Therapies Editorial Board. Aromatherapy With Essential Oils (PDQ®): Health Professional Version. PDQ Cancer Information Summaries. Bethesda, MD: National Cancer Institute; 2002. URL: https://www.ncbi.nlm.nih.gov/books/NBK65874/ [accessed 2022-06-15]
16. Ali B, Al-Wabel NA, Shams S, Ahamad A, Khan SA, Anwar F. Essential oils used in aromatherapy: A systemic review. Asian Pac J Trop Biomed 2015 Aug;5(8):601-611. [doi: 10.1016/j.apjtb.2015.05.007]
17. Burnett KM, Solterbeck LA, Strapp CM. Scent and mood state following an anxiety-provoking task. Psychol Rep 2004 Oct;95(2):707-722. [doi: 10.2466/pr0.95.2.707-722] [Medline: 15587240]
18. Sánchez-Vidaña DI, Ngai SP, He W, Chow JK, Lau BW, Tsang HW. The effectiveness of aromatherapy for depressive symptoms: A systematic review. Evid Based Complement Alternat Med 2017;2017:5869315 [FREE Full text] [doi: 10.1155/2017/5869315] [Medline: 28133489]
19. Blackburn L, Achor S, Allen B, Bauchmire N, Dunnington D, Klisovic R, et al. The effect of aromatherapy on insomnia and other common symptoms among patients with acute leukemia. Oncol Nurs Forum 2017 Jul 01;44(4):E185-E193. [doi: 10.1188/17.ONF.E185-E193] [Medline: 28640576]
20. Karadag E, Samancioglu Baglama S. The effect of aromatherapy on fatigue and anxiety in patients undergoing hemodialysis treatment: A randomized controlled study. Holist Nurs Pract 2019;33(4):222-229. [doi: 10.1097/HNP.0000000000000334] [Medline: 31192834]
21. Kawabata N, Hata A, Aoki T. Effect of aromatherapy massage on quality of sleep in the palliative care ward: A randomized controlled trial. J Pain Symptom Manage 2020 Jun;59(6):1165-1171. [doi: 10.1016/j.jpainsymman.2020.01.003] [Medline: 31981597]
22. Cheng VY, Huang C, Liao J, Hsu H, Wang S, Huang S, et al. Combination of 3-dimensional virtual reality and hands-on aromatherapy in improving institutionalized older adults' psychological health: Quasi-experimental study. J Med Internet Res 2020 Jul 23;22(7):e17096 [FREE Full text] [doi: 10.2196/17096] [Medline: 32706660]
23. Mehndiratta M, Pandey S, Nayak R, Alam A. Posterior circulation ischemic stroke-clinical characteristics, risk factors, and subtypes in a north Indian population: A prospective study. Neurohospitalist 2012 Apr;2(2):46-50 [FREE Full text] [doi: 10.1177/1941874412438902] [Medline: 23983863]
24. Rose JE, Behm FM. Inhalation of vapor from black pepper extract reduces smoking withdrawal symptoms. Drug Alcohol Depend 1994 Feb;34(3):225-229. [doi: 10.1016/0376-8716(94)90160-0] [Medline: 8033760]
25. Jang S, Lee JA, Jang B, Shin Y, Ko S, Park S. Clinical effectiveness of traditional and complementary medicine interventions in combination with nicotine replacement therapy on smoking cessation: A randomized controlled pilot trial. J Altern Complement Med 2019 May;25(5):526-534. [doi: 10.1089/acm.2019.0009] [Medline: 31017453]
26. Sayette MA, Marchetti MA, Herz RS, Martin LM, Bowdring MA. Pleasant olfactory cues can reduce cigarette craving. J Abnorm Psychol 2019 May;128(4):327-340 [FREE Full text] [doi: 10.1037/abn0000431] [Medline: 30985171]
27. López V, Nielsen B, Solas M, Ramírez MJ, Jäger AK. Exploring pharmacological mechanisms of lavender (Lavandula angustifolia) essential oil on central nervous system targets. Front Pharmacol 2017;8:280 [FREE Full text] [doi: 10.3389/fphar.2017.00280] [Medline: 28579958]
28. Zhou W, Fukumoto S, Yokogoshi H. Components of lemon essential oil attenuate dementia induced by scopolamine. Nutr Neurosci 2009 Apr;12(2):57-64. [doi: 10.1179/147683009X388832] [Medline: 19356307]
29. Umezu T, Sakata A, Ito H. Ambulation-promoting effect of peppermint oil and identification of its active constituents. Pharmacol Biochem Behav 2001;69(3-4):383-390. [doi: 10.1016/s0091-3057(01)00543-3] [Medline: 11509195]
30. Agatonovic-Kustrin S, Kustrin E, Gegechkori V, Morton D. Anxiolytic terpenoids and aromatherapy for anxiety and depression. Adv Exp Med Biol 2020;1260:283-296. [doi: 10.1007/978-3-030-42667-5_11] [Medline: 32304038]
31. Dyer J, Cleary L, Ragsdale-Lowe M, McNeill S, Osland C. The use of aromasticks at a cancer centre: A retrospective audit. Complement Ther Clin Pract 2014 Nov;20(4):203-206. [doi: 10.1016/j.ctcp.2013.11.006] [Medline: 25486854]
32. Stringer J, Donald G. Aromasticks in cancer care: An innovation not to be sniffed at. Complement Ther Clin Pract 2011 May;17(2):116-121. [doi: 10.1016/j.ctcp.2010.06.002] [Medline: 21457903]
33. Fukuda K, Kobayashi S. A Manual of the Japanese Version of the Zung SDS (Self-Rating Depression Scale)-The Augmented Edition [document in Japanese]. Kyoto, Japan: Sankyobo; 2011.
34. National Cancer Institute. Common Terminology Criteria for Adverse Events (CTCAE) Version 4.03. Bethesda, MD: US Department of Health and Human Services; 2010 Jun 14. URL: https://searchworks.stanford.edu/view/9100287 [accessed 2022-06-15]
35. Zung WW. A self-rating depression scale. Arch Gen Psychiatry 1965 Jan;12:63-70. [doi: 10.1001/archpsyc.1965.01720310065008] [Medline: 14221692]
36. Dani JA, Heinemann S. Molecular and cellular aspects of nicotine abuse. Neuron 1996 May;16(5):905-908 [FREE Full text] [doi: 10.1016/s0896-6273(00)80112-9] [Medline: 8630247]

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37. Sun J. D-Limonene: Safety and clinical applications. Altern Med Rev 2007 Sep;12(3):259-264. [Medline: 18072821]
38. Cheallaigh AN, Mansell DJ, Toogood HS, Tait S, Lygidakis A, Scrutton NS, et al. Chemoenzymatic synthesis of the intermediates in the peppermint monoterpenoid biosynthetic pathway. J Nat Prod 2018 Jul 27;81(7):1546-1552. [doi: 10.1021/acs.jnatprod.7b01026] [Medline: 29979593]
39. Gostner JM, Ganzera M, Becker K, Geisler S, Schroecksnadel S, Überall F, et al. Lavender oil suppresses indoleamine 2,3-dioxygenase activity in human PBMC. BMC Complement Altern Med 2014 Dec 16;14:503 [FREE Full text] [doi: 10.1186/1472-6882-14-503] [Medline: 25515049]
40. Dosoky NS, Satyal P, Barata LM, da Silva JKR, Setzer WN. Volatiles of black pepper fruits (Piper nigrum L). Molecules 2019 Nov 21;24(23):4244 [FREE Full text] [doi: 10.3390/molecules24234244] [Medline: 31766491]
41. McNair DM. Profile of Mood States. San Diego, CA: Educational and Industrial Testing Service; 1992.
42. Brown RA, Lejuez CW, Kahler CW, Strong DR, Zvolensky MJ. Distress tolerance and early smoking lapse. Clin Psychol Rev 2005 Sep;25(6):713-733 [FREE Full text] [doi: 10.1016/j.cpr.2005.05.003] [Medline: 16023275]
43. Clinical Practice Guideline Treating Tobacco Use and Dependence 2008 Update Panel, Liaisons, and Staff. A clinical practice guideline for treating tobacco use and dependence: 2008 update. A US Public Health Service report. Am J Prev Med 2008 Aug;35(2):158-176 [FREE Full text] [doi: 10.1016/j.amepre.2008.04.009] [Medline: 18617085]
44. Barua RS, Rigotti NA, Benowitz NL, Cummings KM, Jazayeri M, Morris PB, et al. 2018 ACC Expert Consensus Decision Pathway on Tobacco Cessation Treatment: A report of the American College of Cardiology Task Force on Clinical Expert Consensus Documents. J Am Coll Cardiol 2018 Dec 25;72(25):3332-3365 [FREE Full text] [doi: 10.1016/j.jacc.2018.10.027] [Medline: 30527452]
45. Anderson JE, Jorenby DE, Scott WJ, Fiore MC. Treating tobacco use and dependence: An evidence-based clinical practice guideline for tobacco cessation. Chest 2002 Mar;121(3):932-941. [doi: 10.1378/chest.121.3.932] [Medline: 11888979]
46. Hasegawa K, Terashima S, Satoh N, Inoue M, Wada H, Itoh C, et al. [Depressive state of patients on their initial visit to a smoking cessation clinic] [Article in Japanese]. Jpn J Smok Control Sci 2008;2:23-26 [FREE Full text]
47. Wada H, Hasegawa K, Terashima S, Satoh N, Inoue M, Iida Y, et al. [Self-rating depression scale score is a strong independent predictor of smoking cessation outcomes] [Article in Japanese]. Jpn J Smok Control Sci 2008;2(4):4-8. [doi: 10.32213/jascs.vol.2.04_4]

Abbreviations

CO: carbon monoxide
CTCAE: Common Terminology Criteria for Adverse Events
FTND: Fagerström Test for Nicotine Dependence
IRB: Institutional Review Board
NCD: noncommunicable disease
POMS: Profile of Mood States
SDS: Zung Self-Rating Depression Scale
UMIN: University Hospital Medical Information Network

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Protocol

The Development of Videoconference-Based Support for People Living With Rare Dementias and Their Carers: Protocol for a 3-Phase Support Group Evaluation

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Abstract

Background: People living with rarer dementias face considerable difficulty accessing tailored information, advice, and peer and professional support. Web-based meeting platforms offer a critical opportunity to connect with others through shared lived experiences, even if they are geographically dispersed, particularly during the COVID-19 pandemic.

Objective: We aim to develop facilitated videoconferencing support groups (VSGs) tailored to people living with or caring for someone with familial or sporadic frontotemporal dementia or young-onset Alzheimer disease, primary progressive aphasia, posterior cortical atrophy, or Lewy body dementia. This paper describes the development, coproduction, field testing, and evaluation plan for these groups.

Methods: We describe a 3-phase approach to development. First, information and knowledge were gathered as part of a coproduction process with members of the Rare Dementia Support service. This information, together with literature searches and consultation with experts by experience, clinicians, and academics, shaped the design of the VSGs and session themes. Second, field testing involved 154 Rare Dementia Support members (people living with dementia and carers) participating in 2 rounds of facilitated sessions across 7 themes (health and social care professionals, advance care planning, independence and identity, grief and loss, empowering your identity, couples, and hope and dementia). Third, a detailed evaluation plan for future rounds of VSGs was developed.

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Results: The development of the small groups program yielded content and structure for 9 themed VSGs (the 7 piloted themes plus a later stages program and creativity club for implementation in rounds 3 and beyond) to be delivered over 4 to 8 sessions. The evaluation plan incorporated a range of quantitative (attendance, demographics, and geography; pre-post well-being ratings and surveys; psycholinguistic analysis of conversation; facial emotion recognition; facilitator ratings; and economic analysis of program delivery) and qualitative (content and thematic analysis) approaches. Pilot data from round 2 groups on the pre-post 3-word surveys indicated an increase in the emotional valence of words selected after the sessions.

Conclusions: The involvement of people with lived experience of a rare dementia was critical to the design, development, and delivery of the small virtual support group program, and evaluation of this program will yield convergent data about the impact of tailored support delivered to geographically dispersed communities. This is the first study to design and plan an evaluation of VSGs specifically for people affected by rare dementias, including both people living with a rare dementia and their carers, and the outcome of the evaluation will be hugely beneficial in shaping specific and targeted support, which is often lacking in this population.

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KEYWORDS

dementia; Alzheimer disease; frontotemporal dementia; posterior cortical atrophy; Lewy body dementia; Lewy body disease; primary progressive aphasia; young-onset dementia; early-onset dementia; atypical dementia; virtual; web-based; videoconference; videophone; support group

Introduction

Background

Support groups for people caring for or living with dementia (collectively, people affected by dementia) may be characterized as peer support groups facilitated by individuals with lived experience of dementia, educational or psychotherapeutic groups facilitated by professionals, or a combination of these components [1]. Support groups for people affected by dementia have been shown to reduce depression and carer burden as well as improve self-esteem, well-being, and quality of life [2,3]. These benefits have been shown in both in-person and virtual support group contexts [4-8] with multicomponent groups, involving input from peers and professionals, and a focus on psychoeducational and emotional support alongside experience-led guidance being most effective [9].

These groups tend to focus on providing support for the most common forms of dementia such as typical Alzheimer disease and vascular dementia. Although living with or caring for someone with any form of dementia can be a very isolating and lonely experience [6,10], this is a particular concern for people affected by rarer forms of dementia [11-13]. Rare dementia is an umbrella term referring to atypical, inherited, and young-onset conditions, often characterized by progressive difficulties with cognitive symptoms other than memory [14,15]. As individuals diagnosed with rarer dementias tend to be younger than those diagnosed with typical Alzheimer disease and vascular dementia, they have additional concerns including work, mortgages, and young families [16-19]. Rarer dementias also vary with regard to symptom presentation and impact on caregivers [20-22]. In addition, given the wide geographical spread, there is often a lack of tailored and specific local support available to people affected by these dementias, which is exacerbated by the often long journey to receiving a diagnosis [23].

In March 2020, the United Kingdom entered a nationwide lockdown owing to the COVID-19 pandemic caused by SARS-CoV-2. The restrictions resulting from the COVID-19 pandemic lockdown led to an increase in loneliness and isolation for people affected by dementia [24-26] and severely affected those with rarer forms of dementia [27]. For example, individuals with behavioral variant frontotemporal dementia often experience behavioral disinhibition and compulsions, making it difficult to follow government guidelines on social distancing, whereas those with semantic dementia find it difficult to understand the restrictions in place because of difficulties with comprehension. Those diagnosed with posterior cortical atrophy often rely on touch to help with navigation because of difficulties with vision and spatial awareness, which increases the likelihood of spreading the virus [28]. In response to the pandemic, there was a rapid implementation of a number of telehealth and tele-support services [25,29,30]. These services increase accessibility for people with long-term health conditions and those in rural areas, who would usually have to travel long distances to access health and social care services [31]. Online support groups may also provide an additional benefit for people affected by rarer dementias, even as restrictions lift, as due to the typically younger age of onset, carers and those with the diagnosis may still be working, potentially alongside managing childcare needs, and may therefore benefit from the additional flexibility that these groups provide [8,18,19].

Videoconferencing support groups (VSGs) are a type of web-based support [5,8,32]. VSGs have been found to have similar treatment outcomes when compared with in-person groups [32] and have also been shown to improve dementia caregivers' mental health outcomes [7], including a decrease in burden and an increase in perceived social support and positive perceptions of caregiving [33]. In addition, Banbury et al [4], who implemented a 6-session videoconferencing peer support group for isolated carers of people with dementia, found that some group participants were more comfortable with videoconferencing than in-person groups, as they were in their

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own homes during the meeting, which felt like a *safe space* to share.

There is a lack of research on the benefits of VSGs specifically for people with rare dementias. In one of the few studies conducted with caregivers of people living with frontotemporal dementia, O'Connell et al [8] found benefits of VSGs, particularly in terms of being with caregivers who were in a similar situation to themselves with regard to age, relationship with the person with dementia, and their spouse's diagnosis. Importantly, this group did not take place in the individuals' homes but required group members to travel to their local health center to access the group, and group members reported difficulties in social connectivity because of the small screen sizes. Further research is needed to develop virtual support groups that can meet the unique needs of this population in an effective and sustainable way.

Objectives

Considering the barriers to support group access for people with rarer dementias and the additional need for support during the COVID-19 pandemic, we aimed to develop a series of facilitated VSGs tailored to the needs of people affected by rare dementias. Using the study by Hales and Fossey [34] as a guide, along with principles related to user-centered design [35], we describe the development, coproduction, field testing, and evaluation plan for these groups.

Methods

Phase 1

Information, Knowledge Gathering, and Coproduction

Coproduction is an iterative process of discussions with experts by experience, clinicians, and academics to develop VSGs within the context of Rare Dementia Support (RDS). RDS is an organization that supports people affected by posterior cortical atrophy, familial Alzheimer disease, familial frontotemporal dementia, frontotemporal dementia, primary progressive aphasia, young-onset Alzheimer disease, and dementia with Lewy bodies. Before this process, RDS involved large in-person support groups for each disease type; held 3 to 4 times per year in London; smaller regional support groups; as well as one-to-one information, guidance, and advice. The in-person support groups (n=40 to >120) included a mixture of professional and member talks, question and answer, and smaller breakout group sessions (approximately, n=20) covering a range of topics, including postdiagnostic support, communication strategies, legal matters, regional support, activities, and caring in the later stages. It had been a long-held service development plan for RDS to offer smaller group sessions in addition to the larger support group meetings, enabling RDS to address topics in further depth and in a more intimate setting than was possible within the larger support group context because of limited time and large-group size.

Consulting Academic Literature

The development of VSG topics continues to be informed by the literature, along with consultation with academic and clinical experts. The Mental Health America Support Group Facilitation Guide [36] was adapted and used as a framework to guide facilitators throughout the online group discussion process. Given the lack of research into support services for rarer dementias described earlier, we focused on young-onset dementia (YOD) for the literature search because of the higher prevalence of rarer dementias in this population [14,37]. A recent study found that one-third of individuals with YOD receive their diagnosis via the memory clinic, a quarter via neurological services, and less than a fifth via young-onset specialist services [38]. The follow-up support that these individuals receive is incredibly variable, with nearly a third of individuals diagnosed with YOD reporting that they do not have any routine follow-up appointments [38]. Therefore, it is important that those affected by these conditions are educated on how to access health and social care services that may be able to provide additional postdiagnostic and ongoing support, as they may not otherwise be linked with these services. It is also important that people diagnosed with YOD have their own dedicated space [39], where they can share openly with their peers. In addition, people affected by YOD frequently experience feelings of predeath grief, which is associated with perceived stress, depression, and carer burden [40-42]. Predeath grief can include feelings of loss resulting from ongoing changes in roles, relationships, and identities [43,44] and may be of particular concern for individuals affected by YOD because of changes in areas such as employment, finances, and child support [17].

Consulting With Experts by Experience

Building on the initial experience of RDS and understanding the literature, RDS staff had a number of conversations with people affected by rare dementias in the early stages of the national lockdown. These conversations increased the awareness of the lack of support services available and highlighted the need for a support group specifically for people living with a rare dementia. They also highlighted specific themes to be covered (eg, educating RDS members on advance care planning and the role of health and social care professionals), which was particularly important given the lack of literature on support needs related to rare dementias.

Consulting With Clinicians

The subsequent small-group discussion themes were developed based on these discussions and integrated with the views of RDS (consultant) neurologists (n=7) who had years of experience interacting with people affected by rare dementias both individually and at support group meetings.

Consulting With Academic Experts

Clinical academics who worked on the RDS Impact Project [45] had a number of discussions to integrate theoretical perspectives with earlier discussions and consequent adaptations to the planned groups. These discussions with experts by experience, academics, and clinicians led to a decision on initial content and themes for the field-testing round of groups discussed below (Table 1), as well as a model describing flow through the groups and intended inputs and outputs (Figure 1).

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Table 1. Videoconferencing support group (VSG) discussion content.

VSG discussion	Content
Round 1	
Health and social care professionals	• Neurology and memory assessment services • Community support • Postdiagnostic support • Community mental health teams • Support in the later stages
Advance care planning	• LPA[a] • Advance decisions and advance statements • Registering as a carer • Planning for hospital admission • Care in the home and care homes • Contingency planning • Continuing health care • Palliative care
Independence and identity	• Carer independence—challenges in maintaining interests and activities, and ways of managing this • Maintaining independence and identity for people living with a rare dementia • Carer identity—impact on sense of self, identification with the label of "carer"
Grief and loss	• Definition of grief and introduction to the concept of predeath grief • Losses and feelings associated with grief • Ambiguous loss • Anticipatory grief • Approaches to living with grief and loss • Sharing ways members have adapted to grief • Triggers for grief
Empowering your identity	• Health care professionals—who is involved in your care? • Care planning—future planning, LPA, advance decisions and statements, role of general practitioner • Independence and identity—adjusting to diagnosis, strategies for maintaining independence, and accepting help
Round 2 (health and social care professionals and advance care planning groups were combined)	
Couples session	• Independence: activities and interests, strategies to manage with difficulties • Accessing support: navigating the health and social care maze, local support networks • Planning together: advance care planning, choices and decision-making, emergency planning • Living well
Hope and dementia	• What can challenge sense of hope when living with or supporting someone with a rare dementia • Where hope can be found (including an object elicitation component) • How hope changes over time
Round 3	
Later stages program	• This program will be open to those who are currently caring for someone in the later stages of dementia. Sessions will focus on sensory engagement, nutrition and swallowing, continuing health care and legal matters, care considerations, palliative care, pain management, and end of life.
Creativity club	• Intended for people living with dementia, the sessions will encourage members to share their ideas about painting, music, dance, cooking, and even gardening! Each session will include a short creative group activity, and attendees may be asked to bring examples to share or work on themes between sessions.

[a]LPA: Lasting Power of Attorney.

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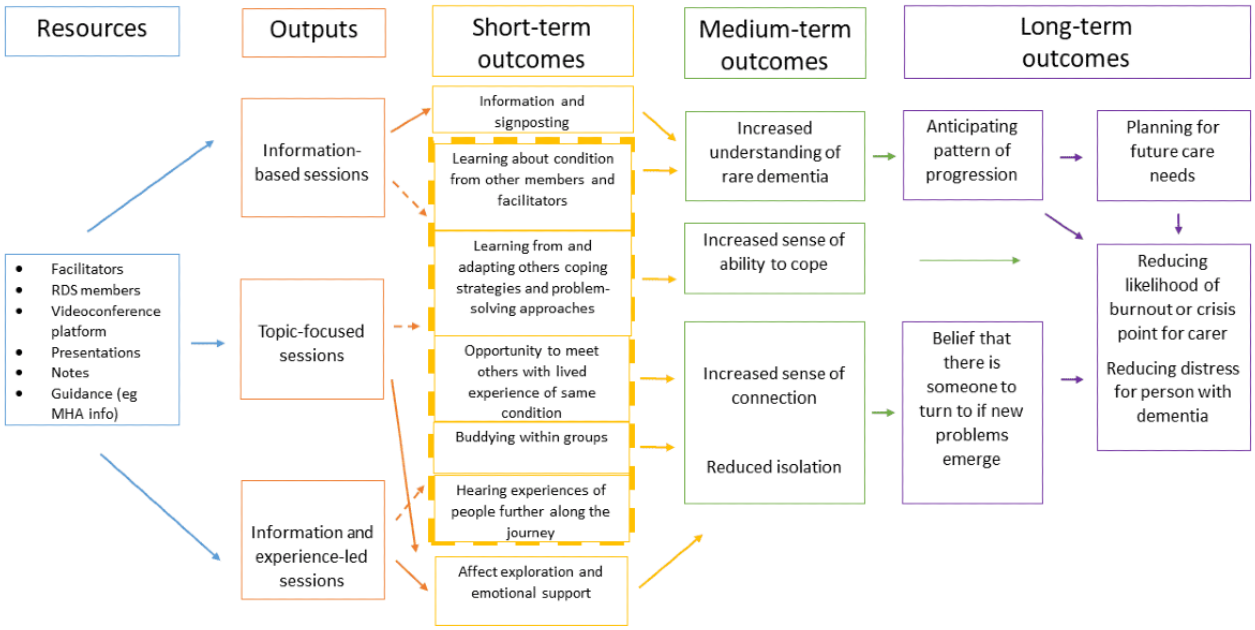
Figure 1. Output from phase 1 information and knowledge gathering. MHA: Mental Health America; RDS: Rare Dementia Support.



Phase 2

Field Testing

The groups, based on the coproduced topics and process model detailed earlier, were subjected to field testing in 2 rounds between May 2020 and September 2020. The aims of field testing were to deliver a service during a pandemic while also making refinements to topics and understanding optimal processes for round 3 of groups where more formal evaluation is proposed.

Recruitment

RDS members (approximately, n=2000) received an email with the dates and a brief description of the VSG topics. They were asked to respond with their preferred groups as soon as possible, and recruitment for the groups was closed when the groups reached capacity (round 1=96 spaces available; round 2=132 spaces available).

Participants

In total, 154 RDS members (N=175; round 1: n=76, 43%; round 2: n=99, 57%) registered across the first 2 rounds of the VSGs, with 21 of those members registering for both rounds. These members included people living (n=27, 15%) or caring for someone now or in the past (n=127, 73%) with a diagnosis of a rare dementia.

Inclusion criteria were participants (1) aged ≥18 years, (2) with the capacity to consent to take part in the VSGs, and (3) with access to a device and internet connection that would enable VSG participation.

Ethics Approval and Consent

The VSGs are part of the larger RDS Impact Project, conducted under the University College London Research Ethics Committee (8545/004: RDS Impact Study). See the study by Brotherhood et al [45] for details on the ethical procedures and consent.

Delivery

The RDS VSGs were conducted virtually using the GoToMeeting (GTM; LogMeIn Inc) videoconferencing platform. The group facilitators determined the number of sessions, with some groups held as one-off sessions, some as a series of 3 to 4 sessions, and other groups as ongoing. The format of the groups was also at the discretion of the facilitators, with some small groups being primarily experience-led and others being topic-focused or information-based.

Learnings From Field Testing

Initially, small online group discussions were offered as one-off, 1-hour-long information and experience-led sessions for RDS members. Sessions were subsequently increased to 1.5 hours to enable sufficient time for experience sharing alongside planned content. In addition, in the *independence and identity*, *grief and loss*, and *empowering your identity* groups, the facilitators felt that the connections made between group members and the scope of what could be covered within the group warranted a series of 4 sessions, rather than a one-off session. Once the 4 sessions were complete, participants were given the opportunity to continue to meet on a fortnightly or monthly basis, with light touch facilitation. Alongside these ongoing sessions, members who were connected with each other during the sessions were offered the option of one-to-one buddying. Further adaptations were made with regard to the timing of the sessions in the *empowering your identity* group for people living with dementia, which initially took place in the afternoon; however, the group members found it very difficult to concentrate at that time, so the facilitators moved the subsequent sessions to midmorning.

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Facilitators also met as a group to provide feedback on challenges arising from VSG facilitation and strategies for managing them. Shared learnings from this discussion included the challenges of facilitating online groups, such as creating a safe and comfortable environment when not meeting face-to-face and assessing risk in a virtual context. There were a number of downsides to the virtual aspect of the groups, such as the anxiety of managing technological issues within the sessions, lack of in-person debriefing and reflection with colleagues, difficulty in trying to read attendees' body language and nonverbal communication, and absence of boundaries between the facilitators' work and home spaces. The benefits of using technology included the depth of conversations and insights shared by group members, indicating that they felt comfortable being open in the context and safety of their own homes, and the ability to privately address any of the individual participant's concerns through the use of the chat function.

Protocol for Round 3

Participants

In round 3, participation in small groups will be offered to the wider RDS membership, with an invitation window of 6 weeks. On the basis of the recruitment for rounds 1 and 2, we estimated 50 to 100 participants per round.

Group Size

In round 3, group size will be reduced from 12 to 10 members per group, in accordance with facilitator feedback and carer preferences in previous research [8].

Topics

The third round of small groups will include the topics from the first 2 rounds of groups, as well as a later stages program for carers and a creativity club for people living with dementia (Table 1).

Sampling Approach

All nonprofessional RDS members will receive an invitation via email to express their interest in the third round of small groups.

Data Handling

All VSGs, apart from the couples' sessions in round 2 and the creativity club in round 3, will be recorded and automatically transcribed via the GTM platform. The recordings and transcriptions are stored securely on the University College London Data Safe Haven, which is only accessed by RDS Impact Study researchers. Once uploaded, the original files are deleted from GTM. As the accuracy of automated transcription is variable, meeting recordings will also be outsourced for professional transcription.

Results

Phase 3: Evaluation Plan

Overview

The first 2 rounds of VSGs were offered as a rapid service response to the pandemic, without a research plan to assess their impact. On the basis of field testing conducted during round 2 (Figure 2), a set of quantitative and qualitative investigations was designed to describe and measure the impact of round 3. Specific hypotheses for the quantitative investigations include (1) that session participation in small groups will be associated with increased in-the-moment well-being and (2) that participation, both within and across sessions, will be associated with enhanced social connectedness. Qualitative analysis will explore questions related to understanding how peer support groups work (eg, How are different types of social support delivered in peer support groups?) and specific questions related to the different themes of the groups (eg, In what ways are carers' senses of identity impacted when supporting someone living with a rare dementia?).

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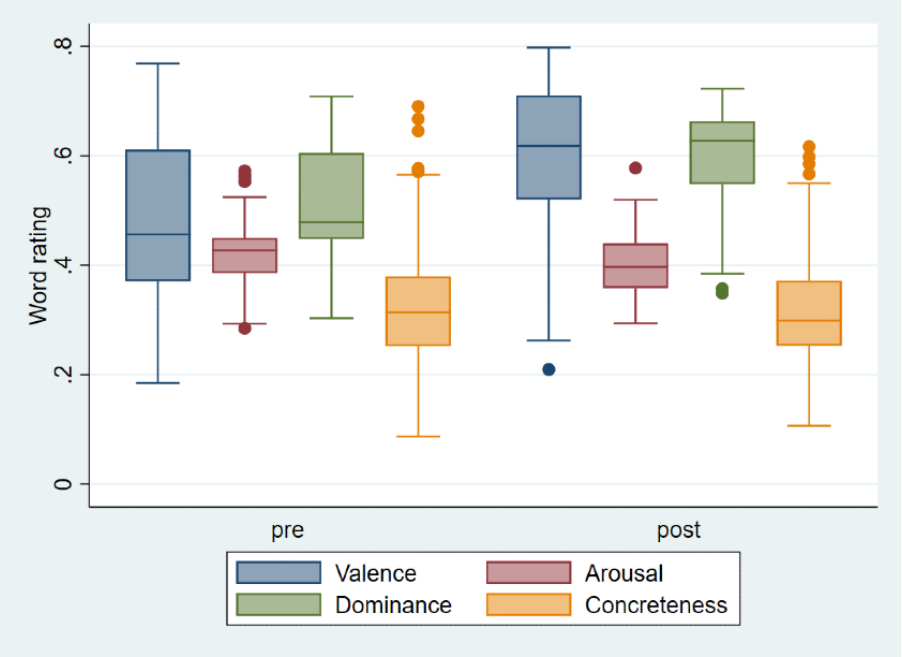
Figure 2. Pilot data from the "3 words" evaluation collected from participants (N=35) in wave 2 small-group conversations. Box and whisker plots show emotional valence, arousal, and dominance plus concreteness ratings of pre- and postsession words (N=301 words; 153 presession words and 148 postsession words). Linear mixed effects models were fitted for each linguistic score using STATA, including participant as a random effect (to account for nonindependence of words produced by each participant) and session theme as a fixed factor, and checking for normality of residuals (independent residual errors for the participants), heteroscedasticity, and linearity of the model. Pre-post differences were significant for all linguistic variables except concreteness, with valence and dominance scores increasing while arousal decreased (coefficients with *P* value, 95% CIs: valence coefficient=0.12, *P*<.001, 0.07 to −0.16; arousal coefficient=−0.02, *P*=.003, −0.04 to −0.01; dominance coefficient=0.08, *P*<.001, 0.04 to −0.11; concreteness coefficient=−0.013, *P*=.31, −0.04 to 0.01). A significantly different proportion of presession and postsession words were categorized by Linguistic Inquiry and Word Count as positive or negative emotion words (χ21=35.0, *P*<.001).



Attendance, Demographics, and Geography

Participation in the groups will be evaluated against a range of factors, including gender, age, relationship to people living with dementia, diagnosis of person living with dementia, severity (judged by RDS facilitators using the Global Deterioration Scale) [46], frequency of RDS service use, and location. Key research questions include whether small online groups facilitate access to support for geographically dispersed members and later-stage carers, relative to standard face-to-face services typically delivered from our central London base.

Participant Ratings and Surveys

At the beginning and end of each session, participants will be asked to click a link to a web survey and (1) choose 3 words that describe how they are feeling in the moment and (2) complete the Canterbury Wellbeing Scale [47]. This will involve moving a web-based visual analog slider on a scale from 0 to 100 to indicate how they are feeling in the moment along the established 5 dimensions of happiness, wellness, interest, optimism, and confidence, including additional scales for stress and social connectedness. Three-word responses will be evaluated for emotional content using normative data for emotional valence, arousal, and dominance plus concreteness [48,49] and the Linguistic Inquiry and Word Count (LIWC) automated classification of positive and negative emotion words [50].

Linguistics

Online support groups also offer rich multimodal data on participants' thoughts, emotions, and behaviors, which can deepen our understanding of support group processes. Voice recordings mean that linguistic analysis tools such as LIWC [50] have been used to explore the relationship between dropout rates and the level of emotional support received within sessions [51], and differences in the manner of expression between online and face-to-face support groups in young adults living with cancer [52].

The recorded conversations will be transcribed and evaluated cross-sectionally (within sessions) and longitudinally (across sessions) for evidence of thematic development and group cohesion. Specific features of interest include (1) participation, in terms of frequency, quantity, and equality of verbal contributions by individual participants and facilitators; (2) emotional content, such as the emotional valence, arousal and dominance of language used (quantified using norms in the study by Hollis and Westbury [48] and LIWC software, as per the "3 words analysis"); and (3) prevalence of specific features, such as incomplete propositions, hedges, signs of agreement (eg, in terms of use of names and grunts), and changes in pronoun (eg, "I" to "we") and tense use (eg, past vs present vs future orientated utterances).

FaceReader

Facial video data have been analyzed with facial emotion recognition software such as FaceReader (version 7.0; Noldus Information Technology) to track changes in emotional

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regulation as markers of therapeutic effectiveness in individuals with borderline personality disorder [53]. Although not previously used with RDS groups, the exploratory use of these tools may yield novel metrics of group behavior, which through automation can be applied efficiently to future evaluations of the impact of online support groups.

Video recordings of the online meetings will be processed using FaceReader software, which classifies expressions into the categories of happy, sad, angry, surprised, scared, disgusted, and neutral and generates measures of the intensity of each individual emotion, valence (intensity of "happy" minus the intensity of the negative expression with the highest intensity), and arousal (based on the activation of 20 facial action units). In addition to quantifying overall differences in valence and arousal within and across sessions as the VSG conversations develop, FaceReader data will be used to explore (1) the relationship between the valence of facial emotion and verbal content of current conversation and (2) the cohesion of the group, taking the statistical variance of valence and arousal metrics among individual listeners to the current speaker in the group as proxies of cohesion.

Facilitator Ratings: Curative Climate Instrument

To complement participant ratings and observational linguistic and video data, facilitators of each group will be asked after each session to complete an adapted version of the Curative Climate Instrument [54] examining the processes of catharsis, cohesion, and insight within a small group. Originally designed as a measure for individual participants, facilitators will be asked to rate 13 of 14 statements reframed from a facilitator perspective (eg, "People were responsive to each other and made contact with each other through language, gesture, etc.") for both levels of agreement (on a Likert scale from 1=strongly disagree to 7=strongly agree) and confidence in their agreement rating (from 1=extremely unconfident to 7=extremely confident).

Phase 3: Qualitative Analysis Plan

The qualitative data (ie, transcriptions of the VSGs) will be analyzed to explore questions related to peer support groups overall, as well as questions that are specific to the different themes of each group, including those in the subsequent sections.

Qualitative Content Analysis

A directed content analysis [55] of all VSGs will be conducted to explore the question "How is social support delivered in peer support groups?," with a coding framework based on the social support categories by Cutrona and Suhr [56] and the Social Support Behavior Code by Suhr et al [57]. Instrumental, tangible, emotional, and esteem support types will be coded for, and examples of each can be seen in Table 2.

Table 2. Qualitative content analysis.

Social support category	Example codes	Example data segments
Instrumental support	Suggestions and advice	"If you're not sure about it (going to a day center), just go and have a look at what's available...we were extremely reluctant and thought 'Oh I don't know'...We'd go through the activities and select what he wanted to do...That was quite helpful."
Tangible support	Direct task	"I'm just going to put (helpful organization's phone number) in the chat and if you (facilitator) could send it to people."
Emotional support	Understanding and empathy	"The biggest problem I see is that we've all got the same problem that, unfortunately, we're watching loved ones deteriorate. We know that there isn't going to be any difference other than a slow deterioration, and we just adjust every time something happens."
Esteem support	Compliments	"I think it is bureaucracy and you have done well to get through it and stand firm...I think you have been brilliant doing that."

Thematic Analysis

Thematic analysis [58] of facilitator peer support sessions will explore the benefits and challenges of offering small peer support group discussions in a web-based format for people affected by rarer dementias to consolidate learning and develop recommendations for other facilitators embarking on similar initiatives. Benefits may relate to increased accessibility for those who would be unable to travel to in-person meetings because of their location, difficulties using public transport, or caring commitments. Challenges such as those relating to technology (eg, managing background noise and feedback), emotional impact (eg, lack of opportunities for informal conversations over coffee before and after meetings), and other factors will also be explored.

Thematic analysis will also be used to explore questions specific to the themes on which the small-group discussions were focused. For example, for the "Hope and dementia" group theme, how is the sense of hope challenged and sustained for people caring for a loved one with a diagnosis of a rare dementia? For the "independence and identity" group theme, how are the individual and shared identities of those living with a rare dementia and their carers impacted by the diagnosis?

Phase 3

Economic Analysis

An exploratory analysis of the costs of developing the small online groups will be conducted using a microcosting approach from a societal perspective. We will microcost the development and delivery of the intervention to provide a clear representation of the costs of establishing these small groups.

Intervention costs will be requested from the groups. This list is not exhaustive but must include (1) cost of setting up the groups, (2) annual overheads, (3) cost of group materials (print costs and design costs), (4) salary costs for group and program facilitators, (5) training costs for facilitators, and (6) support costs for facilitators and volunteers.

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We will also ask the groups to estimate any inputs, financial, time, or otherwise, so that these costs will also be accounted for.

Planned Analysis

We will take guidance from the UK Treasury Office Magenta Book in planning and designing the economic evaluation of this program [59].

This could include the following:

- Cost-benefit analysis using any participant questionnaire results to calculate quality-adjusted life years alongside the costs and benefits calculates the net present value of the program [60]. Cost-benefit analysis undertaken from a societal perspective allows the costs and benefits to be considered separately to consider a net monetary benefit or a ratio of benefits to costs, and considers all the costs and benefits to society [61]. Using deterministic sensitivity analysis, we will adjust the values for individual and multiple parameters and we will vary the discount rate from 0% to 3.5% to generate a range of scenarios, as recommended by the UK Treasury Green Book [62].
- Return on investment analysis, which would estimate, pound for pound, the return on investment from providing the VSGs.
- Cost consequence analysis works well with return on investment to quantify outcomes without traditional market values [61]. Cost consequence analysis allows for the outcomes to be quantified and related to costs for each separate course of action, where the final outcomes may be multidimensional; that is, to consider the range of relevant costs and outcomes, both anticipated and unanticipated.

The health economics component of this study will be written in accordance with the Consolidated Health Economic Evaluation Reporting Standards statement [63].

Discussion

Principal Predictions

We anticipate that connecting people affected by rare dementias together and providing a virtual space where they can share their experiences with others who are affected by the same conditions will be reflected by increased in-the-moment well-being outcomes, as well as an enhancement of social connectedness. We hope to develop a greater understanding of what works and does not in group peer support to improve service delivery for those affected by rare dementias.

To develop support tailored to the specific needs of people affected by rare dementias, it is vital that individuals with lived experience are involved in the design process. RDS members have played a significant role in the development of previous research projects [64,65], and their valuable input continues to shape both the RDS service and associated research, including the development of VSGs.

Although these groups were primarily developed in response to increased support needs during the COVID-19 pandemic, the recordings, pre- and postsession well-being measures, and participant feedback also provided an incredibly rich data source. We described a comprehensive evaluation plan using the data collected from these groups, the outcome of which will be used to further adapt and refine our web-based support provision. In addition, we hope that the learnings from these evaluations will be beneficial for other services that provide support for people with dementia as well as other health conditions, especially those that are rare and where individuals are geographically dispersed.

There are limitations with regard to this study, as the rapid setup of the groups meant that there was limited opportunity for comprehensive feedback and refinement of the group format and delivery ahead of the initial rounds. However, VSG development has also led to rapid learning for RDS staff regarding how to facilitate groups in a web-based context. The evaluation of these groups will further enable the development of a comprehensive framework for the delivery of online support for people affected by rare dementias across one-to-one, family, small-group, and large-group webinar formats.

In addition, because of the setup of the groups, all participants were required to familiarize themselves with the use of videoconferencing software, which likely would have excluded a number of individuals, particularly those living with dementia with additional accessibility needs. The study by O'Connell et al [66] suggests that participants should be provided with the option of joining via phone and video calls when conducting research remotely. This option was made available during the consenting process; however, it was not encouraged during the VSGs. If the participants had issues with internet connectivity during the session, the option of joining via phone was made available at that point. Future iterations might consider providing the option of joining via phone from the outset, rather than purely to overcome technical difficulties, although the impact on group dynamics of members joining via phone versus video may also need to be assessed.

Conclusions and Future Directions

This paper has highlighted the importance of specific and targeted support delivered via VSG for people caring for or diagnosed with a rare dementia, the importance of coproduction, and the need for comprehensive evaluation of these groups to determine their effectiveness, and to further adapt and shape services to meet member needs in future. More broadly, the methods and findings of this work may also be of interest to other dementia-related service providers and providers of other long-term care conditions.

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Conflicts of Interest

None declared.

References

1. Toms GR, Clare L, Nixon J, Quinn C. A systematic narrative review of support groups for people with dementia. Int Psychogeriatr 2015 Sep;27(9):1439-1465. [doi: 10.1017/S1041610215000691] [Medline: 25990373]
2. Chien LY, Chu H, Guo JL, Liao YM, Chang LI, Chen CH, et al. Caregiver support groups in patients with dementia: a meta-analysis. Int J Geriatr Psychiatry 2011 Oct;26(10):1089-1098. [doi: 10.1002/gps.2660] [Medline: 21308785]
3. Leung P, Orrell M, Orgeta V. Social support group interventions in people with dementia and mild cognitive impairment: a systematic review of the literature. Int J Geriatr Psychiatry 2015 Jan;30(1):1-9. [doi: 10.1002/gps.4166] [Medline: 24990344]
4. Banbury A, Parkinson L, Gordon S, Wood D. Implementing a peer-support programme by group videoconferencing for isolated carers of people with dementia. J Telemed Telecare 2019 Oct;25(9):572-577. [doi: 10.1177/1357633X19873793] [Medline: 31631761]
5. Hopwood J, Walker N, McDonagh L, Rait G, Walters K, Iliffe S, et al. Internet-based interventions aimed at supporting family caregivers of people with dementia: systematic review. J Med Internet Res 2018 Jun 12;20(6):e216 [FREE Full text] [doi: 10.2196/jmir.9548] [Medline: 29895512]
6. Kovaleva M, Blevins L, Griffiths PC, Hepburn K. An online program for caregivers of persons living with dementia: lessons learned. J Appl Gerontol 2019 Feb;38(2):159-182. [doi: 10.1177/0733464817705958] [Medline: 28460557]
7. Marziali E, Garcia LJ. Dementia caregivers' responses to 2 Internet-based intervention programs. Am J Alzheimers Dis Other Demen 2011 Feb;26(1):36-43 [FREE Full text] [doi: 10.1177/1533317510387586] [Medline: 21282276]
8. O'Connell ME, Crossley M, Cammer A, Morgan D, Allingham W, Cheavins B, et al. Development and evaluation of a telehealth videoconferenced support group for rural spouses of individuals diagnosed with atypical early-onset dementias. Dementia (London) 2014 May;13(3):382-395. [doi: 10.1177/1471301212474143] [Medline: 24339063]
9. Dam AE, de Vugt ME, Klinkenberg IP, Verhey FR, van Boxtel MP. A systematic review of social support interventions for caregivers of people with dementia: are they doing what they promise? Maturitas 2016 Mar;85:117-130. [doi: 10.1016/j.maturitas.2015.12.008] [Medline: 26857890]
10. Victor CR, Rippon I, Nelis SM, Martyr A, Litherland R, Pickett J, IDEAL programme team. Prevalence and determinants of loneliness in people living with dementia: findings from the IDEAL programme. Int J Geriatr Psychiatry 2020 Aug;35(8):851-858. [doi: 10.1002/gps.5305] [Medline: 32281151]
11. Bruinsma J, Peetoom K, Bakker C, Boots L, Verhey F, de Vugt M. 'They simply do not understand': a focus group study exploring the lived experiences of family caregivers of people with frontotemporal dementia. Aging Ment Health 2022 Feb;26(2):277-285. [doi: 10.1080/13607863.2020.1857697] [Medline: 33325262]
12. Dourado MC, Laks J, Kimura NR, Baptista MA, Barca ML, Engedal K, et al. Young-onset Alzheimer dementia: a comparison of Brazilian and Norwegian carers' experiences and needs for assistance. Int J Geriatr Psychiatry 2018 Jun;33(6):824-831. [doi: 10.1002/gps.4717] [Medline: 28370411]
13. Kaiser S, Panegyres PK. The psychosocial impact of young onset dementia on spouses. Am J Alzheimers Dis Other Demen 2006;21(6):398-402 [FREE Full text] [doi: 10.1177/1533317506293259] [Medline: 17267371]
14. Harvey RJ, Roques P, Fox NC, Rossor MN. Non-Alzheimer dementias in young patients. Br J Psychiatry 1996 Mar;168(3):384-385. [doi: 10.1192/bjp.168.3.384b] [Medline: 8833704]
15. Rare Dementia Support. 2022. URL: https://www.raredementiasupport.org/ [accessed 2021-11-01]
16. Allen J, Oyebode JR, Allen J. Having a father with young onset dementia: the impact on well-being of young people. Dementia 2009 Dec 04;8(4):455-480. [doi: 10.1177/1471301209349106]
17. Gelman C, Rhames K. "I have to be both mother and father": the impact of young-onset dementia on the partner's parenting and the children's experience. Dementia (London) 2020 Apr;19(3):676-690. [doi: 10.1177/1471301218783542] [Medline: 29996672]
18. Svanberg E, Spector A, Stott J. The impact of young onset dementia on the family: a literature review. Int Psychogeriatr 2011 Apr;23(3):356-371. [doi: 10.1017/S1041610210001353] [Medline: 20735892]
19. van Vliet D, de Vugt ME, Bakker C, Koopmans RT, Verhey FR. Impact of early onset dementia on caregivers: a review. Int J Geriatr Psychiatry 2010 Nov;25(11):1091-1100. [doi: 10.1002/gps.2439] [Medline: 20957692]

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20. Diehl J, Monsch AU, Aebi C, Wagenpfeil S, Krapp S, Grimmer T, et al. Frontotemporal dementia, semantic dementia, and Alzheimer's disease: the contribution of standard neuropsychological tests to differential diagnosis. J Geriatr Psychiatry Neurol 2005 Mar;18(1):39-44. [doi: 10.1177/0891988704272309] [Medline: 15681627]
21. Nicolaou PL, Egan SJ, Gasson N, Kane RT. Identifying needs, burden, and distress of carers of people with Frontotemporal dementia compared to Alzheimer's disease. Dementia 2010 Mar 26;9(2):215-235. [doi: 10.1177/1471301209354024]
22. Uflacker A, Edmondson MC, Onyike CU, Appleby BS. Caregiver burden in atypical dementias: comparing frontotemporal dementia, Creutzfeldt-Jakob disease, and Alzheimer's disease. Int Psychogeriatr 2016 Feb;28(2):269-273. [doi: 10.1017/S1041610215001647] [Medline: 26435062]
23. van Vliet D, de Vugt ME, Bakker C, Pijnenburg YA, Vernooij-Dassen MJ, Koopmans RT, et al. Time to diagnosis in young-onset dementia as compared with late-onset dementia. Psychol Med 2013 Feb;43(2):423-432. [doi: 10.1017/S0033291712001122] [Medline: 22640548]
24. Ryoo N, Pyun JM, Baek MJ, Suh J, Kang MJ, Wang MJ, et al. Coping with dementia in the middle of the COVID-19 pandemic. J Korean Med Sci 2020 Nov 02;35(42):e383 [FREE Full text] [doi: 10.3346/jkms.2020.35.e383] [Medline: 33140593]
25. Tousi B. Dementia care in the time of COVID-19 pandemic. J Alzheimers Dis 2020;76(2):475-479. [doi: 10.3233/JAD-200461] [Medline: 32651326]
26. Wang H, Li T, Barbarino P, Gauthier S, Brodaty H, Molinuevo JL, et al. Dementia care during COVID-19. Lancet 2020 Apr 11;395(10231):1190-1191 [FREE Full text] [doi: 10.1016/S0140-6736(20)30755-8] [Medline: 32240625]
27. Suárez-González A, Harding E, Zimmerman N, Hoare Z, Brotherhood E, Crutch S. The impact of the first UK Covid-19 lockdown on carers and people living with low prevalence dementia: results from the Rare Dementia Support survey. medRxiv Preprint posted online December 20, 2020. [doi: 10.1101/2020.12.18.20248455]
28. Suárez-González A, Zimmermann N, Waddington C, Wood O, Harding E, Brotherhood E, et al. Non-memory led dementias: care in the time of covid-19. BMJ 2020 Jun 30;369:m2489. [doi: 10.1136/bmj.m2489] [Medline: 32606068]
29. Cuffaro L, Di Lorenzo F, Bonavita S, Tedeschi G, Leocani L, Lavorgna L. Dementia care and COVID-19 pandemic: a necessary digital revolution. Neurol Sci 2020 Aug;41(8):1977-1979 [FREE Full text] [doi: 10.1007/s10072-020-04512-4] [Medline: 32556746]
30. Goodman-Casanova JM, Dura-Perez E, Guzman-Parra J, Cuesta-Vargas A, Mayoral-Cleries F. Telehealth home support during COVID-19 confinement for community-dwelling older adults with mild cognitive impairment or mild dementia: survey study. J Med Internet Res 2020 May 22;22(5):e19434 [FREE Full text] [doi: 10.2196/19434] [Medline: 32401215]
31. Hoffman DA. Increasing access to care: telehealth during COVID-19. J Law Biosci 2020 Jun 16;7(1):lsaa043 [FREE Full text] [doi: 10.1093/jlb/lsaa043] [Medline: 32843985]
32. Gentry MT, Lapid MI, Clark MM, Rummans TA. Evidence for telehealth group-based treatment: a systematic review. J Telemed Telecare 2019 Jul;25(6):327-342. [doi: 10.1177/1357633X18775855] [Medline: 29788807]
33. Czaja SJ, Loewenstein D, Schulz R, Nair SN, Perdomo D. A videophone psychosocial intervention for dementia caregivers. Am J Geriatr Psychiatry 2013 Nov;21(11):1071-1081. [doi: 10.1016/j.jagp.2013.02.019] [Medline: 23831174]
34. Hales SA, Fossey J. Caring For Me and You: the co-production of a computerised cognitive behavioural therapy (cCBT) package for carers of people with dementia. Aging Ment Health 2018 Oct;22(10):1287-1294. [doi: 10.1080/13607863.2017.1348475] [Medline: 28691520]
35. Walden A, Garvin L, Smerek M, Johnson C. User-centered design principles in the development of clinical research tools. Clin Trials 2020 Dec;17(6):703-711. [doi: 10.1177/1740774520946314] [Medline: 32815381]
36. Support Group Facilitation Guide. Mental Health America. 2016. URL: https://www.mhanational.org/sites/default/files/MHA%20Support%20Group%20Facilitation%20Guide%202016.pdf [accessed 2020-05-01]
37. Alzheimer's Australia. Exploring the Needs of Younger People with Dementia in Australia: Report to the Australian Government. Department of Health and Ageing, Australian Government. 2007. URL: https://catalogue.nla.gov.au/Record/4299602 [accessed 2021-01-17]
38. Stamou V, La Fontaine J, Gage H, Jones B, Williams P, O'Malley M, et al. Services for people with young onset dementia: the 'Angela' project national UK survey of service use and satisfaction. Int J Geriatr Psychiatry 2021 Mar;36(3):411-422. [doi: 10.1002/gps.5437] [Medline: 32979287]
39. Mayrhofer A, Mathie E, McKeown J, Bunn F, Goodman C. Age-appropriate services for people diagnosed with young onset dementia (YOD): a systematic review. Aging Ment Health 2018 Aug;22(8):927-935. [doi: 10.1080/13607863.2017.1334038] [Medline: 28621549]
40. Kobiske KR, Bekhet AK, Garnier-Villarreal M, Frenn M. Predeath grief, resourcefulness, and perceived stress among caregivers of partners with young-onset dementia. West J Nurs Res 2019 Jul;41(7):973-989. [doi: 10.1177/0193945918806689] [Medline: 30343648]
41. Adams KB, Sanders S. Alzheimer's caregiver differences in experience of loss, grief reactions and depressive symptoms across stage of disease: a mixed-method analysis. Dementia 2004 Jun 1;3(2):195-210. [doi: 10.1177/1471301204042337]
42. Holley CK, Mast BT. The impact of anticipatory grief on caregiver burden in dementia caregivers. Gerontologist 2009 Jun;49(3):388-396. [doi: 10.1093/geront/gnp061] [Medline: 19386826]

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43. Lindauer A, Harvath TA. Pre-death grief in the context of dementia caregiving: a concept analysis. J Adv Nurs 2014 Oct;70(10):2196-2207. [doi: 10.1111/jan.12411] [Medline: 24702153]
44. Marwit SJ, Meuser TM. Development of a short form inventory to assess grief in caregivers of dementia patients. Death Stud 2005 Apr;29(3):191-205. [doi: 10.1080/07481180590916335] [Medline: 15816111]
45. Brotherhood EV, Stott J, Windle G, Barker S, Culley S, Harding E, et al. Protocol for the rare dementia support impact study: RDS impact. Int J Geriatr Psychiatry 2020 Aug;35(8):833-841. [doi: 10.1002/gps.5253] [Medline: 31876030]
46. Reisberg B, Ferris SH, de Leon MJ, Crook T. The Global Deterioration Scale for assessment of primary degenerative dementia. Am J Psychiatry 1982 Sep;139(9):1136-1139. [doi: 10.1176/ajp.139.9.1136] [Medline: 7114305]
47. Johnson J, Culverwell A, Hulbert S, Robertson M, Camic PM. Museum activities in dementia care: using visual analog scales to measure subjective wellbeing. Dementia (London) 2017 Jul;16(5):591-610. [doi: 10.1177/1471301215611763] [Medline: 26468054]
48. Hollis G, Westbury C, Lefsrud L. Extrapolating human judgments from skip-gram vector representations of word meaning. Q J Exp Psychol (Hove) 2017 Aug;70(8):1603-1619. [doi: 10.1080/17470218.2016.1195417] [Medline: 27251936]
49. Warriner AB, Kuperman V, Brysbaert M. Norms of valence, arousal, and dominance for 13,915 English lemmas. Behav Res Methods 2013 Dec;45(4):1191-1207. [doi: 10.3758/s13428-012-0314-x] [Medline: 23404613]
50. Pennebaker JW, Boyd RL, Jordan K, Blackburn K. The development and psychometric properties of LIWC2015. The University of Texas at Austin. 2015. URL: https://repositories.lib.utexas.edu/bitstream/handle/2152/31333/LIWC2015_LanguageManual.pdf [accessed 2021-05-04]
51. Wang YC, Kraut R, Levine JM. To stay or leave?: the relationship of emotional and informational support to commitment in online health support groups. In: Proceedings of the ACM 2012 conference on Computer Supported Cooperative Work. 2012 Presented at: CSCW '12; February 11-15, 2012; Seattle, WA, USA p. 833-842 URL: https://doi.org/10.1145/2145204.2145329 [doi: 10.1145/2145204.2145329]
52. Thompson CM, Crook B, Love B, Macpherson CF, Johnson R. Understanding how adolescents and young adults with cancer talk about needs in online and face-to-face support groups. J Health Psychol 2016 Nov;21(11):2636-2646. [doi: 10.1177/1359105315581515] [Medline: 25921477]
53. Arango I, Miranda E, Sánchez Ferrer JC, Fresán A, Reyes Ortega MA, Vargas AN, et al. Changes in facial emotion expression during a psychotherapeutic intervention for patients with borderline personality disorder. J Psychiatr Res 2019 Jul;114:126-132. [doi: 10.1016/j.jpsychires.2019.04.026] [Medline: 31071663]
54. Fuhriman A, Drescher S, Hanson E, Henrie R, Rybicki W. Refining the measurement of curativeness: an empirical approach. Small Group Behav 1986 May 1;17(2):186-201. [doi: 10.1177/104649648601700204]
55. Hsieh HF, Shannon SE. Three approaches to qualitative content analysis. Qual Health Res 2005 Nov;15(9):1277-1288. [doi: 10.1177/1049732305276687] [Medline: 16204405]
56. Cutrona CE, Suhr JA. Controllability of stressful events and satisfaction with spouse support behaviors. Commun Res 1992 Apr 1;19(2):154-174. [doi: 10.1177/009365092019002002]
57. Suhr JA, Cutrona CE, Krebs KK, Jensen SL. The social support behavior code. In: Kerig PK, Baucom DH, editors. Couple Observational Coding Systems. Milton Park, UK: Routledge; 2004.
58. Braun V, Clarke V. Using thematic analysis in psychology. Qual Res Psychol 2006 Jan;3(2):77-101. [doi: 10.1191/1478088706qp063oa]
59. The Magenta Book: guidance notes for policy evaluation and analysis. HM Treasury. 2020. URL: https://dera.ioe.ac.uk/10521/1/complete_Magenta_tcm6-8611.pdf [accessed 2021-05-04]
60. McIntosh E, Baba C, Botha W. Cost–benefit analysis for applied public health economic evaluation. In: Edwards RT, McIntosh E, editors. Applied Health Economics for Public Health Practice and Research. Oxford, UK: Oxford University Press; 2019.
61. Methods for the development of NICE public health guidance (third edition). National Institute for Health and Care Excellence. 2012 Sep 26. URL: https://www.nice.org.uk/process/pmg4/chapter/incorporating-health-economics [accessed 2021-05-04]
62. The green book: appraisal and evaluation in central government. HM Treasury. 2022. URL: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/938046/The_Green_Book_2020.pdf [accessed 2021-05-04]
63. Husereau D, Drummond M, Petrou S, Carswell C, Moher D, Greenberg D, CHEERS Task Force. Consolidated health economic evaluation reporting standards (CHEERS) statement. Int J Technol Assess Health Care 2013 Apr;29(2):117-122. [doi: 10.1017/S0266462313000160] [Medline: 23587340]
64. Crutch S, Herron D, Pickett J, Rosser S, Rossor M, Created Out of Mind team. Inspired by chance: valuing patients' informal contributions to research. BMJ 2020 Dec 14;371:m4478. [doi: 10.1136/bmj.m4478] [Medline: 33318028]
65. Crutch SJ, Yong KX, Peters A, Ocal D, Kaski D, Gonzalez AS, et al. Contributions of patient and citizen researchers to 'Am I the right way up?' study of balance in posterior cortical atrophy and typical Alzheimer's disease. Dementia (London) 2018 Nov;17(8):1011-1022. [doi: 10.1177/1471301218789296] [Medline: 30373456]
66. O'Connell ME, Vellani S, Robertson S, O'Rourke HM, McGilton KS. Going from zero to 100 in remote dementia research: a practical guide. J Med Internet Res 2021 Jan 27;23(1):e24098 [FREE Full text] [doi: 10.2196/24098] [Medline: 33468448]
67. The National Brain Appeal. URL: https://www.nationalbrainappeal.org/ [accessed 2022-06-28]

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Abbreviations

ESRC: Economic and Social Research Council
GTM: GoToMeeting
LIWC: Linguistic Inquiry and Word Count
RDS: Rare Dementia Support
VSG: videoconferencing support group
YOD: young-onset dementia

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Protocol

Salivary Dysfunctions and Consequences After Radioiodine Treatment for Thyroid Cancer: Protocol for a Self-Controlled Study (START Study)

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Abstract

Background: Following radioiodine (^{131}I) therapy of differentiated thyroid cancer, the salivary glands may become inflamed, leading to dysfunctions and decreases in patients' nutritional status and quality of life. The incidence of these dysfunctions after ^{131}I-therapy is poorly known, and no clinical or genetic factors have been identified to date to define at-risk patients, which would allow the delivered activity to be adapted to the expected risk of salivary dysfunctions.

Objective: The aims of this study are to estimate the incidence of salivary dysfunctions, and consequences on the quality of life and nutritional status for patients after ^{131}I-therapy; to characterize at-risk patients of developing posttreatment dysfunctions using clinical, biomolecular, and biochemical factors; and to validate a dosimetric method to calculate the dose received at the salivary gland level for analyzing the dose-response relationship between absorbed doses to salivary glands and salivary dysfunctions.

Methods: This prospective study aims to include patients for whom ^{131}I-therapy is indicated as part of the treatment for differentiated thyroid cancer in a Paris hospital (40 and 80 patients in the 1.1 GBq and 3.7 GBq groups, respectively). The follow-up is based on three scheduled visits: at inclusion (T0, immediately before ^{131}I-therapy), and at 6 months (T6) and 18 months (T18) posttreatment. For each visit, questionnaires on salivary dysfunctions (validated French tool), quality of life (Hospital Anxiety and Depression scale, Medical Outcomes Study 36-Item Short Form Survey), and nutritional status (visual analog scale) are administered by a trained clinical research associate. At T0 and T6, saliva samples and individual measurements of the salivary flow, without and with salivary glands stimulation, are performed. External thermoluminescent dosimeters are positioned on the

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skin opposite the salivary glands and at the sternal fork immediately before ^{131}I administration and removed after 5 days. From the doses recorded by the dosimeters, an estimation of the dose received at the salivary glands will be carried out using physical and computational phantoms. Genetic and epigenetic analyses will be performed to search for potential biomarkers of the predisposition to develop salivary dysfunctions after ^{131}I-therapy.

Results: A total of 139 patients (99 women, 71.2%; mean age 47.4, SD 14.3 years) were enrolled in the study between September 2020 and April 2021 (45 and 94 patients in the 1.1 GBq and 3.7G Bq groups, respectively). T6 follow-up is complete and T18 follow-up is currently underway. Statistical analyses will assess the links between salivary dysfunctions and absorbed doses to the salivary glands, accounting for associated factors. Moreover, impacts on the patients' quality of life will be analyzed.

Conclusions: To our knowledge, this study is the first to investigate the risk of salivary dysfunctions (using both objective and subjective indicators) in relation to organ (salivary glands) doses, based on individual dosimeter records and dose reconstructions. The results will allow the identification of patients at risk of salivary dysfunctions and will permit clinicians to propose a more adapted follow-up and/or countermeasures to adverse effects.

Trial Registration: ClinicalTrials.gov NCT04876287; https://clinicaltrials.gov/ct2/show/NCT04876287

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KEYWORDS

radioiodine; thyroid cancer; epidemiology; self-controlled study; salivary gland; lacrimal gland; dysfunction; protocol; epidemiology

Introduction

Approximately 10,600 new cases of thyroid cancer were diagnosed in France in 2018, and this incidence has increased by an average of 4.4% per year between 1990 and 2018 [1]. Although incidence rates are steadily increasing, mortality rates have declined slightly in recent decades, and thyroid cancer has an excellent prognosis with a 10-year survival rate of over 90% [1].

Standard treatment for differentiated thyroid cancer is thyroidectomy followed by radioiodine (^{131}I) ablation [2]. This ^{131}I complementary therapy aims to destroy thyroid remnant tissues, thus facilitating biological surveillance via the thyroglobulin dosage and reducing the risk of cancer relapse. This therapy also treats possible persistent or metastatic diseases, and enables assessment of disease extension through posttherapy scintigraphy. However, the usefulness of ^{131}I-therapy is debated, especially for cancers with a low risk of recurrence because of their excellent survival rate, and the possibility of adverse effects of this therapy in the short, medium, and long term [3]. The salivary gland might be a site of inflammation after ^{131}I-therapy owing to its ability to capture and concentrate iodine [4], and in particular radioactive iodine, which may be symptomatic in the acute phase, and can be followed by chronic salivary dysfunctions [5]. Such dysfunctions are defined as any quantitative or qualitative change in saliva production, such as a decrease in salivary secretion ranging from minor to severe hypofunction [6]. Nevertheless, saliva is crucial for the maintenance of buccal health. Notably, the incidence of salivary dysfunctions is still unclear, ranging from 2% to 67%, due to major methodological differences between studies, including the method and timing of identification of salivary dysfunctions [4].

Salivary dysfunctions may lead to an increased risk of inflammation and/or oral infection, a change in the taste of food, and difficulties in swallowing and digestion. Lacrimal gland dysfunctions (one of the diagnostic criteria for Sjögren syndrome) have also been reported after ^{131}I-therapy, suggesting that some patients may develop simultaneous lacrimal and salivary gland dysfunctions in the years following ^{131}I-therapy [7]. Quality of life after ^{131}I-therapy requires special attention because of the good prognosis of differentiated thyroid cancer. In the context of ^{131}I-therapy for thyroid cancer, few studies have assessed the long-term quality of life at 6 months or later after ^{131}I-therapy [8-12], whereas it has been shown that salivary dysfunction assessed by a specific questionnaire may occur more than 6 months after therapy for 25% of patients [13]. Moreover, there are inconsistencies in the reported relationships between objective measures of salivary flow (sialometry) and subjective measures of salivary dysfunction (self-questionnaire) [6,11], reinforcing the need to assess salivary dysfunction by creating a composite criterion combining objective and subjective measures.

Additionally, the dose-response relationships between ^{131}I-therapy and the incidence of salivary and lachrymal dysfunctions have been rarely studied, and the administered activity is typically used as a proxy for the dose absorbed by the salivary glands. However, the administered activity does not accurately reflect the dose received by the salivary glands due to the variation in iodine uptake ability of the salivary gland, which could be modified by the size of the thyroid remnant tissues or a potential iodine deficiency of the patient before treatment, along with the inherent interpatient variability affecting the entire biokinetics of iodine. The use of an adapted dosimetric method using thermoluminescent dosimeters and anthropomorphic phantoms would make it possible to better estimate the dose-response relationship by estimating the absorbed dose to the salivary gland.

Finally, while a strong interrelationship between epigenetic processes and genetic factors associated with dry mouth syndrome has been shown [14], the potential existence of

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individual genetic sensitivity to ^{131}I in mediating the relationship between ^{131}I exposure and salivary dysfunctions is important to study, especially as specific epigenetic changes could lead to increased sensitivity to ionizing radiation [15]. Other risk factors of salivary dysfunctions in the context of thyroid cancer treated by ^{131}I-therapy are poorly understood. Only one study investigated the relationship between salivary flow and age, gender, or pathological tumor-node-metastasis (TNM) staging, but did not show any significant relationship, potentially owing to a lack of statistical power due to the small number of patients included (N=67) [11], emphasizing the importance of setting up a study with a large number of patients. Increased knowledge of these factors would help to identify the patients at risk of developing salivary dysfunctions, which could possibly help to adapt the treatment and follow-up accordingly.

In this context, the Salivary dysfuncTions After Radioiodine Treatment (START) study was launched in September 2020, with the following objectives: (1) to estimate the mid- and long-term incidence of salivary dysfunctions in patients with thyroid cancer treated with ^{131}I, using objective, subjective, and mixed criteria; (2) to highlight risk factors of posttreatment salivary dysfunctions using clinical, pathological, biomolecular, and biochemical factors; (3) to validate a dosimetric method to calculate the dose absorbed by the salivary gland; (4) to estimate the dose-response relationship between exposure of the salivary glands to ^{131}I and salivary dysfunctions; and (5) to investigate the consequences of salivary dysfunctions on the quality of life and nutritional status of patients.

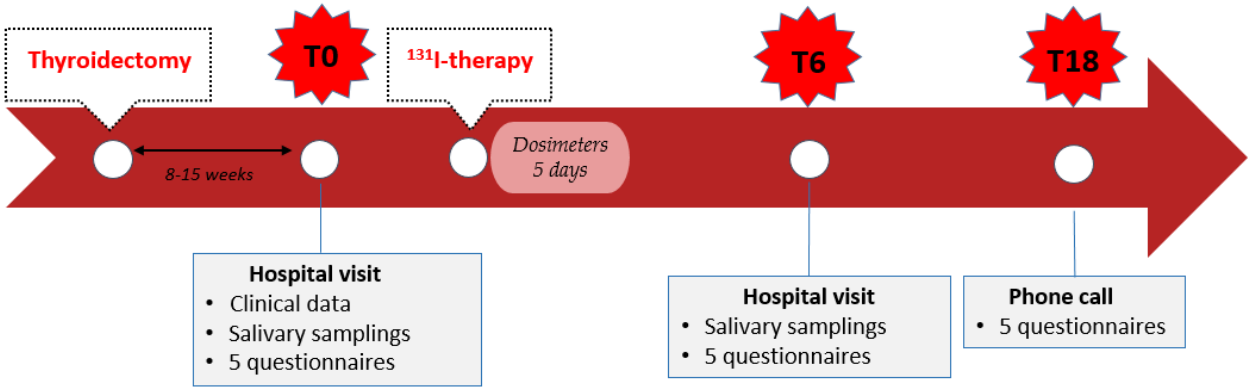
Methods

Study Design

START is a prospective self-controlled study that includes patients with thyroid cancer who underwent thyroidectomy and are candidates for complementary ^{131}I-therapy. This research program aims to enroll 120 patients from the nuclear medicine department of Pitié-Salpêtrière Hospital (Paris, France), divided into two groups of 40 and 80 patients treated with ^{131}I activity of 1.1 GBq and 3.7 GBq, respectively, thus expecting a high number of patients with salivary dysfunctions to provide good statistical power for the analyses.

All consecutive patients awaiting ^{131}I-therapy are systematically invited to participate in the study. They are enrolled just prior to the ^{131}I capsule administration (ie, 1 to 3 months after thyroidectomy), and have three follow-up points: at enrollment (T0), and at 6 months (T6) and 18 months (T18) after ^{131}I-therapy (Figure 1).

Figure 1. Timeline summarizing the study's outline. T0: enrollment; T6: 6 months after radioiodine (^{131}I) therapy; T18: 18 months after radioiodine therapy.



Inclusion and Exclusion Criteria

To be included, patients must have undergone thyroidectomy for the treatment of a differentiated thyroid cancer, be a candidate for complementary ^{131}I-therapy, be over 18 years of age, be willing to participate in the study, and have signed a consent form. Patients who have previously been treated with ^{131}I or who are likely to be treated with multiple ^{131}I therapies within 18 months of inclusion are excluded.

Ethical Considerations

This study will be conducted in accordance with the Declaration of Helsinki (amended at the 64th World Medical Association General Assembly, Fortaleza, Brazil, October 2013) and in accordance with the principles of “Good Clinical Practice” and the Medical Research Involving Human Subjects Act (WMO) [16].

Approvals from the local ethical committee have been received (Comité de Protection de Personnes Sud Mediterranée III, ID 20.01.24.56149; and Agence Nationale de Sécurité des Médicaments, ID 2020-A00208-31). The protocol is registered and will be posted on the ClinicalTrials.gov public website under the number NCT04876287.

Patients included in the study must sign a consent form in which they certify that they have understood the objectives and procedures of the research in which they will participate. They certify that they have had time to think and ask questions to come to an informed decision to participate, and they are aware that this study is not mandatory in the context of their therapy and that they can withdraw at any time.

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Conduct of the Study

Schedule

The START study is expected to be carried out from September 2020 until October 2022, including three measuring points for each patient: at enrollment, and at 6 and 18 months later.

Before Enrollment

The investigating physician in the nuclear medicine department enables first contact with patients during the postsurgery consultation. During this first visit, the physician introduces the START study and its objectives to the patients for whom ^{131}I-therapy is planned, informs them about the nature of the constraints and the expected benefits of the research, and answers all of the patient's questions. The physician ensures that patients meet the inclusion criteria. If the inclusion criteria are fulfilled, a study information leaflet detailing the protocol is given to the patient with the consent form.

Enrollment Visit (T0)

The enrollment visit occurs when an eligible patient has given consent to participate in the study. This visit takes place at the hospital during the consultation prior to the complementary ^{131}I-therapy (on the day of treatment, approximately 2 months after surgery) in a face-to-face manner with a clinical research associate. Clinical and personal data and saliva samples are collected, self-administered questionnaires are provided to patients (see Data Collection section below and Multimedia Appendix 1), and the patients are equipped with thermoluminescent dosimeters (see Dosimetry section below) just before administration of the ^{131}I-therapy. The dosimeters will be removed by the physician 5 days later, immediately before the posttherapy scan.

Six-Month Follow-up (T6)

The 6-month follow-up takes place during the posttherapy consultation at the Thyroid and Endocrine Tumors Unit, Institute of Endocrinology (E3M), Pitié-Salpêtrière Hospital (Paris, France), in a face-to-face manner with a clinical research associate. During this visit, clinical and personal data collection, saliva samples, and self-questionnaires are again carried out

Eighteen-Month Follow-up (T18)

Patients are called by phone to answer the self-questionnaires with a clinical research associate.

Data Collection

All data are collected using paper versions, and are then entered and recorded on a secure server (Table 1).

All questionnaires are completed at each measuring point of the study for each patient. Questionnaires have been selected on the basis of ease and speed of administration by an interviewer, peer-validated, and on the fact that they are the most widely used questionnaires in this type of research (see Multimedia Appendix 1).

Saliva sampling has been performed according to a standardized methodology (see Multimedia Appendix 2).

Table 1. Summary of data collection.

Data type	Qualitative data	Quantitative data
Thyroid cancer information (collected only at the enrollment visit)	Size of the postsurgery remnant, tumor histology, pTNM[a] staging, Tg[b] stimulation protocol, family history of thyroid cancer, patient history of cancer or comorbidities, prescribed activity of ^{131}I (1.1 or 3.7 GBq)	Surgery to therapy duration (months)
Clinical data	Self-rated menopausal status, all medications used during the last 3 months, tobacco and alcohol consumption, self-palpation of the salivary glands (normal, painful, or swollen), self-reported oral carries or infections, observed cracked lips, self-reported use of a saliva substitute, sialagogue	Age, height, weight
Questionnaires	Salivary complaints questionnaire; eye dryness, OSDI[c] questionnaire; questions about nutrition; anxiety and depressive symptoms (HAD[d] scale)	Physical and mental composite scores about quality of life (MOS SF-36[e])
Saliva samples	Not applicable	Weight (precision 0.01 mg), volume (precision 0.01 mL), electrolyte concentrations (mmol/L: sodium, potassium, chloride, amylase, and total protein composition), genetic and epigenetic variant proportions

[a]pTNM: pathological tumor-node-metastasis.

[b]Tg: thyroglobulin.

[c]OSDI: Ocular Surface Disease Index.

[d]HAD: Hospital Anxiety and Depression.

[e]MOS SF-36: Medical Outcome Study Short Form 36 items.

Dosimetry

Immediately before therapy, three thermoluminescent dosimeters (^{7}LiF: Mg,Ti, Thermo Scientific DXT-RAD dosimeter model: DXT-700, provider: APVL) are placed under each earlobe (at the salivary glands level) and at the sternal fork level, protected by an adhesive plastic film (Figure 2). They are removed 5 days later, just before the posttherapy scan.

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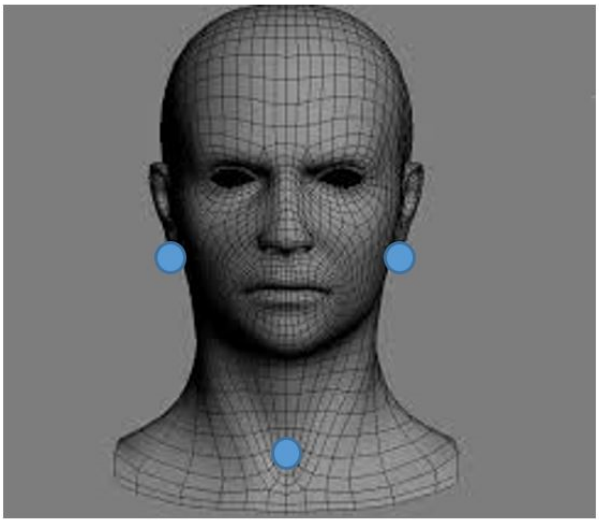
Figure 2. Thermoluminescent dosimeter position.



Subsequently, the dose received specifically by the salivary glands will be estimated from the dosimeter readings. This requires the development of a specific calibration protocol that allows relating the dosimeter readings to the cumulative activity in the salivary glands and thyroid residues, using computational human models [17]. To validate this method, the response of thermoluminescent dosimeters to iodine does not have to deviate significantly from their response under standard calibration conditions.

Study Endpoints

Primary Endpoint

The primary endpoint is a composite criterion combining objective (salivary flow dysfunctions with and/or without stimulation) and subjective (reporting discomfort, pain in the parotid area, difficulty swallowing, or eye dryness) criteria at T6. Salivary flow dysfunctions are defined as an unstimulated salivary flow <0.2 mL/min and/or a stimulated salivary flow <0.7 mL/min [18,19].

Secondary Endpoints

Secondary endpoints are defined as follows: change in quality-of-life score between T0, T6, and T18; change in nutrition between T0, T6, and T18; change in chemical saliva composition between T0 and T6; change in anxiety and depression symptoms between T0, T6, and T18; genetic and/or epigenetic variant identification that may modify the risk of salivary dysfunctions after ^{131}I-therapy; identification of individual factors associated with salivary dysfunctions at T6 and T18; and dose-response analysis between the ^{131}I-dose received precisely at the salivary glands and salivary dysfunctions at T6 and T18.

Statistical Analyses

Sample Size Calculation

A minimum of 120 patients is required to complete the START study. This number is based on a statistical power of 80% with an α risk of 5%, and with theoretical percentages from the literature of salivary dysfunctions of 30% and 60% for the 1.1 GBq and 3.7 GBq therapy groups, respectively [4,20,21]. Thus, the number of patients required is distributed as follows: 40 and 80 patients in the groups treated with delivered activities of 1.1 GBq and 3.7 GBq, respectively. Furthermore, to consider potential losses during follow-up, a final number of 130 patients is required.

Descriptive Analyses

The description of the population (means, SDs, and percentages) at baseline (before ^{131}I-therapy) is presented in this paper. Comparison tests have been performed (*t* test and χ^2 tests) between the two groups of patients (1.1 GBq and 3.7 GBq groups) at T0. This is based on medical and individual data collected in the questionnaire, the ^{131}I dose received precisely at the salivary glands in comparison with the delivered activity, saliva flow descriptions, and responses to the questionnaires.

Planned Analyses

Paired comparison tests will be used to assess differences in data between T0 and T6. Correlations, principal component analyses, and multiple correspondence analyses will be used to study the factors (objective and subjective) common to patients with salivary dysfunctions after ^{131}I-therapy.

All factors significant at a 10% threshold in univariate analyses using different regression models (Textbox 1) will then be entered into multivariate models to measure the risk of developing salivary dysfunctions or other outcomes, adjusted for risk factors previously identified.

The mixed regression models, adjusted for confounders, performed to investigate the temporal evolution for the different outcomes, will be set up using a random intercept for each patient with a first-order autoregressive covariance structure to account for repeated measurements.

The different scores to the questionnaires for quality of life, nutrition, and symptoms of depression and anxiety assessments are calculated and classes are created according to the recommendations for each questionnaire and for each visit (T0, T6, and T18).

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Textbox 1. Synthesis of the planned analyses.

Outcomes

- Categorical

Dry mouth sensation after treatment, dry eye (Ocular Surface Disease Index), Hospital Anxiety and Depression (HAD) anxiety scale, HAD depression scale, changes in nutrition, composite outcome (sum of dysfunctions)

- Continuous

Unstimulated saliva flow (mL/min), stimulated saliva flow (mL/min), saliva pH, electrolyte concentrations in saliva (mmol/L), physical composite score (Medical Outcome Study Short Form 36 items [MOS SF-36]), mental composite score (MOS SF-36), genetic and/or epigenetic variants

Models and tests

- Categorical

χ^2, logistic regression, Poisson regression

- Continuous

Correlations, *t* test, linear regressions, mixed model

Factor of interest

Dose received by the salivary glands, administered dose

Adjustment factors to be tested

Gender, self-rated menopausal status, age, BMI, histology, thyroid remnant tissue, pathological tumor-node-metastasis staging, thyroglobulin stimulation protocol, salivary comorbidities, medication intake, tobacco and alcohol consumption, surgery to therapy duration (months), family history of thyroid cancer

All statistical analyses will be performed using SAS statistical software for Windows (SAS Institute, Cary, NC). An α level of .05 will be accepted as significant.

Results

Patient enrollment took place from September 2020 to April 2021, with a total of 139 patients enrolled, including 45 and 94 patients treated with 1.1 and 3.7 GBq ^{131}I, respectively.

Characteristics of the study participants are displayed in Table 2. The START sample is composed of a large majority of women, with an average age of 47 years (range 18.70-81.80 years). All patients underwent total thyroidectomy with a diagnosis of differentiated thyroid cancer confirmed by pathological examination; the highest proportion in the TNM classification was Tx-T2, followed by Nx-N0, N1, T3, and T4, including approximately 47% of patients with residual thyroid tissue. The ^{131}I-therapy was performed an average 4.11 (SD 3.91) months after the surgery (range 1-35 months). The majority of the included patients were treated for a papillary thyroid cancer.

Concerning the saliva samples, the mean pH was 7.34 (SD 0.48; range 6.00-8.50), with flow rates of 0.76 (SD 0.46; range 0.04-3.00) mL/min and 2.13 (SD 0.88; range 0.40-4.82) mL/min for unstimulated and stimulated saliva, respectively.

Statistically significant differences between the 1.1 and 3.7 GBq treated groups were found in saliva pH and nonstimulated saliva volume.

At the enrollment visit, among all 139 patients, 19 (13.6%) patients had suspicious or obvious symptoms of depression, whereas 67 (48.2%) patients had suspicious or obvious symptoms of anxiety according to the Hospital Anxiety Depression scale (see Table S1 in Multimedia Appendix 3).

When asked if patients experienced changes after thyroid removal surgery, 25 (18.0%) had the sensation of a dry mouth, 48 (34.5%) said they drink more often, and 27 (19.4%) were eating less salty foods.

Regarding lifestyle habits, among the 139 patients, 95 (68.3%) had never smoked, compared to 28 (20.1%) exsmokers and 16 (11.5%) current smokers; 87 (62.6%) never drink alcohol, compared to 45 (32.4%) being occasional drinkers (1-7 drinks/week) and 7 (5.0%) being regular drinkers (7-14 drinks/week) (see Table S1 in Multimedia Appendix 3).

Regarding radioiodine activity, the average doses recorded by the thermoluminescent dosimeters are presented in Table 3. Preliminary results based on the numerical calibration of the dosimeters in terms of cumulated activity provide absorbed doses to the salivary glands after application of the S-factor (self-dose) for salivary glands. There were 43 and 127 patients for which dosimeters were readable in the 1.1 GBq group and 3.7 GBq group, respectively. The doses to the salivary glands were approximately 3-times higher in the 3.7 GBq group than in the 1.1 GBq group (Table 3). For the whole group, the dose to the salivary glands per unit administered activity was 0.63 (SD 0.24) Gy/MBq. The ratio of left/right salivary glands cumulated activity was 0.97 (SD 0.15).

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Table 2. Characteristics of the study population.

Characteristics	1.1 GBq group (n=45)	3.7 GBq group (n=94)	Total (N=139)	*P* value[a]
Gender, n (%)				.24
Women	35 (78)	64 (68)	99 (71.2)	
Men	10 (22)	30 (32)	40 (28.8)	
Age (years), mean (SD)	47.16 (13.86)	47.02 (14.36)	47.07 (14.15)	.96
BMI, mean (SD)	26.88 (5.93)	27.14 (6.12)	27.06 (6.04)	.82
Histology, n (%)				.02
Follicular	2 (4)	18 (19)	20 (14.4)	
Papillary	43 (96)	76 (81)	119 (85.6)	
pTNM[b] staging, n (%)				<.001
Tx-T2	44 (100)	59 (63)	103 (74.6)	
T3	0 (0)	33 (35)	33 (23.9)	
T4	0 (0)	2 (2)	2 (1.5)	
Nx-N0	38 (84)	40 (43)	78 (56.1)	
N1	7 (16)	54 (57)	61 (43.9)	
TSH[c] elevation protocol, n (%)				<.001
L-thyroxin replacement stop	0 (0)	49 (52)	49 (35.2)	
rTSH[d]	45 (100)	45 (48)	90 (64.8)	
Thyroid remnant tissue, n (%)				.07
No	29 (64)	45 (48)	74 (53.2)	
Yes	16 (36)	49 (52)	65 (46.8)	
Family history of thyroid cancer, n (%)				.66
No	37 (82)	80 (85)	117 (84.2)	
Yes	8 (18)	14 (15)	22 (15.8)	
History of systemic disease, n (%)				.19
No	31 (69)	66 (70)	97 (69.8)	
Type 2 diabetes	3 (7)	2 (2)	5 (3.6)	
Dyslipidemia	3 (7)	3 (3)	6 (4.3)	
Diagnosed hypertension	6 (13)	22 (23)	28 (20.1)	
Sjögren syndrome	0 (0)	1 (1)	1 (0.7)	
Brain tumors	1 (2)	0 (0)	1 (0.7)	
Other	1 (2)	0 (0)	1 (0.7)	
History of salivary dysfunctions, n (%)				.15
No	41 (91)	91 (97)	132 (95.0)	
Yes	4 (9)	3 (3)	7 (5.0)	
Delay between surgery and RAI[e] therapy (months), mean (SD)	4.98 (5.15)	3.69 (3.09)	4.11 (3.91)	.07
Unstimulated saliva flow (mL/min), mean (SD)	3.13 (1.82)	4.12 (2.47)	3.8 (2.32)	.02
Stimulated saliva flow (mL/min), mean (SD)	9.65 (3.18)	11.12 (4.83)	10.65 (4.41)	.07
Dry mouth sensation after treatment, n (%)				.67
Yes	9 (20)	16 (17)	25 (18.0)	
No	36 (80)	78 (83)	114 (82.0)	

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Characteristics	1.1 GBq group (n=45)	3.7 GBq group (n=94)	Total (N=139)	*P* value[a]
Saliva pH, mean (SD)	7.2 (0.42)	7.41 (0.50)	7.34 (0.48)	.02
Dry eye (OSDI[f]), n (%)				.29
Normal	34 (79)	78 (86)	112 (83.6)	
Light	3 (7)	8 (9)	11 (8.2)	
Mild	4 (9)	2 (2)	6 (4.5)	
Severe	2 (5)	3 (3)	5 (3.7)	

[a]*P* values are based on the *t* test for continuous variables or the χ^2 test for categorical variables.

[b]pTNM: pathological tumor-node-metastasis.

[c]TSH: thyroid-stimulating hormone.

[d]rTSH: recombinant thyroid-stimulating hormone.

[e]RAI: radioactive iodine.

[f]OSDI: Ocular Surface Disease Index.

Table 3. Dosimetry description.

Variables	1.1 GBq group (n=45)	3.7 GBq group (n=94)
Recorded doses at the left earlobe [Hp(0.07), mSv], mean (SD)	30.07 (9.81)	104.38 (35.43)
Recorded doses at the right earlobe [Hp(0.07), mSv], mean (SD)	30.74 (8.88)	107.72 (42.66)
Recorded doses at the sternal fork [Hp(0.07), mSv], mean (SD)	49.88 (31.47)	173.33 (94.2)
Absorbed doses to the salivary glands (mGy), mean (SD)[a]	702.00 (310.00)	2316.00 (784.00)

[a]N=127.

Further results should be published in 2022. These will be based on comparisons of data from questionnaires and saliva samples between T0 and T6. Individual factors associated with salivary dysfunctions will be presented, as well as the dose-response relationship between absorbed doses to the salivary glands and salivary dysfunctions at T6 and T18.

Discussion

Since many patients treated with ^{131}I for thyroid cancer report salivary disorders, interfering with their quality of life, the START study was launched to detect and evaluate early and mid-term radiation-induced toxicity after ^{131}I-therapy based on a prospective self-controlled study of patients with thyroid cancer. As an original multidisciplinary approach, the START study was designed to combine both objective and subjective parameters of quality of life with clinical and genetic information based on precise dosimetry, which better reflects the heterogeneity of the dose absorbed by the salivary glands. The use of several dosimeters makes it possible to discriminate the contribution coming from the thyroid remnants, after calibration under representative geometrical conditions. This approach further avoids having to perform several imaging examinations for the patients, and to integrate, de facto, the temporal variations of the activity in the salivary glands.

Moreover, this study will be the first to evaluate the genetic and epigenetic variants involved in salivary dysfunctions in patients treated with ^{131}I, which may help to understand some of the biological mechanisms involved in radiation-induced sensitivity. These results should help to better estimate the individualized risk of long-term salivary dysfunctions after ^{131}I-therapy, and thus allow the consideration of potential adverse effects in the choice of treatment.

As the study is still ongoing, this paper presents the protocol and objectives of the START study, as well as descriptive analyses of the included population and the doses recorded by the dosimeters. It is noteworthy that the sex ratio in the study reflects that of the population treated in nuclear medicine departments, which allows for an accurate estimation of the incidence of salivary disorders [22]. Regarding dosimetry, it can be observed that the recorded doses are highly correlated to the administered activities, with a strong earlobes left/right symmetry.

The START study is carried out in collaboration with the Pitié-Salpêtrière Hospital Group, which is the largest European center for the treatment of thyroid cancer, with 10 to 12 patients per week treated with ^{131}I-therapy in the nuclear medicine department. The main limitation of this study is the potentially small number of patients presenting posttherapy salivary dysfunctions. However, the number of subjects to be included was calculated on the basis of 80% statistical power with a first-order risk of 5% and percentages of salivary dysfunctions estimated from the literature [4,20,21]. Nevertheless, salivary complications following ^{131}I-therapy have been poorly studied, and the incidence rate is not very well estimated.

This study will help to deepen knowledge on the risks of salivary dysfunctions after ^{131}I-therapy, as well as provide a better understanding of involved genetic factors. The findings will help target patients at risk of developing salivary dysfunctions

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and possibly adapt the treatment, thus improving the quality of life and nutritional status of patients with thyroid cancer.

Acknowledgments

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Conflicts of Interest

None declared.

Multimedia Appendix 1
Questionnaires.
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Multimedia Appendix 2
Saliva sampling.
[DOC File , 28 KB - resprot_v11i7e35565_app2.doc]

Multimedia Appendix 3
Table S1.
[DOC File , 80 KB - resprot_v11i7e35565_app3.doc]

References

1. Mitton N, Remontet L, Bossard N, Colonna M. Estimations départementales de l'incidence des cancers en 2007 à partir des données des registres et des données du programme de médicalisation des systèmes d'information, France. Rev Épidémiol Santé Publique 2010 Apr;58:S13-S14. [doi: 10.1016/j.respe.2010.02.029]
2. Andresen NS, Buatti JM, Tewfik HH, Pagedar NA, Anderson CM, Watkins JM. Radioiodine ablation following thyroidectomy for differentiated thyroid cancer: literature review of utility, dose, and toxicity. Eur Thyroid J 2017 Jul;6(4):187-196 [FREE Full text] [doi: 10.1159/000468927] [Medline: 28868259]
3. Haugen BR, Alexander EK, Bible KC, Doherty GM, Mandel SJ, Nikiforov YE, et al. 2015 American Thyroid Association Management Guidelines for adult patients with thyroid nodules and differentiated thyroid cancer: The American Thyroid Association Guidelines Task Force on Thyroid Nodules and Differentiated Thyroid Cancer. Thyroid 2016 Jan;26(1):1-133 [FREE Full text] [doi: 10.1089/thy.2015.0020] [Medline: 26462967]
4. Van Nostrand D. Sialoadenitis secondary to ^{131}I therapy for well-differentiated thyroid cancer. Oral Dis 2011 Mar;17(2):154-161. [doi: 10.1111/j.1601-0825.2010.01726.x] [Medline: 21029259]
5. Aliko A, Wolff A, Dawes C, Aframian D, Proctor G, Ekström J, et al. World Workshop on Oral Medicine VI: clinical implications of medication-induced salivary gland dysfunction. Oral Surg Oral Med Oral Pathol Oral Radiol 2015 Aug;120(2):185-206. [doi: 10.1016/j.oooo.2014.10.027] [Medline: 25861957]
6. Pedersen AML, Sørensen CE, Proctor GB, Carpenter GH, Ekström J. Salivary secretion in health and disease. J Oral Rehabil 2018 Sep;45(9):730-746. [doi: 10.1111/joor.12664] [Medline: 29878444]
7. Solans R, Bosch JA, Galofré P, Porta F, Roselló J, Selva-O'Callagan A, et al. Salivary and lacrimal gland dysfunction (sicca syndrome) after radioiodine therapy. J Nucl Med 2001 May;42(5):738-743 [FREE Full text] [Medline: 11337569]
8. Hollingsworth B, Senter L, Zhang X, Brock GN, Jarjour W, Nagy R, et al. Risk factors of I-induced salivary gland damage in thyroid cancer patients. J Clin Endocrinol Metab 2016 Nov;101(11):4085-4093 [FREE Full text] [doi: 10.1210/jc.2016-1605] [Medline: 27533304]
9. Rosario PW, Calsolari MR. Salivary and lacrimal gland dysfunction after remnant ablation with radioactive iodine in patients with differentiated thyroid carcinoma prepared with recombinant human thyrotropin. Thyroid 2013 May;23(5):617-619. [doi: 10.1089/thy.2012.0050] [Medline: 23136908]
10. Grewal RK, Larson SM, Pentlow CE, Pentlow KS, Gonen M, Qualey R, et al. Salivary gland side effects commonly develop several weeks after initial radioactive iodine ablation. J Nucl Med 2009 Oct;50(10):1605-1610 [FREE Full text] [doi: 10.2967/jnumed.108.061382] [Medline: 19759114]
11. Klein Hesselink EN, Brouwers AH, de Jong JR, van der Horst-Schrivers ANA, Coppes RP, Lefrandt JD, et al. Effects of radioiodine treatment on salivary gland function in patients with differentiated thyroid carcinoma: a prospective study. J Nucl Med 2016 Nov;57(11):1685-1691 [FREE Full text] [doi: 10.2967/jnumed.115.169888] [Medline: 27339871]

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12. Fard-Esfahani A, Mirshekarpour H, Fallahi B, Eftekhari M, Saghari M, Beiki D, et al. The effect of high-dose radioiodine treatment on lacrimal gland function in patients with differentiated thyroid carcinoma. Clin Nucl Med 2007 Sep;32(9):696-699. [doi: 10.1097/RLU.0b013e318124fdb6] [Medline: 17710021]
13. Moreddu E, Baumstarck-Barrau K, Gabriel S, Fakhry N, Sebag F, Mundler O, et al. Incidence of salivary side effects after radioiodine treatment using a new specifically-designed questionnaire. Br J Oral Maxillofac Surg 2017 Jul;55(6):609-612. [doi: 10.1016/j.bjoms.2017.03.019] [Medline: 28456449]
14. Charras A. Altérations du méthylome au cours du Syndrome de Gougerot Sjögren, Doctoral thesis in Immunology. Theses. 2018. URL: http://www.theses.fr/2018BRES0049 [accessed 2020-10-14]
15. Chaudhry MA, Omaruddin RA, Kreger B, de Toledo SM, Azzam EI. Micro RNA responses to chronic or acute exposures to low dose ionizing radiation. Mol Biol Rep 2012 Jul 25;39(7):7549-7558 [FREE Full text] [doi: 10.1007/s11033-012-1589-9] [Medline: 22367372]
16. World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. JAMA 2013 Nov 27;310(20):2191-2194. [doi: 10.1001/jama.2013.281053] [Medline: 24141714]
17. Xu X, Eckerman K. Handbook of Anatomical Models for Radiation Dosimetry. Milton Park, UK: Routledge; 2009.
18. Humphrey SP, Williamson RT. A review of saliva: normal composition, flow, and function. J Prosthet Dent 2001 Feb;85(2):162-169. [doi: 10.1067/mpr.2001.113778] [Medline: 11208206]
19. Miranda-Rius J, Brunet-Llobet L, Lahor-Soler E, Farré M. Salivary secretory disorders, inducing drugs, and clinical management. Int J Med Sci 2015;12(10):811-824 [FREE Full text] [doi: 10.7150/ijms.12912] [Medline: 26516310]
20. Van Nostrand D, Neutze J, Atkins F. Side effects of "rational dose" iodine-131 therapy for metastatic well-differentiated thyroid carcinoma. J Nucl Med 1986 Oct;27(10):1519-1527 [FREE Full text] [Medline: 3760975]
21. Clement SC, Peeters RP, Ronckers CM, Links TP, van den Heuvel-Eibrink MM, Nieveen van Dijkum EJM, et al. Intermediate and long-term adverse effects of radioiodine therapy for differentiated thyroid carcinoma--a systematic review. Cancer Treat Rev 2015 Dec;41(10):925-934. [doi: 10.1016/j.ctrv.2015.09.001] [Medline: 26421813]
22. Leenhardt L, Ménégaux F, Franc B, Hoang C, Salem S, Bernier M, et al. Cancers de la thyroïde. EMC Endocrinologie 2005 Feb;2(1):1-38. [doi: 10.1016/j.emcend.2004.10.003]

Abbreviations

^{131}I: radioiodine
START: Salivary dysfuncTions After Radioiodine Treatment
T0: baseline enrollment
T6: 6-month follow-up
T18: 18-month follow-up
TNM: tumor-node-metastasis staging

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Protocol

The World Mental Health International College Student Survey in Canada: Protocol for a Mental Health and Substance Use Trend Study

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Abstract

Background: The World Health Organization World Mental Health International College Student (WMH-ICS) initiative aims to screen for mental health and substance use problems among postsecondary students on a global scale as well as to develop and evaluate evidence-based preventive and ameliorative interventions for this population. This protocol paper presents the Canadian version of the WMH-ICS survey, detailing the adapted survey instrument, the unique weekly cross-sectional administration, the multitiered recruitment strategy, and the associated risk mitigation protocols.

Objective: This paper aims to provide a methodological resource for researchers conducting cross-national comparisons of WMH-ICS data, as well as to serve as a useful guide for those interested in replicating the outlined cross-sectional methodology to better understand how mental health and substance use vary over time among university students.

Methods: The online survey is based on the WMH-ICS survey instrument, modified to the Canadian context by the addition of questions pertaining to Canadian-based guidelines and the translation of the survey to Canadian French. The survey is

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administered through the Qualtrics survey platform and is sent to an independent stratified random sample of 350 students per site weekly, followed by two reminder emails. Upon survey closure every week, a random subsample of 70 nonresponders are followed up with via phone or through a personal email in an effort to decrease nonresponder bias. The survey is accompanied by an extensive risk mitigation protocol that stratifies respondents by the level of need and provides tailored service recommendations, including a facilitated expedited appointment to student counseling services for those at increased risk of suicide. The anticipated sample size is approximately 5500 students per site per year.

Results: In February 2020, the Canadian survey was deployed at the University of British Columbia. This was followed by deployment at Simon Fraser University (November 2020), McMaster University (January 2021), and the University of Toronto (January 2022). Data collection at all 4 sites is ongoing. As of May 6, 2022, 29,503 responses have been collected.

Conclusions: Based on international collaboration, the Canadian version of the WMH-ICS survey incorporates a novel methodological approach centered on the weekly administration of a comprehensive cross-sectional survey to independent stratified random samples of university students. After 27 months of consecutive survey administration, we have developed and refined a survey protocol that has proven effective in engaging students at four Canadian institutions, allowing us to track how mental health and substance use vary over time using an internationally developed university student survey based on the criteria from the Diagnostic and Statistical Manual of Mental Disorders (Fifth Edition).

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KEYWORDS

mental health; substance use; student health; World Mental Health International College Student Initiative; Canada; Canadian; online survey; survey; questionnaire; screen; epidemiology; depression; anxiety; trend

Introduction

The university years coincide with a critical developmental period, a time when many common mental disorders emerge [1]. This developmental period, coupled with life changes that often accompany the transition to university life, such as separation from family and friends, a new environment, and increasing academic pressure, is likely to contribute to increased rates of mental and substance use problems and disorders, potentially overwhelming available services [2-5]. In response to this public health concern, the World Health Organization (WHO) World Mental Health International College Student (WMH-ICS) initiative was developed. The initiative aims to screen for mental health and substance use problems among college and university students on a global scale as well as to develop and evaluate evidence-based preventive and ameliorative interventions for this population. The epidemiologic surveys—a core component of the WMH-ICS initiative—are self-administered online questionnaires that generate diagnostic estimates for a wide range of common mental disorders and include questions that probe symptom severity, help-seeking behaviors, and treatment barriers [6]. To date, the WMH-ICS survey has assessed 95,000 students across 16 countries worldwide [7] and has been repeatedly used in scientific studies [8-13]. Although procedures vary by country and site depending on local resources and priorities, all WMH-ICS surveys include core questions about stressors, disorders, impairments, and treatment.

In February 2020, the Canadian version of the WMH-ICS survey initiative was deployed at the University of British Columbia (UBC). This was followed by deployment at Simon Fraser University (SFU; November 2020), McMaster University (January 2021), and the University of Toronto (UofT; January 2022). Additional Canadian sites are currently in various stages of assessment and implementation. The methodology of these Canadian surveys is notably distinct from the traditional WMH-ICS procedures, which invite all potential respondents (typically first-year students) at one time point and often incorporate follow-up surveys later in their university career. In comparison, the Canadian version is deployed as a repeated cross-sectional survey, where a new stratified random sample of students is invited to participate weekly (additional details provided in the Methods section). Whereas all WMH-ICS surveys aim to provide a detailed picture of the common mental and substance use problems and disorders affecting students, the ongoing administration of the Canadian survey to representative samples of the student population offers the added benefit of providing time-based data that can be used to better understand how these problems vary throughout the year. These data can also be used to understand variation in response to external stressors such as exam periods or global events like the COVID-19 pandemic. The ongoing nature of the survey in Canada also provides the opportunity to add new survey content (eg, related to the COVID-19 pandemic) or revise questions based on existing data and student feedback. Another strength of the Canadian survey design is the use of a multitiered recruitment process, where a subsample of initial nonresponders is selected for follow-up through alternative recruitment strategies, leading to high response rates that minimize nonresponder bias. Finally, the Canadian survey stratifies respondents by level of need and provides tailored service recommendations, including facilitating a follow-up call within 24 hours and a counselling interview within 5 days for those at increased risk of suicide.

This protocol paper presents the Canadian version of the WMH-ICS survey, detailing the adapted survey instrument, the weekly cross-sectional administration, the multitiered recruitment strategy, and the associated risk mitigation protocols. In doing so, it aims to provide a methodological resource for researchers interested in better understanding how mental health

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and substance use vary over time, with an ultimate goal of improving prevention and intervention efforts for mental health problems among university students. In addition, it aims to serve as a useful guide for those interested in replicating the outlined cross-sectional methodology or conducting cross-national comparisons of WMH-ICS data.

Methods

Survey Instrument and Revisions

This survey is administered as part of the WHO WMH-ICS initiative [6] and is a web-based survey tool designed to assess mental health and substance use in postsecondary students. On average, the survey takes students approximately 20 minutes to complete. Questions assess students' well-being (ie, physical and mental health, stresses, self-harm, and suicidal thoughts and behaviors), substance use (ie, alcohol and street drugs), health and social functioning (ie, impairments to daily activities), treatment (ie, use of health services, barriers to help seeking, and readiness for change), and respondent characteristics (eg, sociodemographics or childhood experiences).

The WMH-ICS survey instrument uses validated screening scales to generate lifetime and 12-month prevalence estimates for the following common disorders from the *Diagnostic and Statistical Manual of Mental Disorders*: major depressive disorder, bipolar disorder, generalized anxiety disorder, panic disorder, alcohol use disorder, and substance use disorder [8]. Optional disorder sections used in this survey include screening questions for intermittent explosive disorder, social anxiety disorder, posttraumatic stress disorder, eating disorders, and attention-deficit/hyperactivity disorder [8,14]. While previous publications from the WMH-ICS initiative have used *Diagnostic and Statistical Manual of Mental Disorders* (Fourth Edition) diagnostic criteria [15], a *Diagnostic and Statistical Manual of Mental Disorders* (Fifth Edition) version was recently developed, which is being implemented for the first time in the Canadian survey [7,16]. As is the case with all WMH-ICS surveys, disorder assessments are based on the Composite International Diagnostic Interview Screening Scales [17,18] and the Alcohol Use Disorders Identification Test [19].

In September 2019, the survey was adapted to the Canadian context by a research team based at UBC. During the adaptation process, alcohol and substance use questions were added to generate 30-day estimates, as well as to assess adherence to Canadian low-risk drinking and cannabis use guidelines [20-23]. Additional questions regarding opioid use were also added to obtain information about adherence to the Canadian Opioid Prescribing Guidelines [24]. Additional questions were included on topics of interest to the research team, including past use and willingness to use e–mental health services. A French translation of this Canadian survey was developed using the WMH-ICS France survey as the base content, with adjustments made by native Québécois French speakers to account for the Canadian context and associated regional language variations.

As the survey is deployed on a weekly basis, there is an ongoing opportunity to respond to student feedback. While feedback is not formally requested from respondents, many students from across study sites may contact the principal investigator and research team via email to share feedback on how to improve the survey. Each suggestion is evaluated by the research team to examine feasibility and alignment with the other WMH-ICS surveys. The research team gains additional student feedback by convening a student advisory board consisting of a group of approximately 13 student representatives from organizations, groups, or clubs focused on mental health and substance use issues on campus. Student consultations and the resulting survey adaptations are focused on the language and phrasing of survey questions, ensuring that the survey is inclusive and applicable to the diverse student body (eg, expanding gender identity response options and including content warnings ahead of questions relating to potentially traumatic past experiences and health impacts of COVID-19). Indeed, the flexibility of running weekly surveys allows the research team to keep up with current institutional, local, and global events such as the pandemic. Questions pertaining to COVID-19 were added to the survey more than a month before the declaration of a British Columbia Provincial public health emergency and have allowed continuous measurement of students' exposure to and experience of COVID-19 symptoms, feelings of stress associated with the pandemic, consequences of the pandemic (ie, death of relations/acquaintances and disruption to daily life, housing situations, and classes), the transition to remote learning and then return to in-person learning, and vaccination state. The current versions of the survey can be found in Multimedia Appendices 1 and 2 (English and French, respectively).

Ethics

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2013 [25]. All procedures were approved by the UBC Behavioural Research Ethics Board in a harmonized review process with SFU (approval number H19-02538), the McMaster University Research Ethics Board Office (approval number 3695), and the UofT Research Ethics Board (approval number 39919). Initial approval for the survey was acquired in 2019, and all revisions in both English and French have been approved on an ongoing basis. Written informed consent is obtained from all participants (Multimedia Appendix 3).

Sampling

The following section outlines a general approach to the sampling process. There are slight variations between institutions based on site-specific regulations and preferences for data management. The proposed study duration is 1 year but can be extended by sites based on interest and funding availability. The anticipated sample size is approximately 5500 students per site per year.

Prior to survey launch and at the start of every semester for the duration of the study, a *data pull* process is initiated in which a deidentified data set of students is provided to the research team by the university registrar containing randomly assigned alphanumeric IDs and stratifying variables. All actively enrolled students are included in the data set, with the only exclusion criteria being previously sampled students. Using the software

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SAS (SAS Institute Inc), independent stratified random samples of 350 IDs are drawn for each week of the semester. The stratifying variables—degree type, year of study, international or Canadian student status, gender, and age—are employed in this process to ensure that each weekly sample is representative of the student population, as well as to provide the opportunity to statistically weight final data to reflect the population from which the samples are drawn.

Samples are randomly ordered using Excel's (Microsoft Corporation) random number generator and assigned a week for implementation. The samples are then sent back to the university registrar, and files containing the selected students' first names, email addresses, and phone numbers are returned. To ensure confidentiality of student data, these files returned to the research team do not contain any of the stratifying variables, which are never linked nor linkable by the research team to the student's name, email, or phone. For each sample, a cross check of five random IDs and email addresses is performed by a second university registrar employee to confirm proper data set linkage. This process is repeated each semester and is initiated once the academic deadline for course withdrawal/drop has passed. During each data pull, several additional samples are drawn in case there are processing delays in the subsequent semester, so the additional samples can be used in the interim to prevent disruption to the weekly data collection process.

Online Survey Delivery

The screening tool is programmed into Qualtrics software [26]. The survey is administered from Canadian Qualtrics licenses that store data in cloud-based servers located in Canada. The survey is initially programmed in English, and the Canadian French translation is manually inputted for each question in the "Translate Survey" page of Qualtrics. The "Look and Feel" tool is used to personalize the logo and color scheme of surveys for their respective institutions. Responses are anonymized so that respondents' IP addresses, location data, and contact information are not recorded. Survey access is set to invitation only, and the "prevent multiple submissions" setting is turned on. In Qualtrics, a folder is added for each weekly cohort invited to the survey. Each weekly folder contains three identical copies of the survey: the initial survey, filled by students who responded to the email invitations (I); the survey for initial nonresponders with a phone number on record, also known as "hard to reach" students ("NRa Phones"); and the survey for initial nonresponders without a phone number on record, also known as "very hard to reach" students ("NRb No Phones").

Survey Administration

Every Sunday, a new independent sample of 350 students receives an email invitation to participate in the survey through the online platform. The invitation is codeveloped and cosigned by the principal investigator and a senior-level administrator in charge of the student services portfolio (eg, vice president, students) to convey that the endeavor is a research and quality improvement undertaking with organizational support. After 3 and 7 days, those who have not completed the survey receive similar reminder emails. Three days after the second reminder (ie, 10 days after the initial invitation), the initial survey closes, the distribution history is downloaded, and a random sample of 70 nonresponders is drawn. These students are deemed "hard to reach" and are assigned for follow-up.

Selected students who have a valid North American phone number on file with the university registrar are sent an email that notifies them of their selection for follow-up and includes a new survey link (to the NRa Phones survey). In addition, it informs them that they will be called the following day, with an option to opt-out of receiving the phone call. The next morning, the students are called by a research assistant who explains the importance of the student's participation to increase the validity of the results by including initial nonresponder data, answers any questions, and offers to resend the survey link in case it had been lost or deleted. If the phone call is not answered, the research assistant hangs up and makes a second call several hours later on the same day. If this second call is not answered, a voicemail is left that contains similar content to the phone call, and a callback number is provided in case the student had any questions. In the event that a voicemail system is not set up, a SMS text message is sent with an abbreviated version of the message.

Selected students who do not have a valid North American phone number on file are sent a personalized email from the principal investigator that explains the importance of their response and includes a new survey link to the NRb No Phones survey. These surveys for "hard to reach" and "very hard to reach" students (NRa Phones and NRb No Phones) close 7 days after the follow-up email that contained the new survey link. This process is outlined as a flowchart (Figure 1), and sample email templates and call, voicemail, and text scripts are included in Multimedia Appendix 4.

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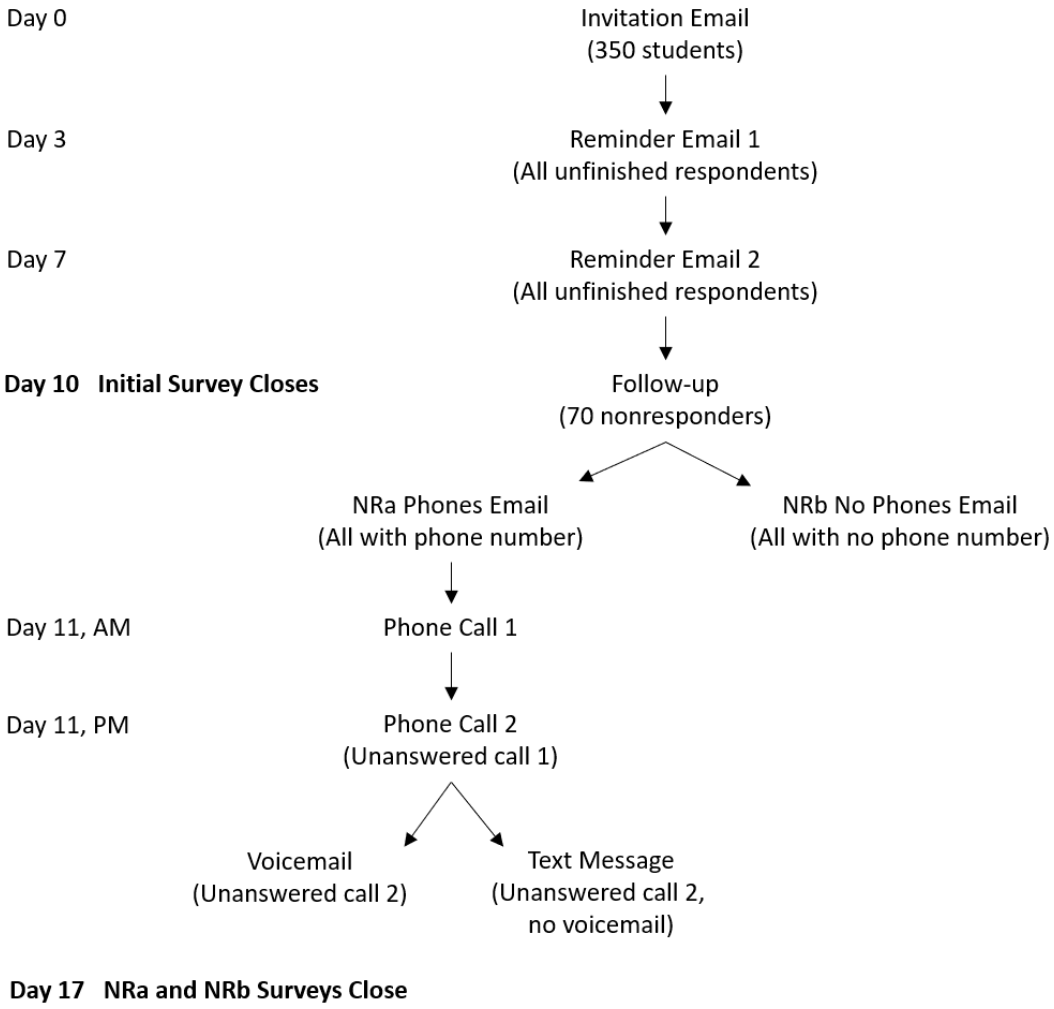
Figure 1. A visual representation of the survey administration process for each weekly sample. NRa: hard-to-reach students; NRb: very hard-to-reach students.



Risk Mitigation Protocol

Upon completion of the survey, all students are redirected to a new page on the Qualtrics platform that provides them with a targeted list of resources based on their survey responses. These lists of resources are from 1 of 6 prespecified protocols and are developed by the research team in collaboration with each study site's university health and counseling services. The protocols are programmed in a hierarchical fashion, with lower numbered protocols taking precedence over all those numbered higher (ie, each respondent triggered only 1 of these protocols as per the hierarchy). A summary of each protocol is provided below (with reference to the specific survey questions used to identify risk), and the full risk mitigation protocol with textboxes and emails can be found in Multimedia Appendix 5.

Protocol 1: Protocol for Participants With Increased Likelihood of Acting on a Recent Suicide Plan in the Coming Year

Participants acknowledging any suicide plan during the past 12 months (response to question G10 different than 0) plus reporting that acting upon such a plan during the coming 12 months was "somewhat likely" or "very likely" (question G11) are presented upon survey completion with a textbox that contains (a) information on relevant clinical resources and support services, as well as (b) a request for the student's consent and permission to contact the university counseling services on their behalf to obtain an expedited appointment. They also receive this information in email format immediately after completing the survey and 28 days later.

If the student consents and provides their contact details, an email containing this information is automatically sent to the designated university counseling services' point person by the online platform. If the student chooses to consent and provide their contact details by replying to the emailed resource list, their reply goes to the designated "Protocol 1 email inbox" and is then automatically forwarded to the designated university counseling services' point person. As a fail-safe mechanism, the principal investigator of the project also receives an automated email notifying them that a Protocol 1 has been triggered, but their email does not contain the student's name or contact details.

The designated counseling services employee reaches out to the student within 1 business day of receiving the email and offers them an appointment within 1 week. This outreach includes up to two phone calls. If the second phone call is unanswered, a voicemail is left. For students without a voicemail

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setup, an email is sent to the address they provide. After completing this outreach, the point person emails the principal investigator to confirm that outreach occurred, identifying the protocol by the date and time it is triggered to maintain student anonymity. If student services does not reach out to confirm to the research team that contact had been attempted or established, the research team follows up with student services to confirm that the automatic Protocol 1 email had been received.

Protocol 2: Protocol for Participants With History of Manic Episodes

Students screening positive for or reporting a lifetime manic episode (shown question E27 or response to question B5b is "yes") receive an automated textbox and email upon survey completion that provides information on the clinical resources and support services available for this level of need as per each site's service provision protocols.

Protocol 3: Protocol for Participants With a History of Psychosis

Students reporting a lifetime history of psychotic experiences (response to question E46 or question E47 is "yes") receive an automated textbox and email upon survey completion that provides information on the clinical resources and support services available for this level of need as per each site's service provision protocols.

Protocol 4: Protocol for Participants With History of Suicide Attempts, a Recent Suicide Attempt (Past Year), Suicide Plan During the Past 12 Months, or Suicidal Ideation During the Past 30 Days

Participants indicating any lifetime history of suicide attempts (response to question G16 is "yes"), any suicide plan during the past 12 months (response to question G10 different than 0), any suicide attempt during the past 12 months (response to question G19 different than 0), or any suicidal ideation during the past 30 days (response to question G6 different than "None of the time") receive an automated textbox and email upon survey completion that provides information on relevant clinical resources and support services.

Protocol 5: Protocol for Participants With Severe Impairment Resulting From Any Mental or Substance Use Disorder

Students screening positive for severe impairments resulting from any mental or substance use disorder (response to question B3b, B3c, B4b, or B4c is "Very severe interference" or "severe interference") receives an automated textbox and email upon survey completion that provides information on the clinical resources and support services available for this level of need as per each site's service provision protocols.

Protocol 6: Standard General Protocol

As a standard general precaution, all participants who do not trigger a specific protocol are shown a textbox that contains information on general mental health and wellness resources and support services. These students are provided the option to have the resources emailed to them if they click on the link to a new online form and input their email address.

Each of the 6 risk mitigation protocols described above are programmed as embedded data in the online platform, and the resource list emails are sent through an automated email trigger function. Emails are programmed to be sent to the respondent using piped text (a line of code that pulls information from different sources; eg, responses to previous questions or embedded data) and selecting "Recipient Email" under "Panels Field" in Qualtrics. Conditions are added to specify the protocol triggered and the language used to complete the survey. Textboxes are programmed into a different survey file, which respondents are redirected to upon completion of the main survey through a query string URL inserted as a "custom end of survey message." The Protocol 1 text includes a checkbox requesting students' consent to contact university health services on their behalf, and a form that requests name, email, and phone numbers. If a student consents by ticking the checkbox, the form responses are emailed to university counseling services using piped text and the email trigger function described above. The form questions are set to "exclude from analysis" so that identifying information is not saved as data and is not accessible to the research team. To deploy the postsurvey protocols, there is one textbox redirect file per institution to ensure only institutionally and locally relevant resources are shown to students.

Data Download

Upon survey closure, the data are exported from the digital platform in SPSS format (IBM Corp). As 3 surveys close each week, 3 SPSS files are uploaded weekly to a secure institutional storage platform. Only specific team members who need access to the data folders are given access, as per the Data Security Protocols (see below).

Data Security

All data—including student contact information and survey responses—related to the project are stored on a secure file storage platform endorsed by the respective university. The secure platforms are stored and hosted in Canada, meeting the Freedom of Information and Protection of Privacy Act's data residency requirements. To ensure that all data are handled securely, the Mental Health Systems and Services Laboratory generated a "Data Management Guidelines" document, which outlines the stringent processes that need to be followed when accessing, storing, and downloading data. As the project works with both student survey responses and student contact information on a weekly basis, it is vital to uphold a high level of security across study sites. Of note, the survey responses are always anonymous (as opposed to anonymized or deidentified) since at no point are the survey responses linked to the student's name or any identifying administrative data.

The primary tenet for data security is that all data access is on a need-to-know basis. This rule is reflected in all facets of data management in the survey administration process and culminates in the data deletion process. When all the survey administration and calls are completed for the week, all documents containing student contact information are deleted while screen recording. This includes any downloaded distribution histories, call history, documents provided by the university registrar, etc. The deletion

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videos are then uploaded to the secure platform for the purpose of auditing by the research team and university administrators.

Remuneration

At most sites, survey participants are entered into a yearly draw for a CAD $1,000 (approximately US $750) gift card. There is one winner per institution per calendar year. The remuneration strategy is open to modification (eg, more draws worth less value) if requested by an institutional research ethics board.

Statistical Analysis Plan

Survey data will be examined independently for Canadian-specific analyses and as part of WMH-ICS cross-national studies. Analyses will aim to provide weighted prevalence estimates for a range of mental disorders, such as major depressive disorder, bipolar disorder, generalized anxiety disorder, panic disorder, alcohol use disorder, and drug use disorder. In addition, associations of demographic determinants and past experiences with meeting criteria for various disorders and suicidality, as well as with accessing mental health services will be evaluated with multivariable regression models. Canadian-specific analyses will be undertaken to explore changes in disorder and symptom prevalence across the calendar and academic years, as well as in response to specific events (eg, natural disasters or pandemics). In line with the WMH-ICS initiative's goals, analyses will also seek to identify areas of unmet treatment need, particularly for marginalized and racialized groups.

Results

Funded in July 2019 by Health Canada, the Canadian version of the WMH-ICS survey was ultimately launched at UBC on February 9, 2020. SFU followed suit on November 29, 2020; McMaster University on January 10, 2021; and the UofT on January 16, 2022. As of May 6, 2022, 29,503 responses have been collected (UBC: n=12,990; SFU: n=8886; McMaster University: n=6505; and UofT: n=1122). Data analysis is ongoing, with the first paper on anxiety and depression during COVID-19 published in March 2021 and additional manuscripts in various stages of the preparation and submission process.

Discussion

In 27 months, the Canadian version of the WMH-ICS survey has provided data from nearly 30,000 students, enabling us to estimate prevalence for a wide range of mental disorders and assess variation throughout the year and in response to specific events. While this survey is grounded in the international WMH-ICS initiative, several methodological features distinguish it from previous work. The weekly administration to independent stratified random samples of university students is a novel approach within the international initiative and is allowing us to track how mental health and substance use vary over time, which has proven to be particularly enlightening in the context of the COVID-19 pandemic that has unfolded during the past 2 years. In addition, the locally developed risk mitigation protocols associated with our survey enables us to offer targeted resources to students who report mental health concerns and facilitate connections to services for students at increased risk of suicide. This feature, facilitated by the digital nature of the survey, provides real-time feedback and an opportunity for preventative efforts to minimize the risk of adverse outcomes such as suicide. These innovative features are in addition to the strengths of the broader WMH-ICS initiative, such as the use of a validated screening tool that has proven effective in engaging students on a global scale.

The Canadian survey data will provide a comprehensive and comparative picture of the common mental and substance use problems affecting students, assist us in identifying the best and most timely ways to engage university students through cost-effective e–mental health interventions, and allow us to explore novel health systems integration strategies between digital and brick-and-mortar services. Collecting data from multiple institutions across Canada as part of the WMH-ICS initiative enables this survey to contribute to knowledge building and service planning on a local, national, and international level. Specifically in Canada, the data collected will contribute to the development of e–mental health intervention resources. We intend for this protocol paper to serve as a guide for institutions considering ongoing mental health and substance use online screening protocols.

Acknowledgments

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Authors' Contributions

DVV developed the concept and design of the study. LBJ, CJ, and KLH wrote the first draft of the manuscript. LBJ edited the manuscript. All authors performed revision of the manuscript.

Conflicts of Interest

CGR reports receiving personal fees from the University of British Columbia during the conduct of this study. In the past 3 years, RCK was a consultant for Datastat, Inc., Holmusk, RallyPoint Networks, Inc., and Sage Therapeutics. He has stock options in Mirah, Prepare Your Mind (PYM), and Roga Sciences. The other authors have no conflicts to declare.

Multimedia Appendix 1

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English survey instrument.
[PDF File (Adobe PDF File), 670 KB - resprot_v11i7e35168_app1.pdf]

Multimedia Appendix 2
French survey instrument.
[PDF File (Adobe PDF File), 695 KB - resprot_v11i7e35168_app2.pdf]

Multimedia Appendix 3
Study cover letter and consent form.
[PDF File (Adobe PDF File), 111 KB - resprot_v11i7e35168_app3.pdf]

Multimedia Appendix 4
Sample recruitment emails and follow-up scripts.
[PDF File (Adobe PDF File), 133 KB - resprot_v11i7e35168_app4.pdf]

Multimedia Appendix 5
Risk mitigation protocol.
[PDF File (Adobe PDF File), 437 KB - resprot_v11i7e35168_app5.pdf]

References

1. Kessler RC, Amminger GP, Aguilar-Gaxiola S, Alonso J, Lee S, Ustün TB. Age of onset of mental disorders: a review of recent literature. Curr Opin Psychiatry 2007 Jul;20(4):359-364 [FREE Full text] [doi: 10.1097/YCO.0b013e32816ebc8c] [Medline: 17551351]
2. Auerbach RP, Alonso J, Axinn WG, Cuijpers P, Ebert DD, Green JG, et al. Mental disorders among college students in the World Health Organization World Mental Health Surveys. Psychol Med 2016 Oct;46(14):2955-2970 [FREE Full text] [doi: 10.1017/S0033291716001665] [Medline: 27484622]
3. Pedrelli P, Nyer M, Yeung A, Zulauf C, Wilens T. College students: mental health problems and treatment considerations. Acad Psychiatry 2015 Oct;39(5):503-511 [FREE Full text] [doi: 10.1007/s40596-014-0205-9] [Medline: 25142250]
4. Beiter R, Nash R, McCrady M, Rhoades D, Linscomb M, Clarahan M, et al. The prevalence and correlates of depression, anxiety, and stress in a sample of college students. J Affect Disord 2015 Mar 01;173:90-96. [doi: 10.1016/j.jad.2014.10.054] [Medline: 25462401]
5. Xiao H, Carney DM, Youn SJ, Janis RA, Castonguay LG, Hayes JA, et al. Are we in crisis? National mental health and treatment trends in college counseling centers. Psychol Serv 2017 Nov;14(4):407-415. [doi: 10.1037/ser0000130] [Medline: 29120199]
6. Cuijpers P, Auerbach RP, Benjet C, Bruffaerts R, Ebert D, Karyotaki E, et al. The World Health Organization World Mental Health International College Student initiative: an overview. Int J Methods Psychiatr Res 2019 Jun;28(2):e1761 [FREE Full text] [doi: 10.1002/mpr.1761] [Medline: 30614123]
7. Bruffaerts R. WMH-ICS Needs Assessment Surveys. 2021 Presented at: WMH Virtual Meeting; 2021; Virtual.
8. Auerbach RP, Mortier P, Bruffaerts R, Alonso J, Benjet C, Cuijpers P, WHO WMH-ICS Collaborators. WHO World Mental Health Surveys International College Student Project: prevalence and distribution of mental disorders. J Abnorm Psychol 2018 Oct;127(7):623-638 [FREE Full text] [doi: 10.1037/abn0000362] [Medline: 30211576]
9. Mortier P, Auerbach RP, Alonso J, Bantjes J, Benjet C, Cuijpers P, WHO WMH-ICS Collaborators. Suicidal thoughts and behaviors among first-year college students: results from the WMH-ICS Project. J Am Acad Child Adolesc Psychiatry 2018 Apr;57(4):263-273.e1 [FREE Full text] [doi: 10.1016/j.jaac.2018.01.018] [Medline: 29588052]
10. Bruffaerts R, Mortier P, Kiekens G, Auerbach RP, Cuijpers P, Demyttenaere K, et al. Mental health problems in college freshmen: prevalence and academic functioning. J Affect Disord 2018 Jan 01;225:97-103 [FREE Full text] [doi: 10.1016/j.jad.2017.07.044] [Medline: 28802728]
11. Ballester L, Alayo I, Vilagut G, Almenara J, Cebrià AI, Echeburúa E, UNIVERSAL study group. Accuracy of online survey assessment of mental disorders and suicidal thoughts and behaviors in Spanish university students. Results of the WHO World Mental Health- International College Student initiative. PLoS One 2019;14(9):e0221529 [FREE Full text] [doi: 10.1371/journal.pone.0221529] [Medline: 31487306]
12. Ebert DD, Mortier P, Kaehlke F, Bruffaerts R, Baumeister H, Auerbach RP, WHO World Mental Health-International College Student Initiative collaborators. Barriers of mental health treatment utilization among first-year college students: first cross-national results from the WHO World Mental Health International College Student Initiative. Int J Methods Psychiatr Res 2019 Jun;28(2):e1782 [FREE Full text] [doi: 10.1002/mpr.1782] [Medline: 31069905]
13. Vigo D, Jones L, Munthali R, Pei J, Westenberg J, Munro L, et al. Investigating the effect of COVID-19 dissemination on symptoms of anxiety and depression among university students. BJPsych Open 2021 Mar 19;7(2):e69 [FREE Full text] [doi: 10.1192/bjo.2021.24] [Medline: 33736744]

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14. Kessler RC, Adler LA, Gruber MJ, Sarawate CA, Spencer T, Van Brunt DL. Validity of the World Health Organization Adult ADHD Self-Report Scale (ASRS) Screener in a representative sample of health plan members. Int J Methods Psychiatr Res 2007;16(2):52-65 [FREE Full text] [doi: 10.1002/mpr.208] [Medline: 17623385]
15. Diagnostic and Statistical Manual of Mental Disorders (Fourth Edition, Text Revision). Washington, DC: American Psychiatric Association; 2000.
16. Diagnostic and Statistical Manual of Mental Disorders (Fifth Edition). Washington, DC: American Psychiatric Association; 2013.
17. Kessler RC, Ustün TB. The World Mental Health (WMH) Survey Initiative Version of the World Health Organization (WHO) Composite International Diagnostic Interview (CIDI). Int J Methods Psychiatr Res 2004;13(2):93-121 [FREE Full text] [doi: 10.1002/mpr.168] [Medline: 15297906]
18. Kessler RC, Calabrese JR, Farley PA, Gruber MJ, Jewell MA, Katon W, et al. Composite International Diagnostic Interview screening scales for DSM-IV anxiety and mood disorders. Psychol Med 2013 Aug;43(8):1625-1637. [doi: 10.1017/S0033291712002334] [Medline: 23075829]
19. Saunders JB, Aasland OG, Babor TF, de la Fuente JR, Grant M. Development of the Alcohol Use Disorders Identification Test (AUDIT): WHO Collaborative Project on Early Detection of Persons with Harmful Alcohol Consumption--II. Addiction 1993 Jun;88(6):791-804. [doi: 10.1111/j.1360-0443.1993.tb02093.x] [Medline: 8329970]
20. Bondy SJ, Rehm J, Ashley MJ, Walsh G, Single E, Room R. Low-risk drinking guidelines: the scientific evidence. Can J Public Health 1999;90(4):264-270 [FREE Full text] [Medline: 10489725]
21. Butt P, Beirness D, Gliksman L, Paradis C, Stockwell T. Alcohol and Health in Canada: A Summary of Evidence and Guidelines for Low-risk Drinking. Ottawa, ON: Canadian Centre on Substance Abuse; 2011.
22. Fischer B, Jeffries V, Hall W, Room R, Goldner E, Rehm J. Lower Risk Cannabis use Guidelines for Canada (LRCUG): a narrative review of evidence and recommendations. Can J Public Health 2011;102(5):324-327 [FREE Full text] [Medline: 22032094]
23. Fischer B, Russell C, Sabioni P, Van den Brink W, Le Foll B, Hall W, et al. Lower-risk cannabis use guidelines (LRCUG): an evidence-based update. Am J Public Health 2017:1.
24. Busse JW, Craigie S, Juurlink DN, Buckley DN, Wang L, Couban RJ, et al. Guideline for opioid therapy and chronic noncancer pain. CMAJ 2017 May 08;189(18):E659-E666 [FREE Full text] [doi: 10.1503/cmaj.170363] [Medline: 28483845]
25. World Medical Association. Declaration of Helsinki, ethical principles for scientific requirements and research protocols. Bull World Health Organ 2013;79(4):373.
26. Qualtrics XM. 2020. URL: https://www.qualtrics.com/ [accessed 2022-06-24]

Abbreviations

SFU: Simon Fraser University
UBC: The University of British Columbia
UofT: University of Toronto
WHO: World Health Organization
WMH-ICS: World Mental Health International College Student

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Original Paper

Physical Activity and Fall Prevention in Geriatric Inpatients in an Acute Care Unit (AGIR Study): Protocol for a Usability Study

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Abstract

Background: Falls are one of the world's top 10 risks associated with disability in people older than 60 years. They also represent more than two-thirds of adverse events in hospitals, mainly affecting patients older than 65 years. Physical activity is a central intervention in fall prevention for older people. Whatever the details of the prevention strategy that is adopted (ie, how a mono- or multifactorial intervention is evaluated, the category of person the intervention targets, and where it is used), it is important to ensure that the proposed intervention is feasible and usable for the patient and the health care team.

Objective: The primary objective is to study the usability of carrying out a physical activity intervention, including 3 types of exercises, in older patients hospitalized in a geriatric acute care unit and categorized according to 3 fall risk levels: low, moderate, and high. The secondary objectives are to determine the difficulty of the physical exercise for patients with different fall risk levels, to study the health care team's perceptions of the intervention's feasibility, and to study the benefits for patients.

Methods: This is an open-label, unicenter, nonrandomized, usability prospective clinical trial. The intervention tested is a daily physical activity program. It consists of 3 types of physical exercise: staying out of bed for at least 3 hours, performing balance exercises while standing for 2 minutes, and the Five Times Sit to Stand transfer exercise. These exercises are carried out under the supervision of the health care team. Fall risk in the patients is classified with the Brief Geriatric Assessment tool. The exercise program starts on the second day of hospitalization after inclusion in the study. Patient assessment continues until the last day of hospitalization or the 20th day of hospitalization, whichever is earlier. For each fall-risk group and each type of exercise, the intervention will be defined as usable if at least 80% of the participants complete 75% or more of the exercises (ie, the ratio between the number of days when the patient completes a type of exercise and the total number of hospitalization days). The perceived feasibility by the health care team is measured with 2 scales, measuring perceived difficulty and time spent with the patient. The intervention benefit is evaluated using the performance of the Five Times Sit to Stand test before and after the intervention.

Results: The first patient was recruited on March 16, 2015. The study enrolled 266 patients, including 75 with low fall risk, 105 with moderate risk, and 85 with high risk.

Conclusions: We have not yet analyzed the results, but our observations suggest that the usability of each type of exercise for a given patient will depend on their fall risk level.

Trial Registration: ClinicalTrials.gov NCT02393014; https://clinicaltrials.gov/ct2/show/NCT02393014

International Registered Report Identifier (IRRID): DERR1-10.2196/32288

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(JMIR Res Protoc 2022;11(7):e32288) doi:10.2196/32288

KEYWORDS

fall prevention; physical activity; older patients; geriatric acute care unit

Introduction

Context

Falls are one of the world's top 10 risks for causing disability in people aged older than 60 years [1]. More than two-thirds of adverse events in hospitals are falls, mainly affecting patients older than 65 years [2,3]. Falls are accompanied by multiple physical and psychological consequences that cause disability, increased length of stay, and increased cost of care [2,3]. Fall risk factors may be classified as (1) biological (related to disease or aging), (2) associated with daily behavior (related to eating, being active, dressing, and other habits), (3) social and economic (related to social isolation, poverty, financial resources, or lack of access to health care), and (4) environmental, including the local environment (building entrances, lack of handrails, type of furniture) and the climate [4]. The management of falls relies on various strategies: avoiding the first fall, fast intervention and treatment when a fall occurs, and preventing additional falls [5].

Physical activity is a central intervention in fall prevention programs for older persons. It contributes to the restoration and maintenance of muscle function and tone, joint mobility, improved balance, and walking ability [5-8]. Physical activity recommendations for older people [9], particularly frail patients at risk of falling [5,6], include moderate-intensity physical activity for 15 to 30 minutes as often as possible during the week; exercise programs based on balance, strength, and gait; group exercise supervised by a professional, to take into account the physical capabilities and health profile of older persons; and regular review of progression to adjust the exercise prescription as appropriate. Recommendations also include multicomponent interventions [10]. It has been shown that multicomponent interventions, which combine physical activity and corrective actions, decrease the annual incidence of falls by 10% to 30% [6,7].

Staying active prevents functional disabilities, particularly in older patients who are hospitalized [11]. These patients quickly lose their ability to perform daily acts by themselves, such as getting up from a low position or walking, causing them to become severely sedentary [6-8,12]. In this context, an intervention can be considered a secondary or tertiary prevention (ie, taking place after confirmation of early-stage risk factors, such as frailty or a history of falls) rather than a primary prevention (ie, before the onset of the disease) [13].

Considering (1) the preventive strategy adopted (ie, the evaluation associated with a mono- or multicomponent intervention), (2) the category of person targeted, and (3) where the intervention takes place (ie, in a home, institution, or hospital), it is important to ensure that the proposed intervention is feasible and usable for the person or the group of people concerned. This is particularly important considering the frailty of older inpatients and the availability of the health care team.

Hypothesis

We hypothesize that in the geriatric acute care unit of a university hospital, it will be possible to carry out a physical activity intervention based on the physical acts of daily life, focusing on strengthening the lower-limb muscles and improving postural balance.

Objectives

Primary Objective

The primary objective is to study the usability of carrying out a physical activity intervention including 3 types of exercise in older inpatients at a geriatric acute-care unit and categorized according to 3 fall risk levels: low, moderate, and high.

Secondary Objectives

There are 3 secondary study objectives. Secondary objective A will be to determine the difficulty level of the physical exercises in each fall risk group and analyze the usability of the intervention in each group to determine the best intervention modality for each group. Secondary objective B will be to determine the health care team's perception of the difficulty of carrying out the intervention and analyze their perceptions with 2 scales. Secondary objective C will be to examine the effects of this physical activity intervention on the patients' lower-limb strength, comparing their ability and time to perform the Five Times Sit to Stand (FTSS) test before (measured during a clinical assessment) and after the intervention (on the last day of hospitalization or the 20th day of hospitalization, if the patient is still hospitalized).

Methods

Design

This is an open-label, unicenter, nonrandomized, usability prospective clinical trial. There is no comparator group (ie, no control group). Figure 1 illustrates the trial design and Table 1 summarizes the timing of the trial. The intervention tested in this study is a physical activity intervention based on the physical acts of daily life that focuses on strengthening the lower-limb muscles and improving postural balance. It consists of 3 types of physical exercise that can be adapted to the fall risk level. It is offered to 3 categories of hospitalized patients, classified according to their risk of falling: low, moderate, and high. It is carried out from the second day of hospitalization after an assessment of the patient's risk of falling until the last day of hospitalization or the 20th day of hospitalization if the patient is still hospitalized. In summary, this study consists of an inclusion visit, a physical activity program performed daily until the 20th day of hospitalization, and an end-of-study visit.

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Figure 1. Trial flow chart. FTSS: Five Times Sit to Stand.

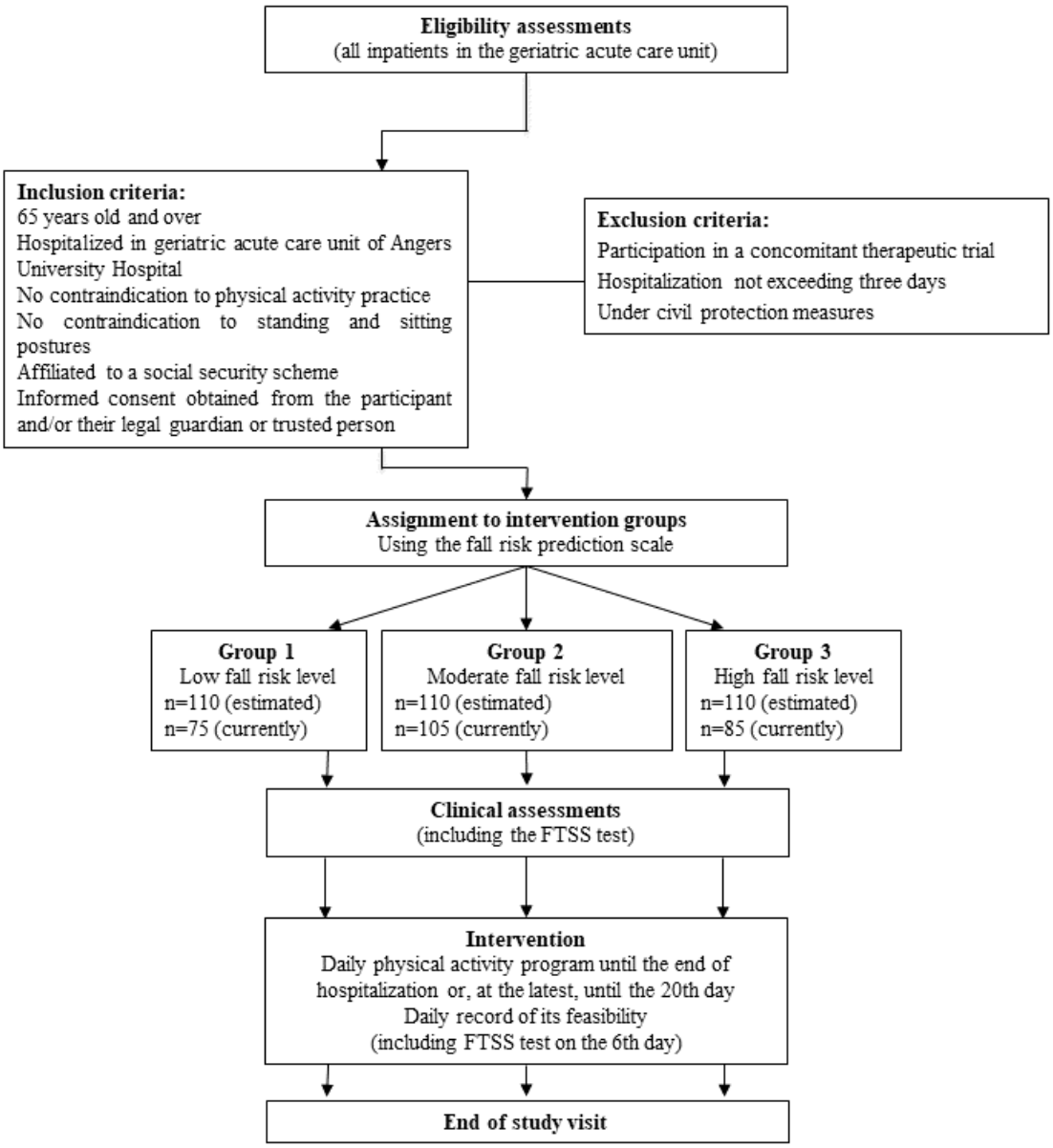

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Table 1. Timeline of the study.

	Enrollment and allocation	Follow up	Study end (last day of hospitalization or 20th day, whichever is earlier)
Inclusion and exclusion criteria applied	✓		
Informed consent obtained	✓		
Group assignment	✓		
Clinical assessment	✓		✓
Five Times Sit to Stand test	✓	✓[a]	✓
Pain	✓	✓[a]	✓
Physical activity intervention		✓[b]	✓

[a]Only measured on the sixth day of follow up.

[b]Performed daily.

Planned Eligibility Criteria

Inclusion Criteria

Patients are included if they are at least 65 years old, hospitalized in a geriatric acute-care unit, and have no contraindications to physical activity, standing, or sitting. Patients must also be covered by a social security scheme and have given and signed an informed consent form to participate in the study (informed consent can also be obtained from a trusted person or legal representative, as appropriate).

Exclusion Criteria

Patients are excluded if their hospitalization was shorter than 3 days, they were participating in a concomitant therapeutic trial, or if they were under any of the 3 French civil protection measures: curatorship, guardianship, and safeguard of justice.

Intervention

This intervention follows the main principles of the latest French National Authority for Health (HAS) recommendations on the prevention of falls in older people [11]. Each fall risk group of participants will receive a physical activity intervention, carried out once a day, consisting of 3 types of exercise. In exercise 1, the participant must stay out of bed for at least 3 hours. This length of time prevents acute postural disorders that increase the risk of falling; these can occur when older patients are bedridden for too long. In exercise 2, the participant stands in static equilibrium for 2 minutes in front of a chair, holding the back of the chair. Depending on the participant's abilities, the exercise is done standing on one or both feet. Exercise 3 requires the participant to switch from sitting on a chair to standing 5 times (this is similar to the FTSS test but is not timed). Depending on the patient's abilities, the exercise is done with or without physical assistance.

This daily intervention is carried out starting on the day after informed consent is obtained from patients fulfilling the selection criteria. It is carried out under the supervision and monitoring of the health care team, specifically nurses and nursing assistants.

Assessments

Fall Risk Assessment

The Brief Geriatric Assessment (BGA) tool [14] is used to assess fall risk level. It consists of six items, coded as binary variables: (1) age (over or under 85 years), (2) gender (male or female), (3) number of medications taken daily (over or under 5), (4) history of falls during the past 6 months (yes or no), (5) cognitive level, assessed as the ability to identify the month and year (yes or no), and (6) use of home help services (yes or no). The BGA tool classifies patients into 3 fall risk levels using an algorithm that consider criteria 4 and 5 as major fall risks and criteria 1, 2, 3, and 4 as minor fall risks: group 1, low fall risk; group 2, moderate fall risk; and group 3, high fall risk. The BGA is used by the health care team as part of usual care.

Clinical Assessments

Clinical assessments are performed at inclusion and during follow up (Table 1). Except for the FTSS test, which is applied during follow up and at the end of the study, all clinical assessments are carried out as part of usual care. Clinical data are collected from the computerized patient medical file or directly from the participant if the data have not yet been added to the file.

The clinical assessment at inclusion will include the reason for hospitalization (including organ failure, musculoskeletal disorders or falls, neuropsychiatric disorders, medicosocial problems, or other causes); age and gender; anthropometric data (ie, weight and height); body mass index (kg/m^2); and the Mini-Mental State Examination (MMSE) [15] score. The MMSE is used to assess cognitive function. It consists of 30 questions in 5 sections (orientation, memory and recall, attention, calculation, and language), with a final score graded out of 30 points. In the absence of memory complaint, (self-reported or non–self-reported), a final score between 27 and 30 indicates the probable absence of a cognitive disorder.

Clinical assessments at inclusion and during follow up will include the use of psychotropic drugs (eg, antidepressants, benzodiazepines, hypnotics, and neuroleptics); the number of different therapeutic classes of drugs taken; the FTSS test; and the patient's overall pain, assessed using a verbal 6-point scale:

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"no pain," "low pain," "moderate pain," "high pain," "extreme pain," and "not assessable." The pain assessment is used to verify changes in pain level during hospitalization. The FTSS test measures a patient's physical transfer ability. The test is to stand up from a chair 5 times as quickly as possible without pushing off. Performance is measured in seconds, from the initial seated position to the final seated position after having completed standing up 5 times. A time longer than 15 seconds is abnormal and is associated with physical and cognitive impairment [16].

Monitoring of the Implementation of the Physical Activity Program

Nurses are in charge of keeping a physical activity monitoring form up to date, which is also digitized in the computerized patient medical file and added to the case report form. This form includes the following information: date of daily physical activity session; level of completion for each type of exercise; reasons why the daily objectives were not reached during the session; perceived feasibility of the daily session by the caregiver; time spent by the caregiver conducting the daily session; and occupational category of the caregiver who supervised the daily session, including nursing assistant, nurse, physiotherapist, occupational therapist, paramedical student, and second-cycle (equivalent to a master's degree in medical sciences) medical student.

Outcomes

Primary Outcome Measure

The primary outcome measure is the number of participants in each fall risk group who complete 75% or more of the physical activity program for each type of exercise during hospitalization. For each type of exercise, success is quantified daily as follows: for exercise 1, the participant was able to stay out of bed for at least 3 hours; for exercise 2, the participant stood in static balance for at least 2 minutes in front of the chair, holding the back of the chair; and for exercise 3, the participant switched from sitting on a chair to standing at least 5 times. The percentage represents the ratio between the number of days when the patient successfully completes a type of exercise and the total number of days of hospitalization. For each fall risk group and each type of exercise, the intervention will be defined as usable if at least 80% of the participants complete at least 75% of the exercise. These thresholds have not been scientifically validated.

Secondary Outcome Measures

The primary outcome will help us to meet secondary objective A. Based on the results for usability, we will establish what types of exercise are usable for each fall-risk group to determine the best intervention modalities for different fall-risk groups in future interventions.

The secondary outcome measures for secondary objective B are the health care team's perception of the difficulty of carrying out the intervention and the time spent by the health care team on the physical activity intervention. A 5-point scale of perceived difficulty will be assessed after each session, including "very easy," "easy," "feasible," "difficult," and "impossible." A scale will also be assessed after each session to quantify the time spent with the patient (ie, the time to complete the physical activity monitoring form, verify the time spent out of bed, and have the patient perform the balance and transfer exercises), including "0 to 2 minutes," "3 to 5 minutes," "6 to 10 minutes," "11 to 20 minutes," and ">20 minutes." These scales have not been scientifically validated.

The intervention will be considered feasible if the health care team consider a majority of sessions to have had a difficulty between "very easy" and "feasible" and if a majority of sessions were shorter than 10 minutes.

The secondary outcome measures for secondary objective C are the percentage of patients who completed the FTSS test before and after the intervention and the time in seconds (measured before and after the intervention) the patients needed to complete the FTSS test. We will consider the intervention beneficial for patients' lower-limb strength in two cases: if the patients can complete the FTSS test more often after the intervention than before, and if those who complete the FTSS test can do so more quickly after the intervention than before.

Sample Size Calculation

The trial aims to recruit 330 patients, with 110 patients in each of the 3 fall risk groups (Figure 1). It is not possible to accurately calculate the needed size of the population to be studied based on the study's primary objective. It can be only estimated empirically (creating a risk of error) based on the typology of older patients attending the geriatric acute-care unit involved in this study. The data available to estimate the needed number of participants with this empirical method are the number of hospitalized patients per year (1000 people), the proportion of these patients who cannot complete the proposed exercises due to poor health (approximately 333 people), and the proportion of these patients who can perform the exercises, based on the *autonomie, gérontologie, groupe iso ressources* (AGGIR) a question grid commonly used nation-wide in France [17]. The AGGIR categorizes individuals into *groupe iso ressources* (GIR) levels to represent their level of autonomy. We aimed to include 133, 333, and 200 participants with GIR levels 5 or 6, 3 or 4, and 1 or 2, respectively. We hypothesize that GIR levels will reflect the fall risk levels estimated by the BGA tool.

Considering the proportion of patients who will likely refuse to participate (estimated at 15%), we consider that the study should include at least 330 patients, with the following distribution: 110 patients with low fall risk (GIR levels 5 or 6); 110 patients with moderate fall risk (GIR levels 3 or 4); and 110 patients with major fall risk (GIR levels 1 or 2).

These numbers should be enough to obtain a sufficient proportion of patients who can perform at least 75% of the exercises in each fall risk group and allow us to better understand the usability of the physical activity intervention we are proposing in this study.

Recruitment/Consent Procedures

The majority of clinical assessments are carried out as part of usual care and as soon as patients enter the geriatric acute-care unit (ie, as soon as possible). This facilitates the preselection

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of patients, partly thanks to the computerized patient medical file. Once a potential participant is identified as meeting the eligibility criteria, a member of the investigation team provides written and oral information on the study in understandable language to the patient (or a family member, trusted person, or legal representative, as appropriate). When possible, fully informed consent is obtained from the patient. When a patient is unable to give fully informed consent, agreement to participate in the study is obtained from the trusted person or the legal representative, but the patient is not enrolled if he or she refuses or shows significant distress. In the case of exclusion or refusal, the investigation team records whether the selection criteria were met and the cause for nonparticipation in the study, and then copies this information into the "registry of eligible and ineligible patients."

Statistical Methods

General

The distribution of quantitative variables will be studied, including the mean, median, mode, minimum, maximum, confidence interval around the mean, and standard deviation. The frequencies of qualitative variables will be calculated. For bivariate analyses, the appropriate statistical tests will be used according to the number and distribution of the variables (ie, normal vs nonnormal distributions) and the number of groups of participants in the comparison. The overall significance level will be set at $P=.05$; all tests will be 2-sided.

Descriptive Analyses

A diagram will be used to summarize the progress of the study as patients are added and to monitor the protocol. All the clinical characteristics of the participants (such as age, sex, and weight) and the results of the investigations carried out will be described. A table will be used to summarize the level of completion of the physical activity intervention for each fall risk group and each type of exercise. This will help us to determine which type of exercise is most usable for each fall risk group (secondary objective A). A contingency table will be used to report, for each fall risk group, the perceived difficulty of the daily sessions by the health care team and the time spent on carrying them out. A contingency table will also be used to report, for each fall risk group, the number of FTSS tests completed by the patients at the beginning of the intervention, the sixth day of the intervention, and at the end of the intervention.

Primary Objective Analysis

For each fall risk group and each type of exercise, the intervention will be considered usable if at least 80% of the participants complete 75% or more of the exercise.

For each parameter, a univariate analysis will be carried out, possibly supplemented by a multivariate analysis, to estimate the effect of physical activity after adjusting for age, sex, and the reason for hospitalization.

Comparison Between Fall Risk Groups

The fall risk groups will be compared for (1) the health care team's perception of their difficulty in carrying out the intervention (secondary objective B) and (2) their results for the FTSS test before and after the intervention (secondary objective C, assessed only in patients who can complete the FTSS test), using parametric and nonparametric tests depending on the distribution of variables.

Safety Parameters

Safety parameters will be set after adverse events are recorded. The record will include the date of the adverse event; its level of seriousness; the type of effects associated with it (and whether they are known, serious, or unexpected); its novelty (ie, whether is a confounding effect or a new effect previously unknown to us); what it is related to (ranging from unrelated to highly likely to be related); and its intensity (ranging from transient and without repercussions to life threatening). All these parameters will be analyzed. All possible measures will be taken by the investigation team to ensure the safety of the patients and to respect relevant laws and ethical rules. In accordance with ethical considerations (more details are provided in the "Ethical Considerations" section), an assessment of whether an adverse event can be assigned to a specific reason will be carried out for all serious adverse events.

Ethical Considerations

The protocol received approval from the West II Ethics Committee in Angers, France (2014/30) and was approved by the French National Agency for the Safety of Medicines and Health Products (ID-RCB: 2014-A01397-40). One amendment to the protocol was submitted and approved by regulatory authorities on June 2015. The trial was conducted in compliance with French laws relating to research involving the human person. The study complied with the E6(R2) and E2B(R3) guidelines of the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH), which address the following topics: good clinical practices and management and electronic transmission of adverse events. The study also complied with the French Public Health Code, the French National Commission for Information Technology and Freedom, the European Union Clinical Trials Directive (2001/20/EC), and the Helsinki Declaration of 1975 and its revisions (including the Ethical Principles for Medical Research Involving Human Subjects, Tokyo 2004) and other requirements, as appropriate. A verification of the consent and emergency procedures was carried out after each inclusion, followed by an auditing of the files at regular time intervals. The study was registered on ClinicalTrials.gov (NCT02393014).

Results

The first participant was included on March 16, 2015. We preselected 278 patients, of whom 266 enrolled in the study (low fall risk group: 75 patients, moderate fall risk group: 105 patients, and high fall risk group: 85 patients).

We will not include more patients. We have not yet analyzed the results, but our first impression is that the high fall risk group was only able to complete exercise 1 (ie, staying out of bed for at least 3 hours daily), the moderate fall risk group was able to complete exercises 1 and 2 (ie, they could also complete the 2-minute balance exercise), and the low fall risk group was able to complete all the physical activity exercises.

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Despite this first impression, the program does not seem to have been perceived as difficult or time consuming by the health care team. Detailed statistical analyses will make it possible to explore in detail the results of this study and to meet its objectives.

Discussion

The objective of this study is to verify the usability of carrying out a physical activity intervention, including 3 types of exercise, in older patients hospitalized at a geriatric acute-care unit who were at low, moderate, or high risk of falls. These exercises focused on strengthening the lower-limb muscles and improving postural balance. We hypothesized that this type of intervention would be usable, which we defined as follows: (1) 80% of the patients would be able to perform each type of daily exercise (the primary objective), and (2) the health care team would perceive the intervention as feasible in terms of its difficulty and the time required to carry it out (secondary objective B). This study also explored two other factors: (1) how the difficulty of each exercise differed for patients with different fall risk levels (ie, secondary objective A, with the intention of improving this type of program in future interventions) and (2) the potential benefits of this type of intervention (ie, secondary objective C) by comparing performance on the FTSS test before and after the intervention. To date, 266 inpatients have been enrolled. We have not analyzed the results, but our initial observations suggest that the usability of each type of exercise for the patients depends on their fall risk level, and that the program has not been perceived as difficult or time consuming by the health care team.

Recently published meta-analyses describing the role of physical activity in preventing falls by patients in posttreatment and rehabilitation wards first reported the effectiveness of exercise programs in 2012 [7], then showed less certainty in 2018 [18]. These meta-analyses also highlighted the fact that there have been very few studies conducted in geriatric acute-care units and that the data were divergent, with some studies showing efficacy and others not. The recent SPRINTT (Sarcopenia and Physical Frailty in Older People: Multi-Component Treatment Strategies) study [19] was a randomized controlled trial aimed, in part, at testing a physical activity intervention that appeared comprehensive (including aerobic endurance, gait, balance, flexibility, and resistance exercises) and monitored the intensity of the exercises to protect the frail, older participants. However, this study does not seem to have been carried out exclusively in a geriatric acute-care unit. Our study focused on the hospital context, for which, to date, there have been few studies attempting to include a significant number of patients [7,18]. If this type of intervention is feasible and “usable” from the point of view of the patients’ abilities and the perceptions of the health care team, we expect that it will reduce the risk of falling. Intervention may also reduce the frequency and severity of iatrogenic events during the hospitalization of older patients. Iatrogenic adverse events can be defined as any unintended injury or complication caused by health care management itself, rather than by the underlying disease process [20]. Sourdet et al [21] recently showed that the majority of iatrogenic events can be prevented, in part by keeping patients active and by engaging them in physical activity interventions. Martinez-Velilla et al [20] pointed out that iatrogenic disability can result from one or more iatrogenic adverse events occurring during hospitalization, including three factors: (1) the patient's pre-existing frailty, (2) the severity of the disorder leading to the admission, and (3) the hospital process of care. They also emphasized the impact of hospitalization itself, which can force the patient to be severely sedentary (ie, to stay in bed or in a chair for a long time), and the positive impact of physical activity intervention. Our physical activity program followed the recommendations of HAS [11]. It partially followed the guidelines of the International Conference on Frailty and Sarcopenia Research (ICFSR) [10]. The ICFSR guidelines focus on frailty and the prevention of sarcopenia. They recommend including aerobic exercises in addition to resistance and balance exercises. Our physical training intervention did not include aerobic exercises. Exercise 1, staying out of bed for at least 3 hours, did not engage the patients in exercise with an intensity and duration sufficient enough to be considered aerobic. Moreover, for some patients with a high fall risk level (who were usually frail), getting them out of bed for at least 3 hours, even if they only stayed seated on a chair or walked a little, was already very difficult to achieve. Another difference with the ICFSR guidelines is that our intervention did not quantify resistance or balance exercises by the number of trials, but rather by the total volume of work (2 minutes of balance and getting up from a chair 5 times). Nevertheless, the ICFSR guidelines conclude that there is currently no data that can be used to identify the optimal physical exercise required in terms of frequency, intensity, time, or type [10]. Our study may provide new information on the frequency, time, and type of physical activity interventions suited to geriatric acute-care units.

Our study presents several limitations that have already been identified. First, it was not possible to quantify the type of activities carried out during exercise 1. Managing the specific activities in this exercise would have taken too much time for the caregivers. Second, the modality of the other two exercises was not well detailed. Because of the diversity of the patients, it was necessary to let the caregivers adapt the exercises. This caused us to lose several interesting types of data (eg, the number of trials needed to reach 2 minutes or the number of times an exercise was performed on one or both feet). Third, we did not use validated scales to evaluate the perceived feasibility from the point of view of the health care team. Nevertheless, we consider that the scales we used were informative. Finally, we used only the FTSS test to assess lower-limb strength. It would have been more interesting to use the Short Physical Performance Battery [22], which includes the FTSS test.

If we verify our hypotheses on usability and if we observe a beneficial effect for the patients, we will plan a larger-scale experiment in which we will investigate the effects of this type of intervention during and after hospitalization on the risk of falling, level of frailty, level of autonomy, length of stay in the geriatric acute-care unit, recurrence of falls, and rehospitalization. Such a study would allow us to better define the frequency, intensity, time, and type of exercise for patients with different fall risk levels.

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Authors' Contributions

FN designed the study, revised the manuscript, and participated in the conduct of the study in the geriatric acute-care unit. RS participated in the development of the methods, the preparation of documents for the ethics committees, revised the manuscript, and participated in the conduct of the study in the geriatric acute-care unit. GBS wrote the first draft and revised the manuscript. CA supervised the study and revised the manuscript.

Conflicts of Interest

None declared.

References

1. World report on ageing and health. World Health Organization. URL: https://apps.who.int/iris/handle/10665/186463 [accessed 2022-05-02]
2. Oliver D, Britton M, Seed P, Martin FC, Hopper AH. Development and evaluation of evidence based risk assessment tool (STRATIFY) to predict which elderly inpatients will fall: case-control and cohort studies. BMJ 1997 Oct 25;315(7115):1049-1053 [FREE Full text] [doi: 10.1136/bmj.315.7115.1049] [Medline: 9366729]
3. Oliver D, Hopper A, Seed P. Do hospital fall prevention programs work? A systematic review. J Am Geriatr Soc 2000 Dec;48(12):1679-1689. [doi: 10.1111/j.1532-5415.2000.tb03883.x] [Medline: 11129762]
4. Pillay J, Riva JJ, Tessier LA, Colquhoun H, Lang E, Moore AE, et al. Fall prevention interventions for older community-dwelling adults: systematic reviews on benefits, harms, and patient values and preferences. Syst Rev 2021 Jan 09;10(1):18 [FREE Full text] [doi: 10.1186/s13643-020-01572-7] [Medline: 33422103]
5. Panel on Prevention of Falls in Older Persons, American Geriatrics Society, British Geriatrics Society. Summary of the Updated American Geriatrics Society/British Geriatrics Society clinical practice guideline for prevention of falls in older persons. J Am Geriatr Soc 2011 Jan;59(1):148-157. [doi: 10.1111/j.1532-5415.2010.03234.x] [Medline: 21226685]
6. Cadore EL, Rodríguez-Mañas L, Sinclair A, Izquierdo M. Effects of different exercise interventions on risk of falls, gait ability, and balance in physically frail older adults: a systematic review. Rejuvenation Res 2013 Apr;16(2):105-114 [FREE Full text] [doi: 10.1089/rej.2012.1397] [Medline: 23327448]
7. Cameron ID, Gillespie LD, Robertson MC, Murray GR, Hill KD, Cumming RG, et al. Interventions for preventing falls in older people in care facilities and hospitals. Cochrane Database Syst Rev 2012 Dec 12;12:CD005465. [doi: 10.1002/14651858.CD005465.pub3] [Medline: 23235623]
8. Kressig RW, Beauchet O, Tharicharu J. [T'ai chi in the elderly: practical aspects]. Rev Med Suisse Romande 2003 Nov;123(11):671-675. [Medline: 15095631]
9. Cornuz J, Bize R, Gobelet C. [Promotion of physical activity: some guidelines for the prevention of osteoporosis]. Rev Med Suisse Romande 2002 Aug;122(8):371-375. [Medline: 12357729]
10. Dent E, Morley JE, Cruz-Jentoft AJ, Woodhouse L, Rodríguez-Mañas L, Fried LP, et al. Physical Frailty: ICFSR International Clinical Practice Guidelines for Identification and Management. J Nutr Health Aging 2019;23(9):771-787 [FREE Full text] [doi: 10.1007/s12603-019-1273-z] [Medline: 31641726]
11. Beauchet O, Dubost V, Revel Delhom C, Berrut G, Belmin J, French Society of Geriatrics and Gerontology. How to manage recurrent falls in clinical practice: guidelines of the French Society of Geriatrics and Gerontology. J Nutr Health Aging 2011 Jan;15(1):79-84. [doi: 10.1007/s12603-011-0016-6] [Medline: 21267524]
12. Beauchet O, Launay C, Annweiler C, Fantino B, Allali G, De Decker L. Physical training-related changes in gait variability while single and dual tasking in older adults: magnitude of gait variability at baseline matters. Eur J Phys Rehabil Med 2013 Dec;49(6):857-864 [FREE Full text] [Medline: 24285023]
13. Health promotion and disease prevention through population-based interventions, including action to address social determinants and health inequity. World Health Organization. URL: http://www.emro.who.int/fr/about-who/public-health-functions/health-promotion-disease-prevention.html [accessed 2022-05-02]
14. Noublanche F, Simon R, Decavel F, Lefort M, Annweiler C, Beauchet O. Falls prediction in acute care units: preliminary results from a prospective cohort study. J Am Geriatr Soc 2014 Aug;62(8):1605-1607. [doi: 10.1111/jgs.12962] [Medline: 25116990]
15. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 1975 Nov;12(3):189-198. [doi: 10.1016/0022-3956(75)90026-6] [Medline: 1202204]
16. Annweiler C, Schott A, Abellan van Kan G, Rolland Y, Blain H, Fantino B, et al. The Five-Times-Sit-to-Stand test, a marker of global cognitive functioning among community-dwelling older women. J Nutr Health Aging 2011 Apr;15(4):271-276. [doi: 10.1007/s12603-011-0037-1] [Medline: 21437558]

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17. Coutton V. Évaluer la dépendance à l'aide de groupes iso-ressources (GIR): une tentative en France avec la grille aggir. Gerontol Soc 2001 Apr;24(99):111-129 [FREE Full text] [doi: 10.3917/gs.099.0111]
18. Cameron ID, Dyer SM, Panagoda CE, Murray GR, Hill KD, Cumming RG, et al. Interventions for preventing falls in older people in care facilities and hospitals. Cochrane Database Syst Rev 2018 Sep 07;9:CD005465 [FREE Full text] [doi: 10.1002/14651858.CD005465.pub4] [Medline: 30191554]
19. Landi F, Cesari M, Calvani R, Cherubini A, Di Bari M, Bejuit R, SPRINTT Consortium. The "Sarcopenia and Physical fRailty IN older people: multi-componenT Treatment strategies" (SPRINTT) randomized controlled trial: design and methods. Aging Clin Exp Res 2017 Feb;29(1):89-100. [doi: 10.1007/s40520-016-0715-2] [Medline: 28144914]
20. Martínez-Velilla N, Herrero AC, Cadore EL, Sáez de Asteasu ML, Izquierdo M. Iatrogenic Nosocomial Disability Diagnosis and Prevention. J Am Med Dir Assoc 2016 Aug 01;17(8):762-764. [doi: 10.1016/j.jamda.2016.05.019] [Medline: 27349623]
21. Sourdet S, Lafont C, Rolland Y, Nourhashemi F, Andrieu S, Vellas B. Preventable Iatrogenic Disability in Elderly Patients During Hospitalization. J Am Med Dir Assoc 2015 Aug 01;16(8):674-681. [doi: 10.1016/j.jamda.2015.03.011] [Medline: 25922117]
22. Guralnik JM, Simonsick EM, Ferrucci L, Glynn RJ, Berkman LF, Blazer DG, et al. A short physical performance battery assessing lower extremity function: association with self-reported disability and prediction of mortality and nursing home admission. J Gerontol 1994 Mar;49(2):M85-M94. [doi: 10.1093/geronj/49.2.m85] [Medline: 8126356]

Abbreviations

AGGIR: Autonomy Gerontology Groups Iso-Resources
BGA: Brief Geriatric Assessment
CHU: Centre Hospitalier Universitaire
COMETE: Cognition, Mobilité Et TEmporalité
CYCERON: Cyclotron-Chimie-Positron
FTSS: Five Times Sit to Stand
GIR: Groupes Iso Ressources
HAS: Haute Autorité de Santé
ICFSR: International Conference of Frailty and Sarcopenia Research
ICH: International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use
INSERM: Institut National de la Santé et de la Recherche Médicale
LPPL: Laboratoire de Psychologie des Pays de la Loire
MMSE: Mini-Mental State Examination
SFR: Structure Fédérative de Recherche
SPRINTT: Sarcopenia and Physical Frailty in Older People: Multi-Component Treatment Strategies
UNICAEN: Université de Caen Normandie

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Original Paper

An Integrated Care Platform System (C3-Cloud) for Care Planning, Decision Support, and Empowerment of Patients With Multimorbidity: Protocol for a Technology Trial

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Abstract

Background: There is an increasing need to organize the care around the patient and not the disease, while considering the complex realities of multiple physical and psychosocial conditions, and polypharmacy. Integrated patient-centered care delivery platforms have been developed for both patients and clinicians. These platforms could provide a promising way to achieve a collaborative environment that improves the provision of integrated care for patients via enhanced information and communication technology solutions for semiautomated clinical decision support.

Objective: The Collaborative Care and Cure Cloud project (C3-Cloud) has developed 2 collaborative computer platforms for patients and members of the multidisciplinary team (MDT) and deployed these in 3 different European settings. The objective of this study is to pilot test the platforms and evaluate their impact on patients with 2 or more chronic conditions (diabetes mellitus type 2, heart failure, kidney failure, depression), their informal caregivers, health care professionals, and, to some extent, health care systems.

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Methods: This paper describes the protocol for conducting an evaluation of user experience, acceptability, and usefulness of the platforms. For this, 2 "testing and evaluation" phases have been defined, involving multiple qualitative methods (focus groups and surveys) and advanced impact modeling (predictive modeling and cost-benefit analysis). Patients and health care professionals were identified and recruited from 3 partnering regions in Spain, Sweden, and the United Kingdom via electronic health record screening.

Results: The technology trial in this 4-year funded project (2016-2020) concluded in April 2020. The pilot technology trial for evaluation phases 3 and 4 was launched in November 2019 and carried out until April 2020. Data collection for these phases is completed with promising results on platform acceptance and socioeconomic impact. We believe that the phased, iterative approach taken is useful as it involves relevant stakeholders at crucial stages in the platform development and allows for a sound user acceptance assessment of the final product.

Conclusions: Patients with multiple chronic conditions often experience shortcomings in the care they receive. It is hoped that personalized care plan platforms for patients and collaboration platforms for members of MDTs can help tackle the specific challenges of clinical guideline reconciliation for patients with multimorbidity and improve the management of polypharmacy. The initial evaluative phases have indicated promising results of platform usability. Results of phases 3 and 4 were methodologically useful, yet limited due to the COVID-19 pandemic.

Trial Registration: ClinicalTrials.gov NCT03834207; https://clinicaltrials.gov/ct2/show/NCT03834207

International Registered Report Identifier (IRRID): RR1-10.2196/21994

(JMIR Res Protoc 2022;11(7):e21994) doi:10.2196/21994

KEYWORDS

multimorbidity; polypharmacy; guidelines reconciliation; clinical decision support; personalized care plans; diabetes mellitus type 2; heart failure; depression; renal failure; acceptability; usability; evaluation; cost-benefit evaluation; predictive modeling

Introduction

Older age is associated with an increased accumulation of multiple chronic conditions called multimorbidity and includes functional and cognitive impairments. More than half of all older people have at least three chronic conditions and a significant proportion have 5 or more [1]. Chronic diseases take many forms such as hypertension, depression, diabetes mellitus type 2, and renal failure. They are the main reasons for poor health and a restricted activity. They impact over one-third of the European population and represent 70% of the health care expenditure in Europe [2].

The management of care for patients with multimorbidity is more complex and time consuming than those with a single disease [3]. Managing multiple diseases concurrently creates an added challenge for health service delivery and provision. Therefore, many individuals with chronic and long-term care needs experience shortcomings in the care they receive. One reason for this is the inconsistency across single-disease clinical guidelines when they cover situations with more than 1 disease. Current European medical models are often dictated by national clinical guidelines, which focus primarily on managing a single disease. Evidently, this can cause inconsistencies and provide contradictory information when providers are following more than 1 guideline for their patient. Furthermore, it can result in avoidable inefficiency for patients and health systems, for example, incompatible treatment regimens and duplicate clinical visits and tests [4].

Polypharmacy, induced by multimorbidity, is itself an important factor that leads to an increased risk of further complications in the provision of safe and effective care for patients, as well as the increased potential for adverse drug interactions and events [5]. Because the polypharmacy redundancy and duplication of medication are common, it not rare for elderly patients to be taking 9 or more medications concurrently [6]. This current approach of managing multimorbidity also fails to integrate care across providers and the interactions of chronic diseases and their treatments are overlooked [7]. As the number and complexity of health conditions increase with age, the type and number of care providers also increase. This often leads to fragmented care: it becomes significantly more difficult for providers to align and coordinate care teams and settings. This is exacerbated by poor interprofessional communication and lack of appropriate information-sharing infrastructure that exists in many health systems and even at local level. Without secure information exchange among the actors involved in health, social, and informal care services, it becomes almost impossible to reconcile potentially conflicting treatment plans or avoid potentially harmful interventions. An insufficient information exchange complicates the application of data-processing techniques developed under paradigms such as data science, machine learning, and artificial intelligence that could support medical decision making with information analysis and predictive models.

Moreover, patients and their informal caregivers often do not have a voice in the management of their own care. This can lead to patients feeling disempowered, less well informed, and therefore less likely to follow the treatment regime "imposed" on them. Among elderly people, noncompliance has a prevalence of 25%-75% and the likelihood rises in proportion to the number of drugs and daily doses prescribed [8]. There is an increasing need to focus care organization on a patient with multiple diseases, rather than targeting each disease separately. This requires a patient-centered approach: considering each patient's multiple physical conditions, psychosocial conditions, and the realities of multimorbidity and polypharmacy. An

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interactive collaborative environment is needed to address these issues in the current care of patients with multimorbidities.

In response, C3-Cloud, a European Commission–supported Horizon 2020 innovation project, was created to pilot test collaborative computer platforms for patients and members of the multidisciplinary teams (MDTs) in 3 different European settings. The aims of the platform are to improve the provision of integrated care for patients with multimorbidity, resolve guideline conflicts (by reconciliation of varying, and potentially conflicting, recommendations from single-disease clinical guidelines), support clinical decision making through clinical decision support services, and facilitate communication among MDT members and with the patients through an interoperable platform (Multimedia Appendix 1). Traditional, "paper-based" health records have strong limitations for the integration of care or collaborative decision making and electronic health records (EHRs) attempt to widen the scope of health records [9]. As the health care landscape is ever changing, EHRs have the potential to replace paper records and add many more capabilities, beyond mere replication of data in an electronic format. New tools such as C3-Cloud can enhance the interaction among MDTs, patients, and their informal caregivers. The objective of this study is to determine the impact the platform will have on patients, MDT members, and health systems with the guiding research question being "Is the use of a personalized ICT tool that facilitates coordinated care planning, treatment optimization, and patient self-management acceptable to patients with multiple long-term conditions and their team of health professionals?". The overall C3-Cloud system architecture is shown in Multimedia Appendix 2 and Multimedia Appendix 3 describes the main components of the C3-Cloud system.

The purpose of this paper is to present the research protocol of the C3-Cloud technology trial as a sustainable protocol guiding the development, testing, and evaluation of other interactive health care platforms targeting patients and MDT members.

Methods

Ethical Considerations

The study received favourable ethical approval from the three pilot regions: In the UK, the North of Scotland Research Ethics Committee approved the study (Integrated Research Application System (IRAS) project ID 224635, 25 May 2018); in Spain, the Basque Ethical Board - Comité de Ética de la Investigación con medicamentos de Euskadi (CEIm-E) - approved the study (PI2018006, 14 May 2018); in Sweden, the Northern Ethical Review Board - Regionala etikprövningsnämnden i Umeå – approved the study (Dnr 2018-3-31M, 5 April 2018). All associated amendments were also approved.

Study Design

The C3-Cloud study used a mixed method research design to gain insights into the usability, acceptance, and usefulness of the C3-Cloud system. The project has developed an innovative care planning system called "C3-Cloud," which was tested with patients, their informal caregivers, and health care professionals in the United Kingdom (South Warwickshire), Sweden (Region Jämtland Härjedalen), and Spain (Basque Country). The tests and evaluation activities generated data to assess the usability and usefulness of the C3-Cloud system as well as its acceptance and satisfaction among user groups. The study was designed to go through 4 evaluation phases. The adoption of phases corresponded to the study's aims to develop the C3-Cloud system together with its users in an iterative approach of testing, feedback, and subsequent improvements, which is in line with the UK's Medical Research Council (MRC) recommendations for carrying out complex interventions. The MRC suggests employing modeling and exploratory trials before aiming to carry out randomized controlled trials [10]. Following this advice, the project was designed to evaluate the system through 4 phases (Figure 1). All 4 phases are methodologically important for the successful testing of the C3-Cloud system. For this work, however, we focus on phases 3 and 4. The first 2 phases of the project will respectively be published in a separate paper. The user-centered design of phase 1 has been published deliberately already [11].

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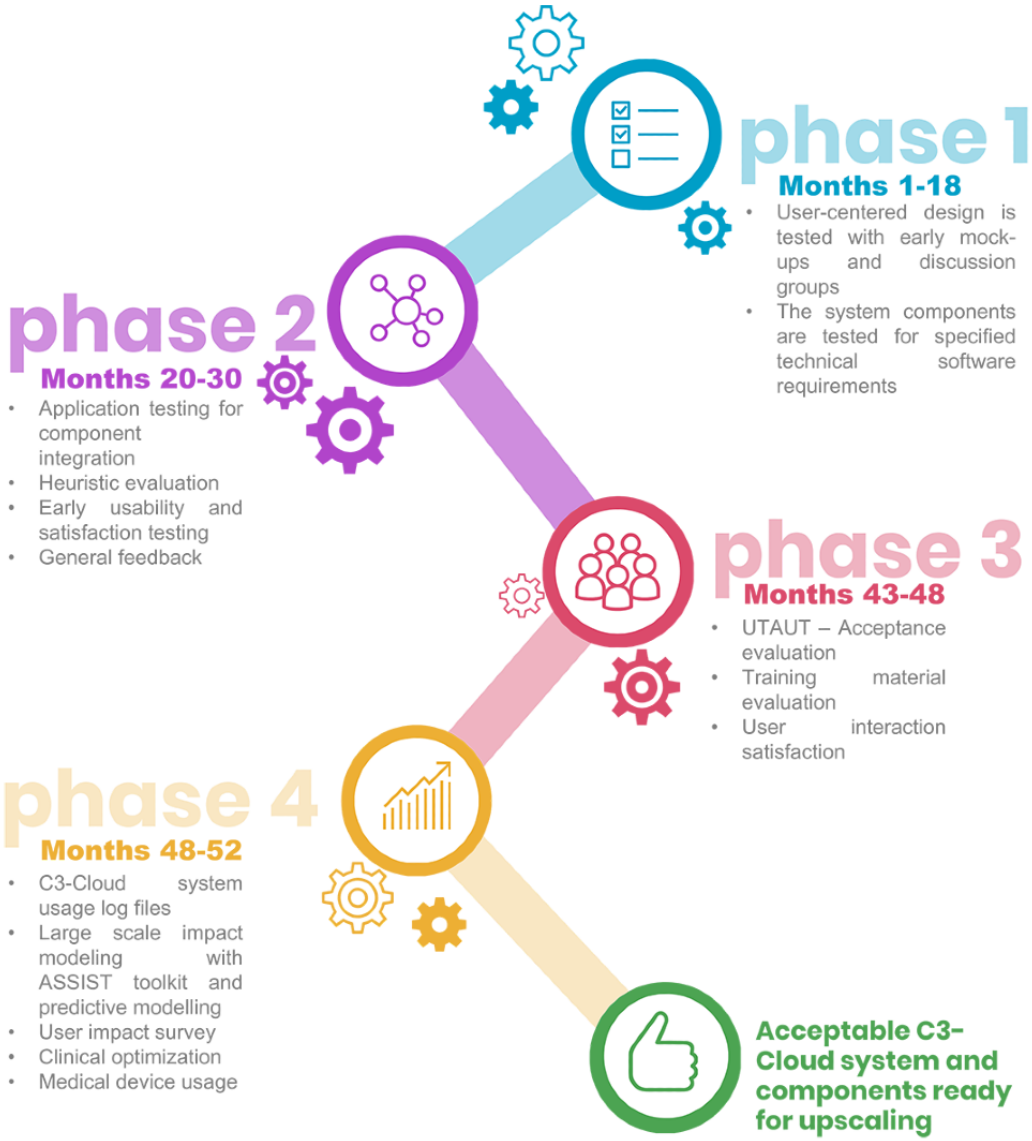
Figure 1. C3-Cloud system evaluation phases. UTAUT: Unified Theory of Acceptance and Use of Technology.



Study Development and Timeline

After the initial evaluations and trials, the C3-Cloud system has been deployed at the pilot sites, which was followed by pilot phase 3 with a larger number of users compared with phases 1 and 2. The project aimed for a 6-month exploratory technology trial (phase 3), followed by a few months for system acceptance analysis and impact assessment of C3-Cloud in phase 4 (Figure 1). All test participants' data as well as patient and clinician data were retrieved anonymously or anonymized and aggregated in the pilot sites before sharing the data sets for analysis. Control group data for the period of phase 4 were extracted from care centers in the pilot sites in April 2020. The anonymously retrieved information was on health care resource consumption. To ensure that data cannot be traced, the data extracts did not include demographic descriptors and identifiers. Data entry of resource utilization dates was manipulated automatically and randomly within a range of ±30 days for each entry.

Study Setting

A technology trial was used to test the C3-Cloud system with MDT members, patients, and their informal caregivers (when available). The technology trial ran for 6 months and took place in 3 European pilot site regions: Basque Country, Spain; Jämtland Härjedalen, Sweden; and South Warwickshire, United Kingdom. Study settings included various locations that are relevant for the provision of health care, for example, health care centers, general practitioner offices, hospitals, and patients' homes. The technology trial is registered at ClinicalTrials.gov (identifier: NCT03834207).

Sampling and Recruitment

The recruitment period for patients started 3 months before the launch of the pilot test to allow sufficient time for the identification of eligible participants and obtaining informed consents, while also keeping the period between recruitment and piloting start as short as possible.

MDT members were contacted individually by pilot site managers using convenience sampling, considering their individual profiles, willingness to participate, and a few general inclusion criteria (Multimedia Appendix 4). This nonprobabilistic sampling involves the sampling of MDT

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members that are nearby, aiming for a total sample size of 62 across the 3 pilot sites.

For the iterative evaluation phase 3 and phase 4, we defined the patient number that we need to observe based on power calculations as the "observation goal," which was 420 patients. An unknown number of patients may withdraw from their participation during the technology trial. Thus, we added a 25% dropout margin to the observation goal, summing up to 526 patients to be recruited for the piloting trial participation (ie, the "recruitment goal"). This dropout margin had been added because the average dropout rate across all clinical trials was expected at around 30% [12]. This, however, varies based on the participants level of income, education, etc. (the higher the income, education, etc., the lower the dropout rate) and because our pilot sites are located in higher-income areas with a comparatively higher level of education, it was concluded that the dropout rate would be slightly lower than the average. Furthermore, there are meta-analytical studies that similarly concluded with approximately 30% dropout rate, although with a wide variability [13]. This conclusion was further supported by the fact that many eligible patients already knew their MDTs; hence, a slightly higher-than-average cooperation and lower dropout rate were expected.

It was anticipated that several patients that were approached for participation would decline from the outset. Accordingly, the number of patients that were approached for participation (ie, the "approaching goal") was 16% larger than the recruitment goal, summing up to 610 intervention patients across the 3 pilot sites. The number of comparator patients whose resource consumption data were monitored anonymously matched the intervention patient numbers at each pilot site.

Potential candidates were selected through each pilot site screening their databases for eligible patients who met the inclusion and exclusion criteria (Multimedia Appendices 4 and 5). No inclusion criteria for informal caregivers have been defined; however, exclusion criteria will be applied (Multimedia Appendix 4). Once the pilot sites have provided a list of eligible patients, they were randomized as study candidates to avoid selection bias. A first randomization round generated candidate lists that were 16% larger than the actual patient recruitment target per pilot site (including a 25% dropout rate), to adjust for patients that were approached but denied their participation.

Table 1 details the number of involved participants per pilot site and evaluation phase. The number of trial participants in each pilot site for evaluation layer 4 reads as follows: "minimum number of trial participants as calculated for the observation goal + 25% dropout rate (recruitment goal) + 16% denial rate (approaching goal)" and sums the total number of trial participants that were approached for participation.

Table 1. Number of trial participants to approach.

Pilot region	Phase 3: Exploratory trial for application evaluation		Phase 4: Monitoring to model large-scale impact		
	Patients	MDT[a] members	Patients	Comparator patients	MDT members
South Warwickshire	50	16	70 + 18 + 14	102	16
Basque Country	50	16	175 + 44 + 35	254	16
Jämtland Härjedalen	50	30	175 + 44 + 35	254	30
Total	150	62	610	610	62

[a]MDT: multidisciplinary team.

Research assistants at each site contacted (email, mail, phone, or face-to-face meetings) the selected study candidates and provided material and information about the study and its objectives. Supportive activities such as videos and presentations were sometimes used in a supplementary role to clarify any questions. Candidates who agreed to participate in the study had to sign an informed consent form for documentation to confirm they have read and understood the information and wanted to participate in the technology trial.

Study Procedure

Early in the pilot technology trial a training was offered for all participants on how to use the platforms. The pilot technology trial was used to evaluate the user experience, satisfaction, and acceptability of the C3-Cloud application as well as the patient training material (phase 3). It also served to obtain anonymous patient data on resource usage for impact modeling and sustainability planning for upscaling C3-Cloud in phase 4. At the start of the trial, the patients had a care plan created on the C3-Cloud system that they developed and managed with their health care professionals during the study. Once the patient's care plan was prepared, they were given access to the C3-Cloud system to view and update their care plan whenever they wished. Moreover, patients were able to send messages to their care team members via the system. The patients care plan in the C3-Cloud system was reviewed and adapted each time they visited a health care professional who was also taking part in the technology trial.

In the final phase of the project a comparison was made on the care and treatment received by patients that have used the system and those that have not (the comparator patient group). The comparator group data were taken from similar patients and retrieved anonymously from the local health care systems. Initial screening showed that a sufficient number of similar patients was available for data retrieval in the systems. These data contributed to determining the full impact of C3-Cloud by assessing the use of health care resources and medication prescription across both groups of patients (phase 4).

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Phase 3

Overview

This phase evaluated the user experience, satisfaction, and acceptance of the C3-Cloud application and patient training material by collecting evaluation data. Data were collected from a subset of participants (150 patients and 52 MDT members) from questionnaires they completed. Data on user experience and satisfaction were collected from the training material questionnaire and the validated Questionnaire on User Interaction Satisfaction (QUIS). The data collected on acceptability of the technology were obtained through a refined version of the validated Unified Theory of Acceptance and Use of Technology (UTAUT) questionnaire. The questionnaires were administered as an online survey a few weeks after the trial start and at the trial end. Trial participants were able to obtain the link to the online survey via the messaging service of the platforms, which ensured that no participant was contacted by the evaluation team directly, thereby avoiding confidentiality breaches. No incentives were provided for completing the surveys. The surveys were open for 3 weeks.

The Training Material Questionnaire

The training material was assessed from the survey that patients answered after the training period to determine whether they and their informal caregivers found the materials useful and informative. Data were gathered on user experience and whether users felt more knowledgeable about their conditions and if they felt enabled to use C3-Cloud to take care of their conditions after the training. It also considered whether the materials are a contributing factor to improve care coordination.

The Questionnaire for User Interaction Satisfaction

Similar to the early usability testing with a limited number of test users, the QUIS7 questionnaire [14] was used for both MDT members and patients when the technology trial was in full scope and it was administered partly after the initial user training at the beginning of the trial and partly at the end of the trial. The results from both questionnaires were compared and used, in an iterative fashion, for shaping the design and re-design of the C3-Cloud platform and for providing recommendations for areas of improvement.

The Unified Theory of Acceptance and Use of Technology Questionnaire

A C3-Cloud–adapted version of the UTAUT questionnaire [15] was used, covering some of the original UTAUT modules. The UTAUT is developed to predict individual adoption and use of new information technologies (ITs). It posits that individuals' behavioral intention to use an IT is determined by 2 beliefs: *perceived usefulness*, which is defined as the extent to which a person believes that using an IT will enhance his or her job performance, and *perceived ease of use*, which is defined as the degree to which a person believes that using an IT will be free of effort. A shortened version of UTAUT was administered at the beginning of the pilot trial, just after participants have had training sessions on how to use the C3-Cloud components. This version included the following UTAUT modules: performance expectancy, effort expectancy, social influence, technology anxiety, adoption timeline, and behavioral intention. The questionnaire was administered again in a more comprehensive manner shortly before the end of the trial. This second version included the additional modules *cultural trends* and *language factors*. The results from the initial UTAUT were compared with the closure UTAUT questionnaire to evaluate the differences in acceptance and use of C3-Cloud technology over the trial duration.

Phase 4

Overview

In Phase 4 modeling for large-scale impact of C3-cloud implementation after the technology trial was performed. The health and economic benefits of the intervention at the population level were evaluated to gain insights into savings that C3-Cloud could generate systemically in the long term. The digitalization of clinical patient histories and the coding of all contacts between patients and their MDTs into the EHR allowed to better understand the health demand of a population and to quantify the health and social burden of the disease. For this quantification, health care resource usage data of all patients were used and compared using modeling techniques with anonymous comparator patient data. The modeling tool used for this analysis has been developed by merging discrete event simulation modeling methods with a cost-benefit assessment tool [16]. The merger tool (Textbox 1) helped predict the return on investment and time to break even for integrated care implementation at a large scale. It was used to inform decision making in the management of integrated care in general and on the expected impact of scaling up the use of C3-Cloud. The aim was to develop a combined tool taking advantage of 2 existing approaches (ASSIST or Assessment and evaluation tools for telemedicine and telehealth [16] and predictive modeling [17,18]) that have been previously applied in other European projects such as CareWell [19] and SmartCare [20]. Merging them aimed to improve reliability and validity of the tool by incorporating the comprehensive perspective applied by ASSIST and the flexible engine developed in predictive modeling to represent mathematically the natural history of the disease. The conceptual model included not only the health system but also the complete set of stakeholders. Model parameterization was a challenge as data required for all stakeholders could not be obtained from evidence-based sources. The data focused on health care resource utilization, frequency of use of C3-Cloud components, and service satisfaction. The data needed for this type of modeling were taken from administering additional questionnaires to participants: the eCare Client Impact Survey (eCCIS) for patients; the eCare User Impact Survey (eCUIS) for MDT members; and a few additional questionnaire items for patients, MDT members, and informal care givers.

In addition, C3-Cloud log files and EHR exports were taken from EHRs of the intervention and comparator patients to evaluate the differences in health care resource utilization during the trial. This included, for example, changes to drug use, readmissions, number of adverse drug events, number of virtual sessions, or resource redistribution. The comparator group was taken from another practice and statistically adjusted for the differences based on historic data.

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Textbox 1. Predictive modeling.

ASSIST Cost-Benefit Analysis Tool

ASSIST (Assessment and evaluation tools for telemedicine and telehealth) is an assessment and evaluation tool originally developed for use in the context of telemedicine and telehealth services, specifically to assess the economic viability of telemedicine pilot projects [16]. During the validation phase, ASSIST was successfully applied by 5 telemedicine projects. A core aim of ASSIST is to facilitate the transposition of a pilot project into routine service operation and to support service providers in achieving a sustainable economic model where service benefits are higher than service costs. It also facilitates the transposition of a pilot project into routine service operation and supports service providers in achieving a sustainable economic model. The assessment process of the tool includes 3 steps:

1. *Service assessment model setup:* the service change is analyzed to identify the key components such as applicable governance and the reimbursement model, stakeholders, and financial impacts (costs and benefits on the stakeholders).

2. Data collection and monetization.

3. *Calculation of performance measure:* the main outcome measure is based on the ratio of total costs to total benefits, that is, including financial costs and benefits, resource costs and benefits, and intangible costs and benefits.

Predictive Modeling

Predictive modeling serves to calculate the budget impact analysis by reproducing the natural history of patients with multimorbidity in both the standard scenario and the new scenario related to the new intervention, which results in implementation, effectiveness (ie, how does the new intervention affect the number of contacts to health professionals), and costs. A budget impact analysis projects the burden of the target population within the conventional or baseline scenario and analyses how this burden would change if the intervention achieved the organizationally defined goal. The list of parameters for the modeling is listed in Multimedia Appendix 6.

The eCare Client Impact Survey and the eCare User Impact Survey

The eCCIS and eCUIS were used to evaluate the utility that the C3-Cloud application brought to the patients and MDT members. It measures how patients and informal carers perceived the utility of C3-Cloud. To this could be added scales addressing time use, willingness-to-pay, and perception of care integration. In addition, the overall satisfaction with the C3-Cloud system as a service, whether the service is worth the effort involved in using it, and whether the respondents would want to continue using the service or to use it again are evaluated.

Additional Questionnaire Items

A few questionnaire items have been added to the surveys to evaluate the impact of C3-Cloud implementation on patients, their informal caregivers, MDT members, and the wider service system. This was administered early in the trial and again at trial closure. The evaluation used open and closed questionnaires, targeting patients and MDT members. It evaluated the impact of the different software components and focused on the following evaluation topics: usefulness, ease of use/usability, safety, process quality and changes, and the respondents' perspective on clinical optimization.

Medical Devices Questionnaire

In addition, medical sensor device usage and connected device usage were evaluated with a subset of patients at the Region Jämtland Härjedalen pilot site only. Patients were individually selected from the group of intervention patients at the discretion of local clinicians. The testing served to evaluate the technical possibility of including sensor and connected devices as part of the patient care planning.

Results

The pilot testing (phase 3) was carried out from November 2019 to April 2020. Difficulties were experienced in recruiting the envisaged number of trial participants, specifically with the intervention patients (Figure 2).

The technology trial protocol was submitted in several revisions to the 3 regional ethics committees in reflection of updates regarding project information that would be communicated to trial participants, the methods of accessing and using control group patient data, the recruitment procedure of patients, trial participants training, or adaptations to some questionnaires.

Data collection was completed in April 2020 with a total of 230 patients and 125 MDT members. The evaluation results of the pilot technology trial were analyzed and reported in a project report in June 2020 [21]. The main challenge with the technology trial evaluation was a limited data basis due to recruitment issues, a trial duration that was too short to show many significant differences in resource use for mild and moderate conditions that were included, and only a small number of returned surveys, mainly due to the COVID-19 pandemic, which dramatically reduced the use of the C3-Cloud platforms, and partially as the surveys were too lengthy. Although the methodological evaluation setup has proven feasible and useful, the evaluation results have limited validity and reliability.

Generally, acceptance and perceived usefulness of the C3-Cloud platforms are just slightly positive with only little variation between patients, informal care givers, and the MDT members.

A follow-up trial confirming the acceptance and evaluation of clinical impacts is also highly recommended.

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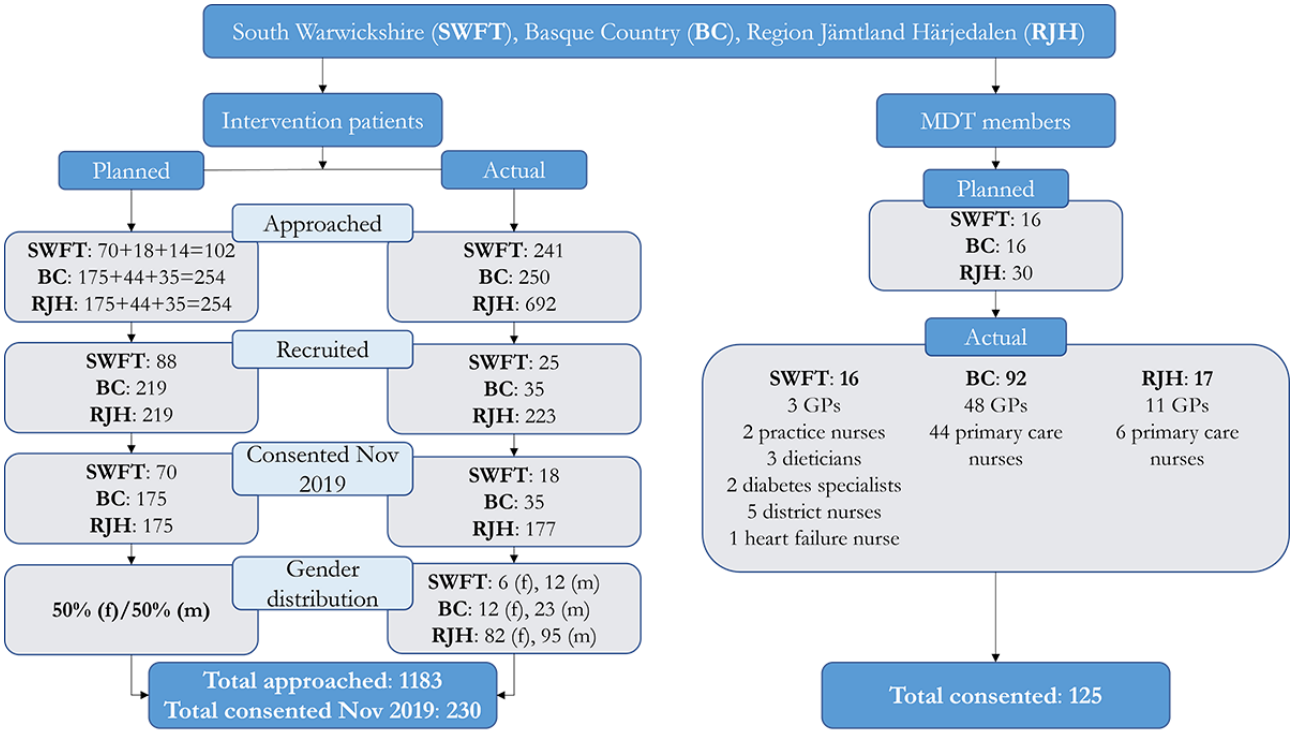
Figure 2. Number of trial participants (summary). GP: general practitioner; MDT: multidisciplinary team.



Strengths of the approach taken are that it allowed for an early feedback to the software developers for further improvement of the software before starting the technology trial with an increased number of patients and MDT members in real settings. The combination of structured and unstructured feedback from the test sessions complemented each other. However, the validity of test results may be reduced based on the dependency on test participant's fluency in the English language and the unequal distribution of test users across the pilot sites. Trial duration, patient and MDT member numbers, and usage frequency during the trial should be carefully considered.

Discussion

This paper has presented the research protocol of the C3-Cloud technology trial as well as the development of the C3-Cloud platforms C3DP (Coordinated Care and Cure Delivery Platform) and PEP (Patient Empowerment Platform). C3-Cloud has developed a modified impact modeling tool in phase 4 (a merger of the ASSIST tool and predictive modeling) for informing integrated care management on a large-scale deployment potential of systems such as C3DP and PEP. The full results were reported in a project report [21]. The number of patients and MDT members varies across the 3 pilot sites based on convenience sampling as participation depends fully on the commitment of the pilot site organizations. Socioeconomically, it was determined that general practitioner and nurse consultations (0.63 and 0.74 times less likely), nurse home visits (0.45 times less likely), and the use of accident and emergency services (0.57 times less likely) have developed positively for patients using C3-Cloud, while nurse telephone consultations increased (1.6 times more likely). An overall positive systemic socioeconomic return of 228% (Basque Country, Spain), 285% (South Warwickshire, United Kingdom), and 399% (Jämtland Härjedalen, Sweden) was modeled for the 3 pilot sites [21].

The C3-Cloud system is designed in such a way that patients can work more closely with their health care professionals to create, develop, and manage their personal care plans. The platforms enable care plans to be personalized for multimorbid conditions through systematic and semiautomatic reconciliation of digitally represented clinical guidelines. Their commitment was crucial to conduct the technology trial throughout the different phases.

The research design leans on the MRC guidance for complex interventions [10]. The usefulness of complex interventions is determined also by the way they are implemented [22]. At the time of running the evaluation, C3-Cloud was in an early development and implementation phase and solutions needed thorough testing along various dimensions to better understand the benefits of information and communication technology in health care and to respond to the challenge of implementing complex interventions.

The results are available as open published results and to some extent as open-source software for other parties to make use of. Parts of the present technical solutions will be used in the follow-up project AdLife [23] or may be offered for routine expanded use in the 3 pilot regions and of course also in a wider scale throughout these countries, using the spin-off entity "C3-Cloud Partnership Ltd."

The strong inclusion and commitment by the public health care organizations in the 3 regions imply that there is a strong probability of the results to be transformed into routine improved health care services for this important group of patients. Future research may include the possible reorganization of multiprofessional care services for elderly patients using collaboration tools such as C3-Cloud as well as by establishment of more decision support tools based on clinical guidelines for other conditions than the 4 diseases tested in the project.

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Acknowledgments

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Conflicts of Interest

None declared.

Multimedia Appendix 1
C3-Cloud platform aims.
[PNG File , 243 KB - resprot_v11i7e21994_app1.png]

Multimedia Appendix 2
Overall C3-Cloud architecture.
[PNG File , 266 KB - resprot_v11i7e21994_app2.png]

Multimedia Appendix 3
C3-Cloud terminology.
[DOCX File , 32 KB - resprot_v11i7e21994_app3.docx]

Multimedia Appendix 4
Inclusion and exclusion criteria for patients and informal caregivers.
[DOCX File , 34 KB - resprot_v11i7e21994_app4.docx]

Multimedia Appendix 5
Diagnosis codes used for patient screening.
[DOCX File , 33 KB - resprot_v11i7e21994_app5.docx]

Multimedia Appendix 6
Full set of parameters for the predictive modeling.
[DOCX File , 27 KB - resprot_v11i7e21994_app6.docx]

References

1. Luppi F, Franco F, Beghe B, Fabbri LM. Treatment of Chronic Obstructive Pulmonary Disease and Its Comorbidities. Proceedings of the American Thoracic Society 2008 Dec 01;5(8):848-856. [doi: 10.1513/pats.200809-101th]
2. European Commission. Communication from the Commission to the European Parliament and the Council: Taking forward the Strategic Implementation Plan of the European Innovation Partnership on Active and Healthy Ageing. European Commission. 2012. URL: https://eur-lex.europa.eu/legal-content/EN/ALL/?uri=CELEX%3A52012DC0083 [accessed 2022-05-10]
3. Australian Institute of Health and Welfare. Comorbidity of cardiovascular disease, diabetes and chronic kidney disease in Australia. Australian Institute of Health and Welfare. 2007. URL: https://www.aihw.gov.au/getmedia/63851abe-7339-4730-bd82-02dc647690be/cocddackdia.pdf.aspx?inline=true [accessed 2022-05-10]
4. Guthrie B, Payne K, Alderson P, McMurdo MET, Mercer SW. Adapting clinical guidelines to take account of multimorbidity. BMJ 2012 Oct 04;345(oct04 1):e6341. [doi: 10.1136/bmj.e6341] [Medline: 23036829]
5. NHS Improvement-Lung. Managing multi-morbidity in practice, what lessons can be learnt from the care of people with COPD and co-morbidities? NHS. 2013. URL: https://www.educationforhealth.org/wp-content/uploads/2015/03/COPD_MultiMorbidities.pdf [accessed 2022-05-10]

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RenderX

6. Haque R. ARMOR: A Tool to Evaluate Polypharmacy in Elderly Persons. Annals of Long-Term Care 2009 Jun:26-30 [FREE Full text]
7. Pavlickova A. EPPOSI AIP-CCM White Paper: Building a Workable Model for the Holistic Management of Chronic Conditions in Europe. Brussels, Belgium: Epposi (European Platform for Patients' Organisations, Science & Industry); 2012.
8. Gellad WF, Grenard JL, Marcum ZA. A systematic review of barriers to medication adherence in the elderly: looking beyond cost and regimen complexity. Am J Geriatr Pharmacother 2011 Feb;9(1):11-23 [FREE Full text] [doi: 10.1016/j.amjopharm.2011.02.004] [Medline: 21459305]
9. Evans RS. Electronic Health Records: Then, Now, and in the Future. Yearb Med Inform 2018 Mar 06;25(S 01):S48-S61. [doi: 10.15265/iys-2016-s006]
10. Craig P, Dieppe P, Macintyre S, Michie S, Nazareth I, Petticrew M, Medical Research Council Guidance. Developing and evaluating complex interventions: the new Medical Research Council guidance. BMJ 2008 Sep 29;337:a1655 [FREE Full text] [doi: 10.1136/bmj.a1655] [Medline: 18824488]
11. Traore L, Assele-Kama A, Keung SNLC, Karni L, Klein GO, Lilja M, et al. User-Centered Design of the C3-Cloud Platform for Elderly with Multiple Diseases - Functional Requirements and Application Testing. Stud Health Technol Inform 2019 Aug 21;264:843-847. [doi: 10.3233/SHTI190342] [Medline: 31438043]
12. Bairu M, Weiner MW. Global Clinical Trials for Alzheimer's Disease. Design, Implementation, and Standardization. Oxford, UK: Academic Press; 2014.
13. Lappan SN, Brown AW, Hendricks PS. Dropout rates of in-person psychosocial substance use disorder treatments: a systematic review and meta-analysis. Addiction 2020 Feb 06;115(2):201-217. [doi: 10.1111/add.14793] [Medline: 31454123]
14. Norman K, Shneiderman B, Harper B, Slaughter L. QUIS: Questionnaire for User Interaction Satisfaction 7.0. Institute for Systems Research. URL: https://isr.umd.edu/news/news_story.php?id=4099 [accessed 2019-09-11]
15. Venkatesh, Morris, Davis, Davis. User Acceptance of Information Technology: Toward a Unified View. MIS Quarterly 2003;27(3):425. [doi: 10.2307/30036540]
16. Hammerschmidt R, Meyer I. Socio-Economic Impact Assessment and Business Models for Integrated eCare. In: Achieving Effective Integrated E-Care Beyond the Silos. Pennsylvania, PA: IGI Global; 2014:135-163.
17. Larrañaga I, Stafylas P, Fullaondo A, Apuzzo GM, Mar J. Economic Evaluation of an Integrated Health and Social Care Program for Heart Failure Through 2 Different Modeling Techniques. Health Serv Res Manag Epidemiol 2018 Dec 03;5:2333392818795795 [FREE Full text] [doi: 10.1177/2333392818795795] [Medline: 30547054]
18. Soto-Gordoa M, Arrospide A, Merino Hernández M, Mora Amengual J, Fullaondo Zabala A, Larrañaga I, [on behalf of the CareWell group]. Incorporating Budget Impact Analysis in the Implementation of Complex Interventions: A Case of an Integrated Intervention for Multimorbid Patients within the CareWell Study. Value Health 2017 Jan;20(1):100-106 [FREE Full text] [doi: 10.1016/j.jval.2016.08.002] [Medline: 28212950]
19. empirica GmbH. CareWell Project. empirica GmbH. URL: http://carewell-project.eu/ [accessed 2019-09-06]
20. empirica GmbH. Smartcare Project. empirica GmbH. URL: http://pilotsmartcare.eu/ [accessed 2019-09-06]
21. Arvanitis TN. C3-Cloud Project. C3-Cloud. 2020. URL: https://c3-cloud.eu/wp-content/uploads/2020/12/D9.6.pdf [accessed 2022-05-09]
22. Soto-Gordoa M, de Manuel E, Fullaondo A, Merino M, Arrospide A, Igartua JI, CareWell Group. Impact of stratification on the effectiveness of a comprehensive patient-centered strategy for multimorbid patients. Health Serv Res 2019 Apr 22;54(2):466-473 [FREE Full text] [doi: 10.1111/1475-6773.13094] [Medline: 30467846]
23. de Manuel Keeno E. ADLIFE. URL: https://adlifeproject.com/ [accessed 2022-05-10]

Abbreviations

ASSIST: Assessment and evaluation tools for telemedicine and telehealth
eCCIS: eCare Client Impact Survey
eCUIS: eCare User Impact Survey
EHR: electronic health record
IT: information technology
MDT: multidisciplinary team
MRC: Medical Research Council
QUIS: Questionnaire on User Interaction Satisfaction
UTAUT: Unified Theory of Acceptance and Use of Technology

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Protocol

Developing, Implementing, and Evaluating an Artificial Intelligence–Guided Mental Health Resource Navigation Chatbot for Health Care Workers and Their Families During and Following the COVID-19 Pandemic: Protocol for a Cross-sectional Study

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Abstract

Background: Approximately 1 in 3 Canadians will experience an addiction or mental health challenge at some point in their lifetime. Unfortunately, there are multiple barriers to accessing mental health care, including system fragmentation, episodic care, long wait times, and insufficient support for health system navigation. In addition, stigma may further reduce an individual's likelihood of seeking support. Digital technologies present new and exciting opportunities to bridge significant gaps in mental health care service provision, reduce barriers pertaining to stigma, and improve health outcomes for patients and mental health system integration and efficiency. Chatbots (ie, software systems that use artificial intelligence to carry out conversations with people) may be explored to support those in need of information or access to services and present the opportunity to address gaps in traditional, fragmented, or episodic mental health system structures on demand with personalized attention. The recent COVID-19 pandemic has exacerbated even further the need for mental health support among Canadians and called attention to the inefficiencies of our system. As health care workers and their families are at an even greater risk of mental illness and psychological distress during the COVID-19 pandemic, this technology will be first piloted with the goal of supporting this vulnerable group.

Objective: This pilot study seeks to evaluate the effectiveness of the Mental Health Intelligent Information Resource Assistant in supporting health care workers and their families in the Canadian provinces of Alberta and Nova Scotia with the provision of appropriate information on mental health issues, services, and programs based on personalized needs.

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Methods: The effectiveness of the technology will be assessed via voluntary follow-up surveys and an analysis of client interactions and engagement with the chatbot. Client satisfaction with the chatbot will also be assessed.

Results: This project was initiated on April 1, 2021. Ethics approval was granted on August 12, 2021, by the University of Alberta Health Research Board (PRO00109148) and on April 21, 2022, by the Nova Scotia Health Authority Research Ethics Board (1027474). Data collection is anticipated to take place from May 2, 2022, to May 2, 2023. Publication of preliminary results will be sought in spring or summer 2022, with a more comprehensive evaluation completed by spring 2023 following the collection of a larger data set.

Conclusions: Our findings can be incorporated into public policy and planning around mental health system navigation by Canadian mental health care providers—from large public health authorities to small community-based, not-for-profit organizations. This may serve to support the development of an additional touch point, or point of entry, for individuals to access the appropriate services or care when they need them, wherever they are.

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KEYWORDS

eHealth; chatbot; conversational agent; health system navigation; electronic health care; mobile phone

Introduction

Background and Rationale

Mental disorders are the leading cause of disability in Canada; approximately 1 in 3 Canadians will experience substance use or mental health disorders in their lifetime [1,2]. Unfortunately, there are also significant gaps in care. According to a 2018 study, 5.3 million Canadians expressed a need for mental health services in a 12-month period [3]. Of these, 43.8% reported that their mental health needs were not being adequately met [3]. Of those reporting unmet or only partially met needs, 78.2% identified personal circumstances, including affordability and not knowing where to receive help, as barriers to care [3].

Barriers to seeking support include stigma, denial, concerns over privacy, and difficulty connecting effectively with a care provider [4-7]. In addition, prominent access issues include fragmented or episodic care, lack of support for navigating the health care system and connecting with an appropriate provider or specialist, and long wait times to access services [4-10].

Canada's publicly funded health care system is administered and delivered by the provinces and territories through public health authorities or entities operating on a nonprofit basis. Hospitals and other health care services deemed medically necessary must be insured by provincial and territorial plans. Many citizens acquire additional private insurance to pay for unfunded services [11]. Mental health care coverage across Canada varies widely, and many available services are not deemed medically necessary despite mental health being increasingly recognized as fundamental to health. Only mental health services received in hospital settings are covered universally by Canada's public health system. Mental health care in Canada is unique as it is provided by a "meshwork" of local hospitals, community programs, residential care centers, private practices, and more [12]. Adding to this complexity, many organizations are particular to 1 jurisdiction or specific to a certain type of mental health concern.

Canada's system has been described as a "labyrinth" where individuals may even resort to paying private sector agents to act on their behalf to find and connect with services, further exacerbating socioeconomic inequalities in access to care [13]. Many Canadians who have received unsatisfactory help for their mental health needs reported "not knowing where to go" as a primary barrier to care [14]. Testimonies of Ontario-based patients and caregivers highlight feelings of confusion in having to navigate this system on their own, resulting in longer delays in care access [15]. Wait times have been as long as 2 and a half years [14], with many individuals receiving no documented care [10]. The Wait Time Alliance 2014 Report Card highlights lack of system coordination and insufficient staff and resources as determinants of long wait times to access mental health services in Canada [15]. Heightened demands for care and lack of navigation toward community services contribute to overcrowding within emergency departments, with a 75% increase in mental health–related visits for patients aged 5 to 24 years since 2006 [16]. System integration and system navigation support services between community-based health and social services and formal health care providers have been identified as a key policy issue in Canada and other jurisdictions such as the United Kingdom [16-23], where lack of knowledge of service options often poses a barrier to referrals from health care providers to community-based services [18,23-26].

The Impact of the COVID-19 Pandemic on Mental Health

In 2019, an outbreak of COVID-19 (SARS-CoV-2) resulted in a global pandemic. By early 2022, COVID-19 had spread worldwide, with >334 million known cases and >5.5 million deaths [27]. In anticipation of a high volume of serious hospitalizations with technical respiratory needs, Canadians were asked to self-quarantine or practice social distancing to reduce the burden on health systems [28]. This intensified the mental health crisis within Canada; according to an Angus Reid Institute poll, 50% of Canadian respondents indicated that their mental health had worsened over the COVID-19 pandemic, with 10% indicating that it had worsened "a lot" [29]. Multiple public surveys deployed during the pandemic reported respondents' experiences of multiple mental health stressors such as economic instability, fear of becoming sick, and life

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disruption as a cause of the COVID-19 pandemic, resulting in stress, anxiety, and depression [30]. A recent Ontario survey revealed that approximately 25% of respondents reported unmet mental health needs as a result of the pandemic, moderate to severe anxiety, and symptoms of loneliness and depression [31].

In accordance with the negative mental health outcomes observed in this and previous epidemics and pandemics [32,33], it is widely agreed by the international medical community that a wave of widespread need for mental health–related services will result from the pandemic that will persist beyond the acute phase [30]. Within the Canadian context, in consideration of the prepandemic prevalence of mental illnesses such as depression (lifetime prevalence of 5% in Canadian men and 10% in Canadian women [34]) and insomnia (12-month prevalence ranging from 9.5% to 24% [35-38]) and existing gaps in service delivery, public health practitioners and policy leaders must urgently consider innovative ways to connect a large portion of the Canadian public with appropriate services in an efficient manner.

In addition to the negative impact on Canadians' mental health, many services have faced disruptions because of adjusting to social distancing and capacity restrictions, often eliminating face to face in lieu of remote service settings [39]. Many countries have developed new web-based mental health information sites or phone lines to provide coping support [40]. For those facing modest mental health burdens, connection with these web-based resources can aid in self-management and may provide a bridge before professional support is available [39]. With these changes in offered services and increased web-based application use, navigation to individual personalized, timely, and relevant resources is increasingly important.

The Mental Health of Health Care Workers

Health care workers and their families are particularly vulnerable during pandemics and, in reflection of anticipated needs, are the target participant group for this pilot study. Health care workers face an increase in mental health risk factors, including anxiety, burnout, and depression, because of factors such as increased exposure and risk of disease transmission to themselves or others (eg, family and friends) and unsafe (eg, personal protective gear shortages) or stressful working conditions [38]. Of concern is the trauma that health care workers witness within the workplace, how their ongoing work limits their ability to address their own mental health concerns, and how they may be processing these experiences when they are outside of the workplace with more time to reprocess what they see. For example, a recent umbrella review of meta-analyses found that the prevalence of anxiety and depression among health care workers was relatively high at 24.94% [39]. A recent survey by the Canadian Centre for Addiction and Mental Health (January 2022) documented an increase in self-reported symptoms of severe anxiety (37% compared with 23.5% in summer 2021) and depression (35.7% compared with 24.8% in summer 2021) among health care workers and other frontline workers [31], suggesting that mental health problems are being exacerbated with time. Together, these risk factors may lead to health care workers resigning from their positions, increasing staff shortages and, in turn, pressures on the remaining employees [40]. On the basis of our findings within this pilot group, we aim to further refine, scale, and spread the implementation of our chatbot to be used by Canada's general public.

Opportunities for Health Chatbots

Digital technologies provide an opportunity to bridge service gaps, increase points of access to and knowledge of the mental health care system and existing services, enhance mental health literacy, and permit greater health system and social system integration, which could improve health and social system coordination, efficiency, patient navigation, satisfaction, and overall health outcomes [41]. In addition, efficiencies realized through the use of new technology may lower health care costs, enabling resources to be redirected to other areas of priority. Artificial intelligence (AI) presents the opportunity to bypass barriers inherent to traditional brick-and-mortar health system structures, meet individuals in need in a discrete and personalized way, and connect them with services in a timely manner regardless of where they are. For example, commonly cited factors identified for why individuals choose to access web-based services include 24-hour accessibility, ease of accessibility despite geographic location, anonymity, and privacy [42-45]. Although further analysis is required in the context of mental health care, research suggests that patients report greater comfort or preference in disclosing sensitive health information to a computer or technological device than to a human [46,47]. AI then presents the opportunity to also address social stigma as a barrier to care, which may hinder an individual's drive or motivation to seek access to care.

Chatbots can be defined as computer programs that use AI methods, including natural language processing (NLP) and machine learning, to simulate conversations with human users. Existing evidence supports the use of health chatbots for empowering users to engage in physical activity and consumption of nutritious food and increasing patient access to health information, among other benefits [48-51]. Although human-computer interaction technology itself is not new as a concept, evaluative research on the use of applied AI as a tool for bridging gaps in mental health care is limited. More specifically, although chatbots currently show promise in a variety of health care settings [52-54], there is limited information on their effectiveness in supporting mental health system navigation [52,55-57]. As such, the use of a conversational chatbot for this general purpose is novel. In addition, existing chatbots are commonly tailored to address one or a limited range of mental health issues [58]. Our conversational chatbot, the Mental Health Intelligent Information Resource Assistant (MIRA), seeks to support a wide range of mental health disorders and considerations.

Most research to date has evaluated constrained client input (options that are provided to the client for input), and research on unconstrained natural language opportunities remains in its infancy [56]. Chatbots in mental health have been characterized or criticized as being predominantly rule-based (chatbot-led and controlled vs user-controlled) and are offered as stand-alone software (vs web-based software, complicating ease of client access). MIRA is a web-based, hybrid NLP and decision tree

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user-controlled AI chatbot. In this context, these features are novel in their application to the mental health space. See the *Methods* section for more details on each of these design elements.

With advances in dialogue management and conversational flexibility enabled through the establishment of complex neural networks that include sentiment analysis, chatbots within the space of mental health have the opportunity to play an important role in patient care.

Fortunately for the emergence of digital health intervention options, the uptake of technology among the general public has been substantive. There are >3.96 billion internet users internationally [59]. In Canada, 91% of the population is estimated to be actively using the internet, and 85% have a cell phone (65% have a smartphone specifically) [60,61]. As such, there remain significant opportunities to use existing and widely adopted technological infrastructure to bridge significant gaps in care and improve health outcomes for Canadians.

The MIRA Project

In this paper, our pan-Canadian, multidisciplinary team of subject matter experts, including individuals with lived experience, members of the Indigenous community, clinicians, and psychiatry and computing science experts, report on the design, implementation, and anticipated evaluation of MIRA, a domain-specific AI-enabled chatbot able to understand common taxonomies in the mental health domain and respond with relevant, appropriate resources aligned with the clients' intents and needs. The MIRA chatbot is an informational chatbot only and does not provide medical advice (ie, it does not diagnose or provide treatment recommendations), nor does it replace a counselor or mental health professional. The population group of interest for this pilot were health care workers and their families in the Canadian provinces of Alberta and Nova Scotia.

In total, 2 additional components have been developed to complement the chatbot's functionality, including a resource management portal (the MIRA Resource Portal) and a Selenium (Software Freedom Conservancy)-based [62] automated testing framework. MIRA does not search for resource recommendations extracted from the open internet. Instead, MIRA draws recommendations from the MIRA Resource Portal, which not only facilitates the input and expert validation of mental health resources for use by the chatbot but also automatically monitors validated resources for any changes after approval and subsequently reports them to the editors. Our Selenium-based testing framework uses AI to automatically generate diverse wording test cases to assess the chatbot with different dialogue flows using diverse wordings and intentional minor spelling errors.

This study will investigate the effectiveness of MIRA in its ability to successfully connect health care workers and their families with appropriate information on mental health issues and local services and programs based on their identified needs. The effectiveness of the technology will be evaluated primarily through data collected via voluntary follow-up surveys and client interactions and engagement with the chatbot. Client satisfaction with the chatbot will also be assessed. We hypothesize that the chat will successfully connect users with appropriate health resources (eg, mental health educational resources, the Mood Disorders Society of Canada [MDSC] peer support program, posttraumatic stress disorder training, and web-based peer support; see the *Outcome Evaluation* section for more details).

Methods

The following subsections describe how the chatbot was developed and implemented and how it will be subsequently evaluated.

Chatbot Development

A Multidisciplinary Team

In recognition of the complex nature of developing and implementing accepted and effective state-of-the-art computing science technologies seeking to support mental health and wellness within the public health domain, a multidisciplinary team is required.

The MIRA Operational Team (including senior leadership, fellows, students, and support staff) and voluntary Expert Advisory Committee include computing science and psychiatry experts, health care workers, and family members and individuals with lived experience. To develop a new technology that is accessible to all Canadians and does not perpetuate the systemic racism inherent within the public health system, MIRA is being cocreated with the Indigenous community and includes an ethnically and culturally diverse team leading and supporting its development from tip to tail. See Multimedia Appendix 1 for a graphical description of this multidisciplinary approach.

Developing MIRA

MIRA was built via Rasa Open Source (Rasa Technologies Inc), an open-source conversational AI platform [63], as team members had familiarity with the platform and it was considered advantageous for the implementation of advanced NLP; owing to its flexibility and ease of integration; and because it was deemed most customizable by our chatbot team in comparison with other platforms such as Botkit, BotPress, MindMeld, and DeepPavlov [64-67]. Its customization would also allow for the incorporation of progressively more complicated or advanced forms of AI and NLP. This is imperative for future iterations of MIRA (beyond this pilot), where the study team intends to program the chatbot to adapt its behavior differently depending on the geographic and linguistic context of the individual using the chatbot or interface. This approach, using base code from Rasa Open Source and enhancing, adding to, and adapting it based on our needs for this project, allows our team to both pilot a state-of-the-art viable product in a reasonable time frame to address an urgent public health need and ensure that more advanced computing science techniques and developments can be incorporated incrementally and tested over several years to further enhance the chatbot capabilities. This also builds on lessons learned from other researchers developing similar technologies in health, where deploying a "working solution"

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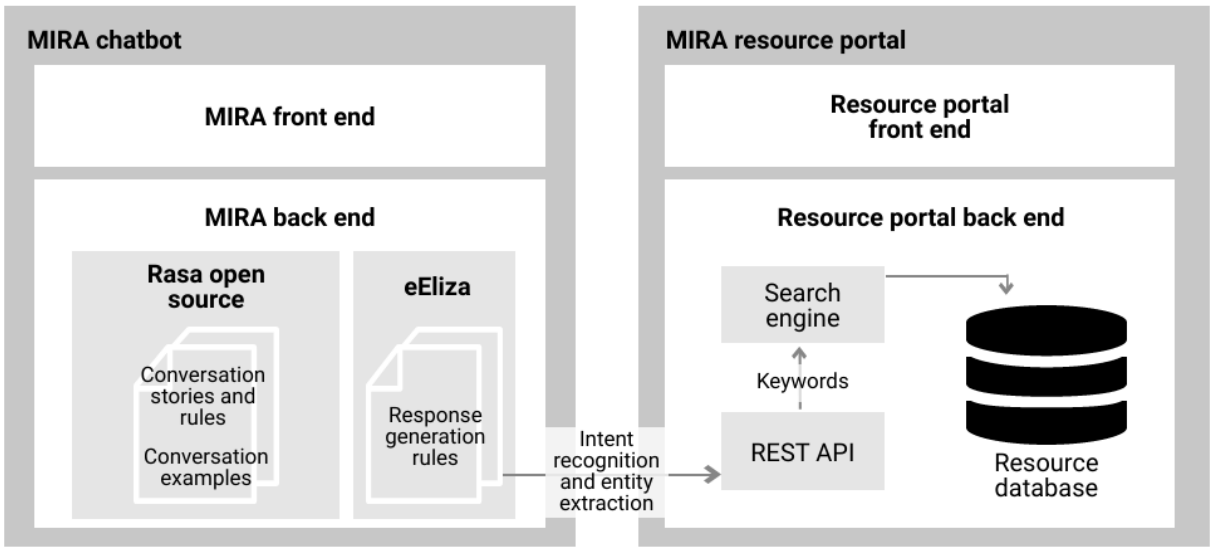
at the time was done at the expense of "...more innovative and potentially better solutions..." [68].

MIRA was built as a web-based chatbot (vs a stand-alone chatbot) to increase accessibility to it as no installation of software or applications is needed to use the chatbot and it can be used on any device regardless of the operating system. This also builds on lessons learned from other research in the field, where stand-alone chatbots were predominantly used [58].

The development of MIRA was guided by a chart-flow diagram via Lucidchart (Lucid) [69], a web-based collaborative design platform. This conversational flow diagram was initially developed by a psychiatry expert (JMN) on our team and then tested and refined by study team members from MDSC, an organization led by individuals with lived experience, including the categorization of anticipated client *intents* (what the client would like to accomplish) and appropriate chatbot *utterances* (the chatbot's responses to a client). Following this preliminary structuring, our computing science team members built the MIRA chatbot to follow the chart-flow diagram as a guide. To further refine the chatbot, the multidisciplinary team was asked to imagine hypothetical questions that could be received by the chatbot. Approximately 200 hypothetical questions were developed (133 distinct questions along with variations in question types). The questions were subsequently organized into *intents*. The chatbot was initially trained on these *intents*. When new intents were revealed, the chart-flow diagram was adjusted to include them. Where possible, *intents* and *utterances* were enhanced using existing open-source libraries on chatbot dialogue. All chatbot *utterances* were reviewed by members of the team from the MDSC to ensure that the language used was at an appropriate reading level, clear, considerate, and respectful. The rationale for approaching the chatbot design and training data in this manner was in reflection of the complicated nature of mental health. The chatbot needed to be tailored to ensure that it behaved in a way that would guide the user to resource recommendations appropriately, effectively, and respectfully. Lucidchart allowed non–computing science team members (eg, psychiatry and lived experience experts) to communicate necessary chatbot conversational flow behaviors to the computing science team clearly and effectively, including any emergency- or urgency-related prompts and responses. The open-source use of big data has been significantly criticized for perpetuating systemic racism and societal inequalities [70]. As such, developing training data using our multidisciplinary team was important to ensure that chatbot behavior remained respectful and reduce existing issues inherent in big data. Furthermore, chatbot behavior was reviewed by members of the team with lived experience to ensure that the chatbot responses were trauma-informed to not exacerbate trauma or challenges individuals accessing services may face.

At the request of the MDSC, the computing science team incorporated additional conversational functionality reflective of ELIZA [71], an early NLP conversational AI algorithm, to add nonscripted responses. This was to reduce the transactional or robotic feel or experience a client had with the chatbot and allow a client to speak freely with the chatbot before asking for assistance in finding specific resources. For the preliminary design, the computing science team adjusted the ELIZA code to include entity extraction (this adjusted code is referred to as *eEliza*, where *e* denotes *enhanced*, and can be found in Figure 1). The extracted entities are then used in conversation back to the client (to acknowledge the information shared by the client) as well as to refine resource recommendations to be provided later in the interaction. The use of Generative Pre-trained Transformer [72], an open-source AI algorithm that translates input from clients and generates at times human-like output, is currently being explored to further enhance the conversational functionality of the chatbot for this pilot phase.

Figure 1. Architectural diagram of the Mental Health Intelligent Information Resource Assistant (MIRA) chatbot and resource portal system. API: application programming interface; REST: Representational State Transfer.



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Of importance is the use of both NLP (via text-based entry) and decision trees (rule-based responses based on the use of predetermined button options) to support response generation. Most chatbots in mental health use either one or the other, whereas MIRA uses a hybrid approach to enhance functionality and end-user experience by offering them the choice or control to use both interchangeably during their exchange with MIRA. It is our understanding at the time of writing this paper that this approach in itself (using NLP and rule-based responses and allowing users to control the conversation) is a novel application of AI within the mental health field [58].

The chatbot was built to associate various terms or phrases as being of an urgent or serious nature and has been prompted to immediately provide information on emergency services should this association be triggered. For example, if the client indicates that they are experiencing suicidal thoughts, the chatbot will immediately provide them with emergency contact information and the Crisis Services Canada phone number, chat line, and texting information. This emergency response was flagged by mental health experts on our team and our Expert Advisory Committee as being of critical importance in supporting individuals experiencing urgent mental health–related challenges. Hypothetical phrases used for baseline training data were developed with the assistance of these members as well.

Following this work, our computing science team members worked on the incorporation of data augmentation (ie, the use of an AI algorithm that, using existing examples and hypothetical questions, can create new variations of hypothetical questions that could be asked to further refine chatbot functionality) as well as web browser automation via the Selenium platform to test chatbot functionality to mimic anticipated and unanticipated client questions, responses, and behaviors. Over 20 different data augmentation algorithms were used, including contextual word embeddings, random character errors, and synonym augmentations. Stanford's CoreNLP (Stanford NLP Group), an open-source NLP tool, will be used to further enhance entity extraction [73].

The two main purposes of MIRA are to provide individuals with (1) information or education on substance use and mental illnesses generally (simple educational information including general definitions and descriptions of symptoms written at a lay audience level) and (2) information on services and programs in Canada or, if voluntarily provided, in the specific city or village, region, or province of the identified end user. The level of specificity of the information, services, or programs provided is dependent on the level of information voluntarily shared by the client. For example, the client may ask for a definition of mood disorders or, alternatively, for an in-person group therapy program for individuals managing major depressive disorder in Edmonton, Alberta. The programming of these 2 components requires different approaches, as detailed below.

The education resource component of the chatbot was developed by first identifying common mental health ailments or challenges. A list of psychiatric disorders was extracted from the Diagnostic and Statistical Manual of Mental Disorders by a psychiatry expert on the team, who then extracted common language used on the web by reputable (known government and not-for-profit, government-supported) organizations whose websites were tailored to a lay audience and linked clinical and common language. This linking was helpful both to train the chatbot on relationships between lexicons used in the psychiatric field and audiences and to serve as a preliminary list of common ailments. Following the development of these lists, volunteers at the MDSC supported the collection of web-based resources that provided the following information on each specific ailment: definition of the disorder or ailment, list of associated symptoms, and a description of common associated treatments. These web-based resources and their relevant informational data were individually logged in the MIRA portal (MIRA portal details outlined below) and subject to review by a 30-member Expert Advisory Committee.

The service and program resource component was developed by first logging a resource list provided on the MDSC website. The act of logging was conducted by MDSC volunteers. Following this, government websites were reviewed by team members and volunteers for additional resource lists. Where lists of recommended resources were provided, volunteers were asked to log these resources. These web-based resources were also subject to review by a 30-member Expert Advisory Committee. The MIRA portal currently has >750 fully vetted resources.

Testing MIRA

The MIRA core team collaboratively determined a quality threshold for the release of a minimum viable chatbot prototype based on a variety of performance metrics. Performance measures, including accuracy of intent recognition and entity extraction as well as average rending time, were used by the computing science team to monitor the progress of chatbot training and refinement. Where needed, the team strategically addressed particular elements of the chatbot that they felt may enhance measures reporting lower than acceptable metrics.

The chatbot was in alpha testing from December 2021 to February 2022. The chatbot was then beta tested by members of our 30-member, multidisciplinary Expert Advisory Committee from February 7, 2022, to May 1, 2022. Comments were logged, and changes were made to the chatbot in real time. Testing was enhanced using automation via Selenium, a web browser automation tool, to repeatedly test anticipated end-user behavior and log programming bugs and errors.

The chatbot was launched for the pilot population on May 2, 2022. Data collection is anticipated to take place from May 2, 2022, to May 2, 2023. The publication of a preliminary synthesis of the results will be sought in spring or summer 2022, followed by a more comprehensive evaluation in spring 2023.

Interacting With MIRA

Once the client clicks on the MIRA URL [74], they are directed to a webpage with the MIRA chatbot interface. MIRA begins by welcoming the client and asks them for their consent to use anonymized data from the conversation to evaluate and improve its services, with a link to a pop-up with consent information (Multimedia Appendix 2). If the client provides consent, the chatbot then asks a short series of demographic-related questions—employment type, location, and end user (eg, for

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the client or for someone else; if *someone else*, then the age of the end user is also collected; Multimedia Appendix 3). Following these preliminary questions, the chatbot asks in an open-ended manner (eg, "How can I help you?") and provides some examples of questions that could be asked in the form of button options (eg, "I want to find programs and services" or "I want to learn coping skills"; Multimedia Appendix 4). If a client asks to "chat" with MIRA or begins expressing feelings opposed to an obvious request for information, eEliza programming will be prompted (Multimedia Appendix 5). The MIRA website, MIRA chatbot, and MIRA Resource Portal (renamed the MIRA Resource Library for the May 2 launch) were tested for compatibility with multiple electronic devices, including tablets, smartphones, and desktop computers, as well as multiple browser applications, including Safari and Chrome.

The MIRA Portal

The internet may contain information with inaccurate content, bias, and insufficient evidence [75,76]. This is why MIRA does not draw resource recommendations via the open internet and, instead, provides resource recommendations drawn from the MIRA Resource Portal. The MIRA Resource Portal is a resource repository in which MDSC volunteers have cataloged and annotated metadata of >750 resources to date. These resources were assessed for quality by a 30-member Expert Advisory Committee using an approach reflecting the academic peer-review process. More specifically, resources were assigned to committee members by an editor (the study coordinator). Each resource was subject to review by at least two different reviewers. Reviewers were guided by an evaluation matrix developed using a hybrid of items that were drawn from existing validated tools [75,77,78]. The factors assessed included (1) readability, (2) accessibility, and (3) quality [75,77,78]. This hybrid approach was taken as our definition of *resource* was broad (see the *Resource Types* section) and included many types of resources (eg, phone number, website links, videos, audio recordings, images, and apps) and, as such, to our knowledge, no validated tool existed at the time of writing this paper. To date, >1600 resource reviews have been conducted, resulting in 750 resources that have been fully vetted and approved by the Expert Advisory Committee and are now accessible by the chatbot.

For the purposes of this study, *resource* is defined as evidence-supported, relevant, and reliable information that would satisfy an end user of the chatbot in retrieving general mental health information or connecting with the appropriate mental health services for their identified needs and circumstances. A recommended resource can be provided at the end of a dialogue as the final outcome or at any time during the exchange.

Resource Types

The types of resources included in the MIRA Resource Portal are shown in Textbox 1.

Textbox 1. Types of resources included in the Mental Health Intelligent Information Resource Assistant Resource Portal.

Resource types

- Health system navigation: information that connects clients with programs and services—includes a textual description of the resource and any of the elements of a typical contact record (email address, phone number, physical address of in-person service, hours of operation, and URL if it is a website)
- Informational or education reference: includes a textual description of the resource and the website URL or the URL to an audio, video, image, or PDF attachment
- Simple answer: just a textual description that can be provided as an answer to a direct factual question

If a resource received a mixed review, it was then subject to review by a third reviewer (a tiebreaker who was also a member of the Expert Advisory Committee). Reviews were made anonymous to everyone with the exception of the editor, who was responsible for assigning resources, to allow reviewers to be candid, and all reviewers were asked to acknowledge any conflicts of interest before being permitted to review a resource. See Figure 1 for an architectural diagram of the MIRA chatbot and portal system.

Participants

For the purposes of this project, the definition of the target sample was broadened to capture all health-related personnel and their respective families who may be affected by heightened mental health burden in light of the ongoing pandemic. In addition, direct or vicarious trauma or psychological distress in a health care environment is not limited to medical staff [79,80]. Therefore, *health care worker* will be defined as outlined in Textbox 2.

Textbox 2. Definition of health worker for this study.

***Health worker* definition**

- "Any health professionals and any staff member, contract worker, student or trainee, registered volunteer, or other essential caregiver currently working in a healthcare organization, including workers that are not providing direct patient care and are frequently in the patient environment. This includes cleaning staff, food services staff, information technology staff, security, research staff, and other administrative staff.
- Workers providing healthcare service or direct patient service in a congregate, residential or community setting outside of a healthcare organization (e.g., nurse providing patient care in a school, worker performing personal support services in an assisted living facility, medical first responder in the community, peer worker in a shelter)" [81].

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The definition of health care worker varies considerably by health authority or administrator. As such, the following numbers were used to determine a general goal post for a target sample size recognizing that the data sources (Alberta Health Services and Nova Scotia Health Authority) may have differing inclusion criteria for what is categorized as a health care worker. There are approximately 240,000 frontline Alberta Health Services workers in Alberta [82], and there are 23,400 health care workers in Nova Scotia [83]. To include family members into sample size calculations, 2011 Statistics Canada estimates on the average number of individuals in a household were used (2.5 per household) [84]. With a 95% CI and 3% margin of error, the sample size target was estimated to be 1066 for Alberta and 1048 for Nova Scotia. More specifically, this sample size refers to the number of participants who consent to using the chatbot. This study will seek to slightly oversample from each province (Alberta: n=1100; Nova Scotia: n=1100). In reflection of the general experiences of other researchers with participation rates for web-based surveys (34%-43% [85-89]), we will aim to collect between 374 and 473 partial and complete baseline surveys and 110 partial and complete follow-up surveys per province. To the authors' knowledge at the time of writing this paper, this study is the first to evaluate the use of conversational agents or chatbots to support mental health system navigation; as such, the effect size is unknown at the time of the design phase of the study, and power analysis will need to be conducted as the study team actively gathers data to ensure that our sample size is adequate. Therefore, the sample size is subject to re-estimation during the course of this study.

Participant recruitment will be conducted through snowball sampling via word of mouth, social media advertisements, physical advertisements (study posters and study information posted on physical bulletin boards in hospital staff rooms as well as in newsletters to staff where possible), and referrals via our network and partners (including medical professional organizations). After consenting to take part in the study via a web-based consent form, the participants will be asked if they would like to take part in voluntary follow-up surveys following the use of the chatbot. Regardless of their response, they will then be able to immediately engage with the chatbot. The inclusion criteria are being aged >18 years at the start of the study, being a health care worker or a family member of a health care worker, being located in Alberta or Nova Scotia, being able to speak and read English, and having access to the internet. The chatbot will be developed with the option of adding French and other languages of peoples geographically located within the settlement of Canada in future iterations of the chatbot (eg, Cree, Inuktitut, and Ojibway). The exclusion criteria are individuals aged <18 years, individuals in provinces outside Alberta and Nova Scotia, those with limited comprehension of English, and those without internet access. However, if a client tries to access this service to support an individual aged <18 years or outside the 2 provinces indicated, the chatbot will include cross-Canadian resources that could support them.

Procedures

This project was initiated on April 1, 2021. Data collection began on May 2, 2022, and will continue until May 2, 2023. The publication of preliminary results will be sought following the synthesis of data in spring or summer 2022. A final report will be developed in spring 2023.

Health care workers from the provinces of Nova Scotia and Alberta will be invited to use the chatbot service. Family members of health care workers will also be welcome to participate in the study. Participant recruitment will be conducted via snowball sampling through word of mouth, social media advertisements, physical advertisements, and referrals via our network and partners (including medical professional organizations). Potential participants will be asked to provide informed consent before receiving services from the virtual assistant. Although the participants will be encouraged to register their email address so that the study team can send them voluntary follow-up surveys to evaluate program performance (more on the surveys below), registration will be voluntary. Regardless of registration, the participants will be provided with access to MIRA following the provision of consent.

If a participant registers their email address, they will be provided with 2 voluntary surveys: one at baseline (immediately following use of the chatbot) and a second one at 24 hours following the initial use of the chatbot. The surveys will collect demographic information (eg, year of birth, gender identity, and visible minority status); ask the participants whether they followed through with a recommended resource and the perceived appropriateness of that resource (eg, "Were the resource(s) that MIRA recommended to you during your conversation appropriate?" or "After your conversation with the MIRA, did you follow-up or connect with the resource(s) that the chatbot recommended?"); and assess baseline mental and physical health via the Clinical Outcomes in Routine Evaluation System (CORE-10), a brief, validated 10-item assessment and outcome measurement tool used to assess conditions including anxiety, depression, physical problems, and risk to self [90]. Select items from the Embodied Conversational Agent Trust Questionnaire (ETQ)—for example, "Did you feel that MIRA was competent?" (4-point Likert scale from 0=not at all to 3=completely)—and Acceptability E-scale (AES)—for example, "How much do you agree with the following statements? MIRA gave me information that was relevant to my concern" (5-point Likert scale from "strongly agree" to "strongly disagree")—are used to assess client satisfaction and acceptability, including perceived usability, benevolence, credibility, and trustworthiness [91].

In addition to the voluntary survey, data will be extracted in aggregate of the general use of the technology to assess effectiveness and engagement, including topics most frequently raised, average time spent on the service, number of resources provided in an average conversation, number of client interactions with links, most frequent recommendations by the chatbot to clients, number of resources recommended by the chatbot in an average conversation, average number of objections raised by clients in conversations, and intent identification and entity extraction accuracy. The use of aggregate data in this manner will be flagged in the consent form preceding the use of the virtual assistant. Participation on the platform will remain anonymous with the exception of the satisfaction surveys (voluntary), which may be temporarily linked via email address to track survey responses at different

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time intervals (baseline and 24 hours). Following linkages, emails will be permanently deleted and replaced with a randomized participant number to further protect anonymity. Transcripts between clients and the chatbot will be used anonymously to further train and refine the chatbot. The transcripts do not contain any identifiable information and will only be used to improve chatbot functionality. The use of transcripts by the chatbot to serve as a form of memory from which the chatbot will learn and teach itself to perform in a more refined manner is outlined in the consent form provided to the participants. To further protect anonymity, the chatbot has been programmed to remove any personally identifiable information from the transcripts before saving them (eg, if a name is provided, it is omitted from the saved transcript).

There is no standardized approach to evaluate chatbots within the field of health [56,92]. To determine which variables to collect for analysis, our team aggregated findings from several academic studies and reviews that described the technical characteristics, applications, and evaluation measures of chatbots in the field of health [56,92]. In reflection of the findings of these studies, where applicable for the purposes of our study, we chose items from validated tools or items used to evaluate other chatbots (eg, CORE-10, ETQ, AES, and classifier performance measures such as accuracy and precision) to permit cross-comparability where possible between this and existing research and to support efforts to align evaluative measures within the field [56,89,92-94].

Data Analysis

The effectiveness of the technology will be assessed primarily through data collected via voluntary follow-up surveys and client interactions and engagement with the chatbot. As the use of the chatbot is anonymous, it is not possible to conduct direct follow-up via electronic medical records to confirm the use of any particular service. As such, the research team will primarily rely on information volunteered by clients via the follow-up surveys and chatbot analytics to assess whether clients are successfully connected with recommended resources (by asking them directly).

Outcome Evaluation

The primary outcome measure will be an analysis of participant responses to follow-up survey questions on a successful connection with resources recommended by the chatbot and the perceived appropriateness of the resources recommended. More specifically, we ask the participants the following questions: (1) “Was/were the resource(s) the MIRA chatbot recommended to you during your conversation appropriate?” (response options: “yes”; “no”; and “other, please specify”) and (2) “After your conversation with the MIRA chatbot, did you follow-up or connect with the resource(s) that MIRA recommended?” (response options: “yes”; “no”; “other, please specify”; and “I prefer not to answer”; if “no,” then the respondent is asked the subsequent question “why not?”).

Assessment of whether the chatbot successfully connected the respondent with appropriate resources will be the number of respondents who answer “yes” to both of these questions. Further consideration will be given to “no” or “other, please specify” responses, where additional detail is shared by the client, to assess rationale for a failed connection (eg, personal choice not to connect or could not successfully reach the resource after attempting to do so). In reflection of previous reports that approximately 24% to 44% of Canadians do not feel that their mental health needs are being adequately met [3,31], we have set a minimum threshold for successful connection with appropriate resources of >50%.

Secondary outcome measures will be an analysis of mental and physical well-being (CORE-10) at the time of use and 24 hours following use, client satisfaction and acceptability (including perceived usability, benevolence, credibility, and trustworthiness), intergroup variation, drop-off and engagement rates, general chatbot use patterns, and exploration of why this intervention may or may not have been supportive or helpful for particular groups.

Chatbot performance will also be evaluated based on additional technical measures identified in reflection of other evaluative works within the field of chatbots in health to allow for the cross-comparability of the findings [56,92,95-97], including an analysis of intent classification accuracy scores, entity recognition accuracy scores, client URL engagement, chatbot rending and response speed, conversational completes, task completion rates measured via binary responses to questions such as “is this what you were looking for?” and “is there anything else I can help you with?,” star ratings by clients at the end of a conversation, client objections, and prompt interruptions.

Ethics Approval

Ethics approval was granted on August 12, 2021, by the University of Alberta Health Research Board (case Pro00109148) and on April 21, 2022, by the Nova Scotia Health Authority Research Ethics Board (case 1027474). All data and computer code will be password-protected and stored on a secure server at the University of Alberta in Canada.

Results

On April 1, 2021, this project was initiated by partners MDSC, the University of Alberta, Dalhousie University, the University of Saskatchewan, the International Indigenous Health Research and Training Centre, the Asia-Pacific Economic Cooperation Digital Hub for Mental Health, AI4Society, and the Alberta Machine Intelligence Institute. A Mathematics of Information Technology and Complex Systems Accelerate grant to support student involvement in this project was successfully awarded on August 11, 2021, with a secondary award granted on March 23, 2022, to support research activities for this project until spring 2024. For this study, ethics approval was sought and granted by the University of Alberta Health Research Board and the Nova Scotia Health Authority Research Ethics Board on August 12, 2021, and April 21, 2022, respectively. On May 2, 2022, data collection began and is anticipated to continue until May 2, 2023. Preliminary results will be published in spring or summer 2022, with a more comprehensive evaluation using a larger data set to be completed by spring 2023.

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Discussion

Overview

The world is undergoing a period of significant growth in technological innovation. Starting with the internet, technological networks and systems have emerged as so complex and disruptive that they have transformed not only our governing and economic structures but also our perception of self, community, and day-to-day life. With 8 million global deaths attributed annually to mental illness [12], there is urgency to identify effective and timely service options that reduce and eliminate barriers, including through health system navigation, as well as to investigate innovations where technology may present constructive, novel solutions.

In this paper, we describe our experience to date with the development of MIRA, a chatbot designed to guide clients who experience mental health challenges to appropriate information and services available to them. Our development process includes a broad team of stakeholders and experts (in mental health and computing science) and addresses a number of challenges that one should consider to develop a realistic and practical solution.

This paper also describes our anticipated methodology to evaluate MIRA, including its ability to connect health care workers and their families with relevant, high-quality mental health services and information. As noted, we hypothesize that the chatbot will effectively connect clients with appropriate information on mental health issues, services, and programs based on personal needs. If proven effective, in the spirit of the Canadian universal health care system, the chatbot will be offered free of charge to the Canadian public. To our knowledge, there have been no similar studies in this field. If successful, this innovation has the potential to offer significant benefits to the Canadian public and demonstrate a solution that can be adopted by other international health care systems.

Future Directions

There are several considerations that could be made for future research, some of which our team seeks to touch upon in future work related to this study, outlined in this section.

Research evaluating health chatbots is commonly criticized for being inconsistent in terms of outcome measures, which hinders opportunities for cross-comparability with other evaluations. As such, through the careful review of previous studies and the publication of our protocol, we hope to help support a movement toward consistency by using evaluative measures consistent with those reported in systematic and scoping reviews of chatbots in mental health where possible and appropriate [56,92,95-97]. Further consideration should be given by other researchers to the development of a standardized approach to evaluate chatbots within the field of health.

Discussions on the development and implementation of ethical AI and prioritizing health equity throughout the life cycle of an AI system are of critical importance. AI has been criticized for being "no more than human behaviour reflected back to us" [98]. Inherent to this argument is the ability of AI to "reflect the biases present in our collective conscience" [70]. The discourse on guidelines to rectify and prioritize health equity in the development life cycle of an AI system [99], as well as around ethical AI applications generally, is becoming more prolific. This project uses a multidisciplinary core team and advisory committee that includes members of the Indigenous community and other communities of color, individuals with lived experience, and other experts. This cocreation of a mental health chatbot (including efforts to action the First Nations Principles of Ownership, Control, Access, and Possession) with the support of an advisory group to assist usability testing and the development of a controlled training ground truth data set is novel and presents an interesting and rich opportunity to conduct an analysis and exploration of mental health equity in the digital space through a lens of different existing and potential end users. Researchers should be encouraged to continue to explore these topics further in the context of applied AI design and implementation to support health equity and racial justice.

This study will also explore other areas of interest, such as the analysis of health information–seeking behavior (HISB). HISB is a coping strategy individuals use involving the gathering of information about a health topic in response to a recent diagnosis or for other health-related reasons, such as general health promotion. The personal and contextual considerations of HISB have not been adequately explored. More specifically, further analysis is needed of the cultural, contextual, and demographic influences that may play a role in HISB [97,100]. As the perceived level of quality of information accessed can influence individuals' intention to seek further information, additional considerations must be made for quality review and assurance of any resources recommended by the chatbot. As such, resources that the chatbot recommends must be vetted by experts, including health professionals and individuals with lived experience [97,101,102]. Our team has sought to address this through the development and use of the MIRA Resource Portal and vetting, supported by an Expert Advisory Committee that includes a diverse set of voices. Thus, further analysis of the topic of HISB is possible as a result of this work.

Although deep learning models currently have the ability to conduct language processing tasks such as tagging, text classification, machine translation, and question answering, existing state-of-the-art models are criticized for lacking *explainability*—more specifically, being able to describe how the algorithm came to a particular result or action, which is considered a key pillar in discourse around ethical AI development [103-105]. This and future studies must seek to improve the methods of explainable NLP.

Another direction for future consideration is the incorporation of emotional intelligence into dialogue generation to better imitate human conversational patterns and appropriately respond to emotional input. Existing neural dialogue systems such as sequence-to-sequence have been criticized for being limited in response length or for producing generic or noncommittal versus empathetic or emotionally intelligent outputs [106,107]. Future studies should explore the integration of empathetic response generation that appropriately categorizes a client's current emotional state based on their input utterance, considers a desired target emotion to guide clients toward, and subsequently generates an emotionally intelligent response back to clients

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incorporating these considerations [106,107]. Multilabel emotion mining may be considered to support this categorization [108]. Our team will seek to improve the emotional intelligence of future iterations of MIRA following this pilot through the further enhancement of *eEliza*.

Limitations

There are several anticipated limitations of note that we consider unavoidable. First, digital interventions are not accessible to all Canadians, and there are barriers to their use, including technical issues with connectivity; lack of access to electrical or technological infrastructure because of cost, service provision, and natural disasters; and distrust of technology regarding the use of data or protection of anonymity [11].

Second, consistent adaptation and refinement are inherent in innovations using AI as the technology is programmed to remember interactions with clients and will evolve or learn. In addition, there will be a number of technological bugs or errors in the programming code for the chatbot that will become apparent as it is being piloted. As such, it is anticipated that the technological device itself will require ongoing adaptation with implementation. Any changes observed or made by the study team will be carefully documented and made available upon request.

There is potential for selection bias as participant recruitment includes the use of snowball sampling or chain-referral sampling using the research team's network or referrals through affiliated organizations (listed with the authors of this paper) to help encourage participant recruitment. In addition, individuals who are more familiar or comfortable with technology may be more likely to participate in this study. To reduce this form of bias, the study team plans to use multiple methods of participant recruitment, including printing hard copies of the study poster for use on bulletin boards in staff rooms in hospitals as well as asking hospital operations staff, with approval from the respective health authorities, to share information about the study with their staff widely.

There is a risk of response bias. As such, our team will seek to oversample in each province; ensure that the anonymity of the survey is clear to the users by outlining anonymity in the welcome message of the chatbot as well as in the consent documentation; primarily use validated tools or items extracted from validated tools to assess baseline mental and physical health as well as user satisfaction and acceptability, including perceived usability, benevolence, credibility, and trustworthiness (ie, the CORE-10, ETQ, and AES); and ensure that the Likert-scale questions include a neutral response option. Data will then be weighted where possible according to the Statistics Canada Census Profile data.

Acknowledgments

This study received funding to support student involvement through the Mood Disorders Society of Canada and the Mathematics of Information Technology and Complex Systems Accelerate grant. In addition, OZ is supported by the Amii Fellow Program and the Canadian Institute for Advanced Research Artificial Intelligence Chair Program. This study includes multiple partnerships, including support from a committee of experts entitled the Expert Advisory Committee, as well as Mood Disorders Society of Canada volunteers. The authors would like to give thanks to these members for volunteering their time to validate resources that the chatbot will ultimately draw from as well as for the insights provided in the beta testing of the chatbot itself.

Data Availability

The data sets generated and analyzed during this study are available from the corresponding author upon reasonable request.

Conflicts of Interest

None declared.

Multimedia Appendix 1
A multidisciplinary approach to mental health chatbot development.
[PNG File , 52 KB - resprot_v11i7e33717_app1.png]

Multimedia Appendix 2
Chatbot storyboard—screenshots of the chatbot interface with details on chatbot functions and features.
[PNG File , 185 KB - resprot_v11i7e33717_app2.png]

Multimedia Appendix 3
Chatbot storyboard—screenshots of the chatbot interface with details on chatbot functions and features.
[PNG File , 85 KB - resprot_v11i7e33717_app3.png]

Multimedia Appendix 4
Chatbot storyboard—screenshots of the chatbot interface with details on chatbot functions and features.

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[PNG File , 100 KB - resprot_v11i7e33717_app4.png]

Multimedia Appendix 5
Chatbot storyboard—screenshots of the chatbot interface in eEliza.
[PNG File , 124 KB - resprot_v11i7e33717_app5.png]

References

1. Mood Disorders Society of Canada. 2019. URL: https://mdsc.ca/docs/MDSC_Quick_Facts_4th_Edition_EN.pdf [accessed 2021-09-15]
2. Pearson C, Janz T, Ali J. Mental and substance use disorders in Canada. Statistics Canada. 2015. URL: https://www150.statcan.gc.ca/n1/en/pub/82-624-x/2013001/article/11855-eng.pdf?st=d8oRDqRq [accessed 2021-09-15]
3. Health fact sheets: Mental health care needs, 2018. Statistics Canada. 2019 Oct 7. URL: https://www150.statcan.gc.ca/n1/pub/82-625-x/2019001/article/00011-eng.htm [accessed 2021-10-02]
4. Understanding the impact of alcohol on human health and well-being. National Institute on Alcohol Abuse and Alcoholism. Bethesda, MD, USA: National Institute on Alcohol Abuse and Alcoholism; 2014. URL: https://www.niaaa.nih.gov/publications/brochures-and-fact-sheets/understanding-alcohol-impact-health [accessed 2021-09-01]
5. Simpson CA, Tucker JA. Temporal sequencing of alcohol-related problems, problem recognition, and help-seeking episodes. Addict Behav 2002;27(5):659-674. [doi: 10.1016/s0306-4603(01)00200-3] [Medline: 12201375]
6. Narrow WE, Regier DA, Rae DS, Manderscheid RW, Locke BZ. Use of services by persons with mental and addictive disorders. Findings from the National Institute of Mental Health Epidemiologic Catchment Area Program. Arch Gen Psychiatry 1993 Feb;50(2):95-107. [doi: 10.1001/archpsyc.1993.01820140017002] [Medline: 8381266]
7. Wild TC, Roberts AB, Cooper EL. Compulsory substance abuse treatment: an overview of recent findings and issues. Eur Addict Res 2002 Apr;8(2):84-93. [doi: 10.1159/000052059] [Medline: 11979011]
8. Sunderland A, Findlay LC. Perceived need for mental health care in Canada: results from the 2012 Canadian Community Health Survey-Mental Health. Health Rep 2013 Sep;24(9):3-9 [FREE Full text] [Medline: 24258361]
9. Sanmartin C, Houle C, Tremblay S, Berthelot JM. Changes in unmet health care needs. Health Rep 2002;13(3):15-21. [Medline: 12743957]
10. Peachey D, Hicks V, Adams O. An imperative for change: access to psychological services for Canada – a report to the Canadian Psychological Association. Health Intelligence. 2013 Mar. URL: https://cpa.ca/docs/File/Position/An_Imperative_for_Change.pdf [accessed 2021-10-01]
11. Strudwick G, Sockalingam S, Kassam I, Sequeira L, Bonato S, Youssef A, et al. Digital interventions to support population mental health in Canada during the COVID-19 pandemic: rapid review. JMIR Ment Health 2021 Mar 02;8(3):e26550 [FREE Full text] [doi: 10.2196/26550] [Medline: 33650985]
12. Walker ER, McGee RE, Druss BG. Mortality in mental disorders and global disease burden implications: a systematic review and meta-analysis. JAMA Psychiatry 2015 Apr;72(4):334-341 [FREE Full text] [doi: 10.1001/jamapsychiatry.2014.2502] [Medline: 25671328]
13. Kelly G. When the sick need to hire a squeaky wheel: the Canadian public health-care system has become so labyrinthine that some are paying for advocacy and navigation expertise. The Globe and Mail. 2017 Apr 15. URL: https://www.proquest.com/docview/1888167203?accountid=14474&parentSessionId=DkTuRXllvgFINcxV%2FlrHgMxVkZYqgQmb%2Frah%2Bd3FNcQ%3D [accessed 2021-09-15]
14. Kids can't wait: 2020 report on wait lists and wait times for child and youth mental health care in Ontario. Canadian Mental Health Association (CMHA). 2020. URL: https://cmho.org/wp-content/uploads/CMHO-Report-WaitTimes-2020.pdf [accessed 2021-09-15]
15. Position paper on the occasion of the 10th Anniversary of the 2004 10-Year Plan to Strengthen Health Care in Canada. Wait Time Alliance. 2014 Sep 23. URL: https://www.waittimealliance.ca/wp-content/uploads/2014/09/WTA-Fall-Event-2014-Position-Paper-English-FINAL.pdf [accessed 2021-09-15]
16. Chappell NL, McDonald L, Stones M. Aging in Contemporary Canada. 2nd edition. Toronto, ON, Canada: Pearson-Prentice Hall; 2008.
17. Denton M, Ploeg J, Tindale J, Hutchison B, Brazil K, Akhtar-Danesh N, et al. Where would you turn for help? Older adults' awareness of community support services. Can J Aging 2008;27(4):359-370. [doi: 10.3138/cja.27.4.359] [Medline: 19416797]
18. Ploeg J, Denton M, Tindale J, Hutchison B, Brazil K, Akhtar-Danesh N, et al. Older adults' awareness of community health and support services for dementia care. Can J Aging 2009 Dec;28(4):359-370. [doi: 10.1017/S0714980809990195] [Medline: 19925701]
19. Hutchison B, Levesque JF, Strumpf E, Coyle N. Primary health care in Canada: systems in motion. Milbank Q 2011 Jun;89(2):256-288 [FREE Full text] [doi: 10.1111/j.1468-0009.2011.00628.x] [Medline: 21676023]

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20. Commission on the Reform of Ontario's Public Services: Public services for Ontarians: a path to sustainability and excellence. Queen's Printer for Ontario. 2012. URL: https://www.opsba.org/wp-content/uploads/2021/02/drummondReportFeb1512.pdf [accessed 2021-09-15]
21. Key observations 2014-15 quality improvement plans: primary care. Health Quality Ontario. 2014. URL: https://www.hqontario.ca/portals/0/Documents/qi/qip-analysis-pc-en.pdf [accessed 2021-09-15]
22. McGinnis P, Davis MM, Howk S, DeSordi M, Thomas M. Integrating Primary Care Practices and Community-based Resources to Manage Obesity. Agency for Healthcare Research and Quality. Rockville, MD, USA: Agency for Healthcare Research and Quality; 2014. URL: https://www.ahrq.gov/sites/default/files/publications/files/obesity-pcpresources.pdf [accessed 2021-09-15]
23. Birrell D, Heenan D. Implementing the transforming your care agenda in Northern Ireland within integrated structures. J Integr Care 2012;20(6):359-366. [doi: 10.1108/14769011211285156]
24. Mossabir R, Morris R, Kennedy A, Blickem C, Rogers A. A scoping review to understand the effectiveness of linking schemes from healthcare providers to community resources to improve the health and well-being of people with long-term conditions. Health Soc Care Community 2015 Sep;23(5):467-484. [doi: 10.1111/hsc.12176] [Medline: 25494621]
25. MacAdam M. Moving toward health service integration: provincial progress in system change for seniors – CPRN research report. Canadian Policy Research Networks. 2009 May. URL: http://globalag.igc.org/health/world/2009/canada.pdf [accessed 2021-09-01]
26. Valaitis R, Cleghorn L, Ploeg J, Risdon C, Mangin D, Dolovich L, et al. Disconnected relationships between primary care and community-based health and social services and system navigation for older adults: a qualitative descriptive study. BMC Fam Pract 2020 Apr 23;21(1):69 [FREE Full text] [doi: 10.1186/s12875-020-01143-8] [Medline: 32326880]
27. WHO Coronavirus (COVID-19) Dashboard. World Health Organization. URL: https://covid19.who.int/ [accessed 2021-07-19]
28. Drolet M. How Canada is encouraging self-isolation to prevent the spread of COVID-19. Global News. 2020 Mar 5. URL: https://globalnews.ca/news/6634584/canada-coronavirus-covid-19-self-isolation [accessed 2021-09-15]
29. Angus Reid Institute. 2020 Apr 27. URL: https://angusreid.org/covid19-mental-health/ [accessed 2021-09-15]
30. Moreno C, Wykes T, Galderisi S, Nordentoft M, Crossley N, Jones N, et al. How mental health care should change as a consequence of the COVID-19 pandemic. Lancet Psychiatry 2020 Sep;7(9):813-824 [FREE Full text] [doi: 10.1016/S2215-0366(20)30307-2] [Medline: 32682460]
31. Centre for Addiction and Mental Health. Anxiety, feelings of depression and loneliness among Canadians spikes to highest levels since Spring 2020. Centre for Addiction and Mental Health (CAMH). 2022. URL: https://www.camh.ca/en/camh-news-and-stories/anxiety-depression-loneliness-among-canadians-spikes-to-highest-levels [accessed 2022-02-10]
32. A national commitment to recovery from the disease of addiction in Canada. Canadian Centre on Substance Abuse. 2015. URL: https://www.ccsa.ca/sites/default/files/2019-04/CCSA-Recovery-Oriented-System-of-Care-Resource-2017-en.pdf [accessed 2021-09-15]
33. Uguen-Csenge E. Mental illness will be 'next wave' of COVID-19 pandemic, epidemiologist says. CBC News. 2020 Apr 4. URL: https://www.cbc.ca/news/canada/british-columbia/months-isolation-mental-health-covid-1.5521649 [accessed 2021-09-15]
34. Dobson K. "Psychology Works" Fact Sheet: Depression. Canadian Psychological Association. 2021 Jan 12. URL: https://cpa.ca/psychology-works-fact-sheet-depression/ [accessed 2021-09-15]
35. Tjepkema M. Insomnia. Health Rep 2005 Nov;17(1):9-25. [Medline: 16335690]
36. Sutton DA, Moldofsky H, Badley EM. Insomnia and health problems in Canadians. Sleep 2001 Sep 15;24(6):665-670. [doi: 10.1093/sleep/24.6.665] [Medline: 11560179]
37. Morin CM, LeBlanc M, Daley M, Gregoire JP, Mérette C. Epidemiology of insomnia: prevalence, self-help treatments, consultations, and determinants of help-seeking behaviors. Sleep Med 2006 Mar;7(2):123-130. [doi: 10.1016/j.sleep.2005.08.008] [Medline: 16459140]
38. Cabarkapa S, Nadjidai SE, Murgier J, Ng CH. The psychological impact of COVID-19 and other viral epidemics on frontline healthcare workers and ways to address it: a rapid systematic review. Brain Behav Immun Health 2020 Oct;8:100144 [FREE Full text] [doi: 10.1016/j.bbih.2020.100144] [Medline: 32959031]
39. Sahebi A, Nejati-Zarnaqi B, Moayedi S, Yousefi K, Torres M, Golitaleb M. The prevalence of anxiety and depression among healthcare workers during the COVID-19 pandemic: an umbrella review of meta-analyses. Prog Neuropsychopharmacol Biol Psychiatry 2021 Apr 20;107:110247 [FREE Full text] [doi: 10.1016/j.pnpbp.2021.110247] [Medline: 33476692]
40. Months of abuse, exhaustion have burnt-out nurses leaving their jobs. CBC News. 2021 Sep 13. URL: https://www.cbc.ca/player/play/1945590851847 [accessed 2021-09-15]
41. The Integration Imperative: reshaping the delivery of human and social services. KPMG and Mowat. 2013. URL: https://assets.kpmg/content/dam/kpmg/nz/pdf/October/integration-imperative-kpmg-nz.pdf [accessed 2021-09-15]
42. Kypri K, McAnally HM. Randomized controlled trial of a Web-based primary care intervention for multiple health risk behaviors. Prev Med 2005;41(3-4):761-766. [doi: 10.1016/j.ypmed.2005.07.010] [Medline: 16120456]

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RenderX

43. Linke S, Murray E, Butler C, Wallace P. Internet-based interactive health intervention for the promotion of sensible drinking: patterns of use and potential impact on members of the general public. J Med Internet Res 2007 May 08;9(2):e10 [FREE Full text] [doi: 10.2196/jmir.9.2.e10] [Medline: 17513281]
44. Humphreys K, Klaw E. Can targeting nondependent problem drinkers and providing internet-based services expand access to assistance for alcohol problems? A study of the moderation management self-help/mutual aid organization. J Stud Alcohol 2001 Jul;62(4):528-532. [doi: 10.15288/jsa.2001.62.528] [Medline: 11513231]
45. Lieberman DZ, Huang SW. A technological approach to reaching a hidden population of problem drinkers. Psychiatr Serv 2008 Mar;59(3):297-303. [doi: 10.1176/ps.2008.59.3.297] [Medline: 18308911]
46. Bucci S, Schwannauer M, Berry N. The digital revolution and its impact on mental health care. Psychol Psychother 2019 Jun;92(2):277-297. [doi: 10.1111/papt.12222] [Medline: 30924316]
47. Lucas GM, Gratch J, King A, Morency LP. It's only a computer: virtual humans increase willingness to disclose. Comput Human Behav 2014 Aug;37:94-100 [FREE Full text] [doi: 10.1016/j.chb.2014.04.043]
48. Bickmore TW, Silliman RA, Nelson K, Cheng DM, Winter M, Henault L, et al. A randomized controlled trial of an automated exercise coach for older adults. J Am Geriatr Soc 2013 Oct;61(10):1676-1683. [doi: 10.1111/jgs.12449] [Medline: 24001030]
49. Bickmore TW, Schulman D, Sidner C. Automated interventions for multiple health behaviors using conversational agents. Patient Educ Couns 2013 Aug;92(2):142-148 [FREE Full text] [doi: 10.1016/j.pec.2013.05.011] [Medline: 23763983]
50. Watson A, Bickmore T, Cange A, Kulshreshtha A, Kvedar J. An Internet-based virtual coach to promote physical activity adherence in overweight adults: randomized controlled trial. J Med Internet Res 2012 Jan 26;14(1):e1 [FREE Full text] [doi: 10.2196/jmir.1629] [Medline: 22281837]
51. Edwards RA, Bickmore T, Jenkins L, Foley M, Manjourides J. Use of an interactive computer agent to support breastfeeding. Matern Child Health J 2013 Dec;17(10):1961-1968. [doi: 10.1007/s10995-013-1222-0] [Medline: 23329167]
52. Vaidyam AN, Wisniewski H, Halamka JD, Kashavan MS, Torous JB. Chatbots and conversational agents in mental health: a review of the psychiatric landscape. Can J Psychiatry 2019 Jul;64(7):456-464 [FREE Full text] [doi: 10.1177/0706743719828977] [Medline: 30897957]
53. Cameron G, Cameron D, Megaw G, Bond R, Mulvenna M, O'Neill S, et al. Assessing the usability of a chatbot for mental health care. In: Proceedings of the 2018 International Workshops on Internet Science. 2019 Presented at: INSCI '18; October 24–26, 2018; St. Petersburg, Russia p. 121-132. [doi: 10.1007/978-3-030-17705-8_11]
54. Cameron G, Cameron D, Megaw G, Bond R, Mulvenna M, O'Neill S, et al. Towards a chatbot for digital counselling. In: Proceedings of the 31st British Computer Society Human Computer Interaction Conference. 2017 Presented at: HCI '17; July 3-6, 2017; Sunderland, UK p. 1-7. [doi: 10.14236/ewic/hci2017.24]
55. Abd-Alrazaq AA, Rababeh A, Alajlani M, Bewick BM, Househ M. Effectiveness and safety of using chatbots to improve mental health: systematic review and meta-analysis. J Med Internet Res 2020 Jul 13;22(7):e16021 [FREE Full text] [doi: 10.2196/16021] [Medline: 32673216]
56. Laranjo L, Dunn AG, Tong HL, Kocaballi AB, Chen J, Bashir R, et al. Conversational agents in healthcare: a systematic review. J Am Med Inform Assoc 2018 Sep 01;25(9):1248-1258 [FREE Full text] [doi: 10.1093/jamia/ocy072] [Medline: 30010941]
57. Provoost S, Lau HM, Ruwaard J, Riper H. Embodied conversational agents in clinical psychology: a scoping review. J Med Internet Res 2017 May 09;19(5):e151 [FREE Full text] [doi: 10.2196/jmir.6553] [Medline: 28487267]
58. Abd-Alrazaq AA, Alajlani M, Alalwan AA, Bewick BM, Gardner P, Househ M. An overview of the features of chatbots in mental health: a scoping review. Int J Med Inform 2019 Dec;132:103978. [doi: 10.1016/j.ijmedinf.2019.103978] [Medline: 31622850]
59. Field Listing - Internet Users. Central Intelligence Agency. 2018 Jul. URL: https://www.cia.gov/the-world-factbook/field/internet-users/ [accessed 2021-09-15]
60. Canadian Internet Use Survey. Statistics Canada. 2019 Oct 29. URL: https://www150.statcan.gc.ca/n1/daily-quotidien/191029/dq191029a-eng.htm [accessed 2020-03-27]
61. Communications Monitoring Report 2016: Canada's Communication System: An Overview for Canadians. Canadian Radio-television and Telecommunications Commission. 2016. URL: https://publications.gc.ca/collections/collection_2016/crtc/BC9-9-2016-eng.pdf [accessed 2021-09-15]
62. Selenium. URL: https://www.selenium.dev/ [accessed 2022-02-10]
63. Rasa X. URL: https://rasa.com/docs/rasa-x/ [accessed 2022-02-10]
64. BotKit. GitHub. URL: https://github.com/howdyai/botkit [accessed 2022-02-10]
65. Botpress. URL: https://botpress.com/ [accessed 2022-02-10]
66. MindMeld. URL: https://www.mindmeld.com/ [accessed 2022-02-10]
67. DeepPavlov. URL: https://deeppavlov.ai/ [accessed 2022-02-10]
68. Azevedo Chagas B, Ferreguetti K, Ferreira TC, Marcolino MS, Ribeiro LB, Pagano AS, et al. Chatbot as a telehealth intervention strategy in the COVID-19 pandemic. CLEI E J 2021 Dec 13;24(3). [doi: 10.19153/cleiej.24.3.6]
69. Lucid Chart. Lucid. URL: https://www.lucidchart.com/ [accessed 2022-02-10]

XSL•FO
RenderX

70. Thomasian NM, Eickhoff C, Adashi EY. Advancing health equity with artificial intelligence. J Public Health Policy 2021 Dec;42(4):602-611 [FREE Full text] [doi: 10.1057/s41271-021-00319-5] [Medline: 34811466]
71. Weizenbaum J. ELIZA—a computer program for the study of natural language communication between man and machine. Commun ACM 1966 Jan;9(1):36-45 [FREE Full text] [doi: 10.1145/365153.365168]
72. Solaiman I, Brundage M, Clark J, Askell A, Herbert-Voss A, Wu J, et al. Release Strategies and the Social Impacts of Language Models. arXiv 2019 Nov 13 [FREE Full text]
73. Core NLP. Stanford University. 2021. URL: https://stanfordnlp.github.io/CoreNLP/ [accessed 2022-02-10]
74. The Mental Health Virtual Assistant. Mood Disorders Society of Canada. URL: https://www.mymira.ca/ [accessed 2022-07-12]
75. Kirby PL, Reynolds KA, Walker JR, Furer P, Pryor TA. Evaluating the quality of perinatal anxiety information available online. Arch Womens Ment Health 2018 Dec;21(6):813-820. [doi: 10.1007/s00737-018-0875-5] [Medline: 29931445]
76. Ipser JC, Dewing S, Stein DJ. A systematic review of the quality of information on the treatment of anxiety disorders on the Internet. Curr Psychiatry Rep 2007 Aug;9(4):303-309. [doi: 10.1007/s11920-007-0037-3] [Medline: 17880862]
77. Chung M, Oden RP, Joyner BL, Sims A, Moon RY. Safe infant sleep recommendations on the Internet: let's Google it. J Pediatr 2012 Dec;161(6):1080-1084 [FREE Full text] [doi: 10.1016/j.jpeds.2012.06.004] [Medline: 22863258]
78. Devine T, Broderick J, Harris LM, Wu H, Hilfiker SW. Making quality health websites a national public health priority: toward quality standards. J Med Internet Res 2016 Aug 02;18(8):e211 [FREE Full text] [doi: 10.2196/jmir.5999] [Medline: 27485512]
79. Tan BY, Chew NW, Lee GK, Jing M, Goh Y, Yeo LL, et al. Psychological impact of the COVID-19 pandemic on health care workers in Singapore. Ann Intern Med 2020 Aug 18;173(4):317-320 [FREE Full text] [doi: 10.7326/M20-1083] [Medline: 32251513]
80. Li Z, Ge J, Yang M, Feng J, Qiao M, Jiang R, et al. Vicarious traumatization in the general public, members, and non-members of medical teams aiding in COVID-19 control. Brain Behav Immun 2020 Aug;88:916-919 [FREE Full text] [doi: 10.1016/j.bbi.2020.03.007] [Medline: 32169498]
81. COVID-19: Guidance for Prioritizing Health Care Workers for COVID-19 Vaccination. Ontario Ministry of Health. 2021. URL: https://www.health.gov.on.ca/en/pro/programs/publichealth/coronavirus/docs/Guidance_for_Prioritizing_HCW_covid19_vaccination_2020-01-08.pdf [accessed 2021-09-15]
82. Small K. Alberta's COVID-19 vaccine rollout expands to front-line health-care workers on Monday. Global News. 2014 Apr 10. URL: https://globalnews.ca/news/7750610/alberta-covid-19-vaccine-rollout-2c/ [accessed 2021-09-15]
83. Nova Scotia Health by the Numbers 2019-20. Nova Scotia Health. 2019. URL: https://www.nshealth.ca/AnnualReport2019-20/numbers.html [accessed 2021-09-15]
84. The shift to smaller households over the past century. Statistics Canada. 2018 May 17. URL: https://www150.statcan.gc.ca/n1/pub/11-630-x/11-630-x2015008-eng.htm [accessed 2022-01-19]
85. Burgard T, Bošnjak M, Wedderhoff N. Response rates in online surveys with affective disorder participants. Z Psychol 2020 Mar 31;228(1):14-24 [FREE Full text] [doi: 10.1027/2151-2604/a000394]
86. Shih TH, Fan X. Comparing response rates from Web and mail surveys: a meta-analysis. Field Methods 2008 Mar 03;20(3):249-271 [FREE Full text] [doi: 10.1177/1525822x08317085]
87. Daikeler J, Bosnjak M, Lozar Manfreda K. Web versus other survey modes: an updated and extended meta-analysis comparing response rates. J Surv Stat Methodol 2019 May 13;8(3):513-539 [FREE Full text] [doi: 10.1093/jssam/smz008]
88. Fan W, Yan Z. Factors affecting response rates of the Web survey: a systematic review. Comput Human Behav 2010 Mar;26(2):132-139 [FREE Full text] [doi: 10.1016/j.chb.2009.10.015]
89. Noble JM, Vuong W, Surood S, Urichuk L, Greenshaw AJ, Agyapong VI. Text4Support mobile-based programming for individuals accessing addictions and mental health services-retroactive program analysis at baseline, 12 weeks, and 6 months. Front Psychiatry 2021 May 28;12:640795 [FREE Full text] [doi: 10.3389/fpsyt.2021.640795] [Medline: 34122173]
90. Connell J, Barkham M. CORE-10 User Manual, Version 1.1. CORE System Trust & CORE Information Management Systems Ltd. 2007. URL: https://pdf4pro.com/amp/cdn/core-10-user-manual-john-butler-96b16.pdf [accessed 2021-09-01]
91. Philip P, Dupuy L, Auriacombe M, Serre F, de Sevin E, Sauteraud A, et al. Trust and acceptance of a virtual psychiatric interview between embodied conversational agents and outpatients. NPJ Digit Med 2020 Jan 7;3:2 [FREE Full text] [doi: 10.1038/s41746-019-0213-y] [Medline: 31934646]
92. Abd-Alrazaq A, Safi Z, Alajlani M, Warren J, Househ M, Denecke K. Technical metrics used to evaluate health care chatbots: scoping review. J Med Internet Res 2020 Jun 05;22(6):e18301 [FREE Full text] [doi: 10.2196/18301] [Medline: 32442157]
93. Philip P, Micoulaud-Franchi JA, Sagaspe P, De Sevin E, Olive J, Bioulac S, et al. Virtual human as a new diagnostic tool, a proof of concept study in the field of major depressive disorders. Sci Rep 2017 Feb 16;7:42656 [FREE Full text] [doi: 10.1038/srep42656] [Medline: 28205601]
94. Philip P, Bioulac S, Sauteraud A, Chaufton C, Olive J. Could a virtual human be used to explore excessive daytime sleepiness in patients? Presence (Camb) 2014 Nov 01;23(4):369-376 [FREE Full text] [doi: 10.1162/pres_a_00197]

XSL•FO
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95. Martínez-Miranda J, Martínez A, Ramos R, Aguilar H, Jiménez L, Arias H, et al. Assessment of users' acceptability of a mobile-based embodied conversational agent for the prevention and detection of suicidal behaviour. J Med Syst 2019 Jun 25;43(8):246. [doi: 10.1007/s10916-019-1387-1] [Medline: 31240494]
96. Fulmer R, Joerin A, Gentile B, Lakerink L, Rauws M. Using psychological artificial intelligence (Tess) to relieve symptoms of depression and anxiety: randomized controlled trial. JMIR Ment Health 2018 Dec 13;5(4):e64 [FREE Full text] [doi: 10.2196/mental.9782] [Medline: 30545815]
97. Zimmerman MS, Shaw Jr G. Health information seeking behaviour: a concept analysis. Health Info Libr J 2020 Sep;37(3):173-191. [doi: 10.1111/hir.12287] [Medline: 32052549]
98. Blackwell AF. Objective functions: (in)humanity and inequity in artificial intelligence. HAU 2019 Mar;9(1):137-146 [FREE Full text] [doi: 10.1086/703871]
99. Dankwa-Mullan I, Scheufele EL, Matheny ME, Quintana Y, Chapman WW, Jackson G, et al. A proposed framework on integrating health equity and racial justice into the artificial intelligence development lifecycle. J Health Care Poor Underserved 2021 May;32(2S):300-317. [doi: 10.1353/hpu.2021.0065]
100. Syan A, Lam JY, Huang CG, Smith MS, Darnay K, Hawke LD, et al. The Wellness Quest: a health literacy and self-advocacy tool developed by youth for youth mental health. Health Expect 2021 Apr;24(2):659-669 [FREE Full text] [doi: 10.1111/hex.13214] [Medline: 33636052]
101. Chang SJ, Im EO. A path analysis of Internet health information seeking behaviors among older adults. Geriatr Nurs 2014;35(2):137-141. [doi: 10.1016/j.gerinurse.2013.11.005] [Medline: 24332965]
102. Ellis J, Mullan J, Worsley A, Pai N. The role of health literacy and social networks in arthritis patients' health information-seeking behavior: a qualitative study. Int J Family Med 2012;2012:397039 [FREE Full text] [doi: 10.1155/2012/397039] [Medline: 22997575]
103. Sun X, Yang D, Li X, Zhang T, Meng Y, Qiu H, et al. Interpreting deep learning models in natural language processing: a review. arXiv 2021 Oct 25 [FREE Full text]
104. Murphy KP. Machine Learning: A Probabilistic Perspective. Cambridge, MA, USA: MIT Press; 2012.
105. Kim MY, Atakishiyev S, Babiker HK, Farruque N, Goebel R, Zaïane OR, et al. A multi-component framework for the analysis and design of explainable artificial intelligence. Mach Learn Knowl Extr 2021 Nov 18;3(4):900-921 [FREE Full text] [doi: 10.3390/make3040045]
106. Dong C, Huang C, Zaiane OR, Mou L. Simulated annealing for emotional dialogue systems. In: Proceedings of the 30th ACM International Conference on Information & Knowledge Management. 2021 Oct Presented at: CIKM '21; November 1-5, 2021; Virtual p. 2984-2988 URL: https://doi.org/10.1145/3459637.3482182 [doi: 10.1145/3459637.3482182]
107. Huang C, Zaiane OR, Trabelsi A, Dziri N. Automatic dialogue generation with expressed emotions. In: Proceedings of the 2018 Conference of the North American Chapter of the Association for Computational Linguistics: Human Language Technologies. 2018 Presented at: NAACL '18; June 1-6, 2018; New Orleans, LA, USA p. 49-54. [doi: 10.18653/v1/n18-2008]
108. Farruque N, Huang C, Zaiane OR, Goebel R. Basic and depression specific emotion identification in Tweets: multi-label classification experiments. In: Proceedings of the 20th International Conference on Intelligent Text Processing and Computational Linguistics. 2019 Presented at: CICLing '19; April 7-13, 2019; La Rochelle, France URL: https://doi.org/10.48550/arXiv.2105.12364

Abbreviations

AES: Acceptability E-scale
AI: artificial intelligence
CORE-10: Clinical Outcomes in Routine Evaluation System
ETQ: Embodied Conversational Agent Trust Questionnaire
HISB: Health information–seeking behavior
MDSC: Mood Disorders Society of Canada
MIRA: Mental Health Intelligent Information Resource Assistant
NLP: natural language processing

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Protocol

Pediatric Research Observing Trends and Exposures in COVID-19 Timelines (PROTECT): Protocol for a Multisite Longitudinal Cohort Study

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Abstract

Background: Assessing the real-world effectiveness of COVID-19 vaccines and understanding the incidence and severity of SARS-CoV-2 illness in children are essential to inform policy and guide health care professionals in advising parents and caregivers of children who test positive for SARS-CoV-2.

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Objective: This report describes the objectives and methods for conducting the Pediatric Research Observing Trends and Exposures in COVID-19 Timelines (PROTECT) study. PROTECT is a longitudinal prospective pediatric cohort study designed to estimate SARS-CoV-2 incidence and COVID-19 vaccine effectiveness (VE) against infection among children aged 6 months to 17 years, as well as differences in SARS-CoV-2 infection and vaccine response between children and adolescents.

Methods: The PROTECT multisite network was initiated in July 2021, which aims to enroll approximately 2305 children across four US locations and collect data over a 2-year surveillance period. The enrollment target was based on prospective power calculations and accounts for expected attrition and nonresponse. Study sites recruit parents and legal guardians of age-eligible children participating in the existing Arizona Healthcare, Emergency Response, and Other Essential Workers Surveillance (HEROES)-Research on the Epidemiology of SARS-CoV-2 in Essential Response Personnel (RECOVER) network as well as from surrounding communities. Child demographics, medical history, COVID-19 exposure, vaccination history, and parents/legal guardians' knowledge and attitudes about COVID-19 are collected at baseline and throughout the study. Mid-turbinate nasal specimens are self-collected or collected by parents/legal guardians weekly, regardless of symptoms, for SARS-CoV-2 and influenza testing via reverse transcription-polymerase chain reaction (RT-PCR) assay, and the presence of COVID-like illness (CLI) is reported. Children who test positive for SARS-CoV-2 or influenza, or report CLI are monitored weekly by online surveys to report exposure and medical utilization until no longer ill. Children, with permission of their parents/legal guardians, may elect to contribute blood at enrollment, following SARS-CoV-2 infection, following COVID-19 vaccination, and at the end of the study period. PROTECT uses electronic medical record (EMR) linkages where available, and verifies COVID-19 and influenza vaccinations through EMR or state vaccine registries.

Results: Data collection began in July 2021 and is expected to continue through the spring of 2023. As of April 13, 2022, 2371 children are enrolled in PROTECT. Enrollment is ongoing at all study sites.

Conclusions: As COVID-19 vaccine products are authorized for use in pediatric populations, PROTECT study data will provide real-world estimates of VE in preventing infection. In addition, this prospective cohort provides a unique opportunity to further understand SARS-CoV-2 incidence, clinical course, and key knowledge gaps that may inform public health.

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KEYWORDS

COVID-19; SARS-CoV-2; vaccine effectiveness; vaccine; efficacy; effectiveness; cohort study; pediatric; child; inoculation; vaccination; public health; children; health care professional; health care; caregiver; health data; online survey; incidence

Introduction

COVID-19 cases among US children continue to rise, with over 12.7 million reported cases as of March 3, 2022 (representing 19% of all US cases) [1]. Although infection with SARS-CoV-2 typically results in milder symptoms in children than in adults, severe illness resulting in hospitalization, admission to intensive care units, or need for respiratory support can still occur [2-4].

The Pfizer-BioNTech BNT162b2 mRNA COVID-19 vaccine received emergency use authorization (EUA) for individuals aged 16 years and older on December 11, 2020; aged 12-15 years on May 10, 2021; aged 5-11 years on October 29, 2021; and aged 6 months through 5 years June 18, 2022. However, as of March 3, 2022, only 57% and 26% of US adolescents aged 12-17 years and children aged 5-11 years, respectively, are fully vaccinated [5-7].

Randomized controlled clinical trials have shown that the Pfizer-BioNTech COVID-19 vaccine is highly immunogenic and efficacious in preventing infection and severe illness in children and adolescents [8-10]. However, few studies to date have documented vaccine effectiveness (VE) against symptomatic and asymptomatic infection among pediatric populations in real-world conditions. Moreover, sociodemographic and clinical risk factors for SARS-CoV-2 infection in pediatric populations are not well characterized, particularly among those with milder illness; most studies to date have identified risk factors among hospitalized children only [11]. Given the predominance of mild to moderate COVID-19 illness in this age group, assessing the full clinical, immunological, and epidemiological impact of COVID-19 among pediatric populations requires prospective monitoring of both symptomatic and asymptomatic infection.

The HEROES-RECOVER network (Arizona Healthcare, Emergency Response, and Other Essential Workers Surveillance [HEROES] study and the Research on the Epidemiology of SARS-CoV-2 in Essential Response Personnel [RECOVER] study) established a protocol that continues to prospectively collect data on SARS-CoV-2 infections in approximately 6000 health care workers, first responders, and other essential workers [12-14]. Modeled on the HEROES-RECOVER protocols, Pediatric Research Observing Trends and Exposures in COVID-19 Timelines (PROTECT) is a longitudinal prospective pediatric cohort study designed to estimate symptomatic and asymptomatic SARS-CoV-2 incidence and COVID-19 VE against infection among children aged 6 months to 17 years [12,15]. In addition, several secondary objectives are to identify risk factors for SARS-CoV-2 infection and describe the clinical course of COVID-19 in children, such as examining the kinetics of immune responses to SARS-CoV-2 infection. The PROTECT cohort will also be leveraged to monitor influenza infections and vaccine effectiveness, given the similarity in clinical presentation and importance of evaluating influenza vaccines annually.

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Methods

Study Design

Using a prospective longitudinal cohort design, approximately 2305 children aged 6 months to 17 years will be enrolled, with a planned study duration of at least 15 months after study start. Enrollment began in July 2021 and surveillance is expected to continue through April 2023. Additional study objectives include describing the incidence of SARS-CoV-2 infections by age, sociodemographic characteristics, health status, and other risk factors. Primary and secondary study objectives can be found in Textbox 1.

Textbox 1. Primary and secondary objectives of the PROTECT (Pediatric Research Observing Trends and Exposures in COVID-19 Timelines) study.

Primary Objectives

- Contribute to estimates of vaccine effectiveness (VE) of authorized COVID-19 vaccines in preventing laboratory-confirmed symptomatic and asymptomatic SARS-CoV-2 virus infections among children aged 6 months to 17 years.
- Contribute to estimates of the incidence of laboratory-confirmed SARS-CoV-2 infection, including asymptomatic and symptomatic infections, using molecular, virologic, and serologic diagnostics, and describe differences by age and other sociodemographic characteristics, health status, and/or other risk factors.

Secondary Objectives

- Contribute data to explore the VE, impact, and uptake of authorized COVID-19 vaccines.
- Describe associations between COVID-19 vaccination and SARS-CoV-2 infection and symptoms by vaccine product, number of doses, and timing of vaccination.
- Describe VE by age and other sociodemographic characteristics, health status, and/or other risk factors.
- Examine the association between vaccination and illness severity, duration, and infectiousness (or viral shedding) among children with SARS-CoV-2 infection.
- Describe child-reported adverse reactions following vaccination.
- Contribute data to explore clinical and epidemiological factors of SARS-CoV-2 infection.
- Examine the kinetics of immune responses to SARS-CoV-2 infection.
- Describe the association between preexisting SARS-CoV-2 antibodies and subsequent risk of SARS-CoV-2 reinfection.
- Describe the clinical characteristics and functional impact associated with COVID-19 illness among children.
- Contribute data to characterize knowledge, attitudes, and practices of parents/guardians related to COVID-19 vaccines, and examine associations with vaccine hesitancy and uptake or adherence to vaccination recommendations.
- Contribute data to examine the duration of viral RNA detection associated with symptomatic and asymptomatic SARS-CoV-2 infection using quantitative molecular methods.
- Contribute data to examine the incidence and outcomes of other respiratory virus infections, including influenza virus infection.
- Contribute to VE estimates of influenza vaccines in preventing influenza virus infection and influenza illness.

Setting

PROTECT is an ancillary study to the HEROES-RECOVER network, which includes prospective cohorts from two studies: the HEROES study and the RECOVER study [12,15]. The RECOVER sites encompass five US states: Florida (Miami), Minnesota (Duluth), Oregon (Portland), Texas (Temple), and Utah (Salt Lake City). The HEROES study is based in Arizona (Phoenix, Tucson, and other areas). Study teams from the Arizona, Florida, Texas, and Utah sites are recruiting children into the PROTECT study, and principal investigators from all sites, including the Minnesota and Oregon sites, provided input on study design. PROTECT recruits children from households within the HEROES-RECOVER cohort as well as from the surrounding community. The Minnesota and Oregon sites do not recruit participants for PROTECT.

Eligibility Criteria

Eligible children include children aged 4 months to 17 years at the date of recruitment with plans to stay in the area for the next 12 months, although children 4-5 months old do not enroll and start study activities until they are 6 months old. If a child turns 18 years of age during the study period, they are either reconsented or have consent waived depending on site institutional review board (IRB) requirements and can continue to participate.

The child's parent or legal guardian must have access to a smartphone or internet-connected computer, a mailing address where they can receive study supplies, willingness and ability to complete periodic data collection activities, and the ability to speak and understand English or Spanish (they must sign the English- or Spanish-language study consent form).

Exclusion criteria include receiving both doses of a two-dose COVID-19 vaccine (or one dose of a single-dose COVID-19 vaccine if authorized during the study period) ≥14 days prior to enrollment (for those enrolled at the Texas, Utah, and Florida study sites) or participating in a vaccine trial within 3 months of the enrollment date. To ensure representation of both vaccinated and unvaccinated children, children recruited from

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the community are required to be either unvaccinated or only partially vaccinated. The HEROES study site (Arizona) used a target ratio of 1:6 participants vaccinated against COVID-19 to unvaccinated participants to direct the recruitment strategy. Some recruitment for the pediatric cohort occurred prior to vaccine availability for those under 12 years of age (see Table 1).

Table 1. PROTECT (Pediatric Research Observing Trends and Exposures in COVID-19 Timelines) study sites and site characteristics.

Characteristics	University of Arizona	Baylor Scott & White Health	University of Miami	University of Utah
Location	Tucson, Arizona	Temple, Texas	Miami, Florida	Salt Lake City, Utah
Recruitment area	Entire state of Arizona	Bell, Burnet, Coryell, Falls, Lampasas, McLennan, Milam, and Williamson counties in Texas	Miami-Dade county	Salt Lake, Davis, Utah, Summit, Morgan, Weber, and Tooele counties
Population of children <18 years of age in the recruitment area[a] [16]	1,609,000	363,000	546,000	758,000
Recruitment goal	1500	200	330	275
Recruitment strategies	Websites, social media, press releases, outreach to community members and interested parties, current HEROES[b] households	Radio, websites, search engines, social media, targeted phone banking, outreach to community members and interested parties, current RECOVER[c] households	Radio, websites, search engines, social media, targeted phone banking, outreach to community members and interested parties, current RECOVER households, address-based sampling mailers	Radio, websites, search engines, social media, outreach to community members and interested parties, current RECOVER households
Eligibility related to vaccination status[d]	Varied based upon vaccine availability at the time of enrollment	Not fully vaccinated at enrollment unless parents/legal guardians participate in RECOVER	Not fully vaccinated at enrollment unless parents/legal guardians participate in RECOVER	Not fully vaccinated at enrollment unless parents/legal guardians participate in RECOVER

[a]Rounded to the nearest thousand. Data from April 2020.

[b]HEROES: Healthcare, Emergency Response, and Other Essential Workers Surveillance study.

[c]RECOVER: Research on the Epidemiology of SARS-CoV-2 in Essential Response Personnel study.

[d]See Table 3 for definitions of vaccination status.

Recruitment Strategy

The PROTECT study's enrollment goal of 2305 children is intended to assure adequate statistical power (see detailed power calculations below) after accounting for nonresponse and attrition. Sites enroll children across three age groups: children aged 6 months to 6 years, aged 7-11 years, and aged 12-17 years. Each site has recruitment goals based on its catchment area (see Table 2). Site-specific enrollment targets are reflective of the current enrollment totals of the parallel cohort study among frontline workers from which children would be recruited. Sites were asked to project an additional number of participants that could be recruited from community engagements of the sites. Study sites implement a multipronged recruitment strategy, including: (1) enrolling from the existing HEROES-RECOVER cohort; (2) sharing study information with health care systems and providers, community organizations, school districts, and vaccination sites; and (3) accepting self-referrals from community marketing tailored to the site, which may include press releases, social media, radio ads, and Google banners.

Table 2. PROTECT (Pediatric Research Observing Trends and Exposures in COVID-19 Timelines) enrollment goal by study site and age group.

Age group	Arizona HEROES[a]	Texas	Florida	Utah	All PROTECT
6 months to 6 years	300	63	70	105	538
7-11 years	700	63	105	105	973
12-17 years	700	74	155	40	969
Total	1500	200	330	Up to 275	2305

[a]HEROES: Healthcare, Emergency Response, and Other Essential Workers Surveillance study.

Recruitment and enrollment activities vary by site but may be conducted by a telephone call with study staff, a virtual call center, or in-person at study site clinics. Participants' parents/legal guardians may opt to complete a screening interview during recruitment or via the study website to determine eligibility and interest. Study staff inform parents/legal guardians of the participation incentives, including gift cards or Clin cards (reloadable prepaid gift cards) for completion of study activities, quarterly gift cards, or raffles, varying by site and local IRB guidance (see Table S1 in Multimedia Appendix 1).

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Data Collection

Data are collected and managed through REDCap (Research Electronic Data Capture), a secure, online Health Insurance Portability and Accountability Act–compliant data management platform, which is only accessible through a password-protected REDCap account [17,18]. Sites use Mosio or Twilio to automate the process of sending regular text messages or emails containing specimen collection reminders and links to the secure data collection platform [19,20]. For the Utah and Texas study sites, data are stored through a centralized REDCap project managed by Abt Associates and housed at Vanderbilt University. The Florida and Arizona study sites maintain their own REDCap databases through their universities.

All study-related documents and samples contain a unique identifier for each child. Additionally, a unique identifier is created at the household level, given that multiple children from a household may enroll in PROTECT. Study data are linked with this household identifier to help facilitate the distribution of study supplies to parents/legal guardians and allow for clustering analysis.

Enrollment

An electronic copy of the study consent and assent forms is sent to parents/legal guardians for review. Study staff review all information and study procedures with the parents/legal guardians. Study staff document written permission from a parent/legal guardian for the child to participate in the study, allow study staff to store biospecimens (nasal specimens and blood samples) after PROTECT ends, and obtain written consent for their participation in study survey data collection. Study staff also obtain and document written assent from children aged 12-17 years or verbal assent from children aged 7-11 years prior to starting enrollment activities. The parent/legal guardian must provide permission for each eligible child if multiple children from their household participate in PROTECT.

After consent, an enrollment survey for each child enrolled in PROTECT is completed by the parent/legal guardian to record information on household composition, household members' COVID-19 vaccination status, perceptions of COVID-19 and COVID-19 vaccines (and intent if the child is not vaccinated), COVID-19 illness history, sociodemographic information (such as household income, race/ethnicity, and current gender identity), school and/or daycare attendance, participation in extracurricular and work-related activities, health insurance coverage, percent of time masks are worn in school/daycare and the community, medical history (eg, influenza and other routine childhood vaccines, medical conditions, daily medication use, and any hospitalizations in the past 12 months), and self-reported overall health status and sleep quality (see Table S2 in Multimedia Appendix 2).

Parents/legal guardians are provided with multiple respiratory specimen collection kits per enrolled child. These kits include study information and all specimen collection materials. Specimen collection kits are replenished periodically to ensure participants do not run out. Parents/legal guardians are given written and visual detailed instructions for collecting, storing, and submitting specimens. Depending on the study site, parents/legal guardians may drop specimens off at a specified location, have them picked up by an at-home courier, or ship them according to FDA guidance and specifications.

The parent/legal guardian also selects which day of the week they agree to collect and return the kit. They will do this on the same day every week, regardless of whether the child is experiencing illness symptoms or not. The evening prior to collecting the child's nasal specimen, parents/legal guardians may receive a reminder email or text message, depending on the study site.

Active Surveillance

Each week, children enrolled in PROTECT provide a mid-turbinate nasal specimen and the parent/legal guardian responds to three questions in writing on the specimen collection bag: the collection date of the respiratory specimen, whether the child is experiencing COVID-like illness (CLI) symptoms, and how many days ago CLI symptoms began (if appropriate). For PROTECT, CLI is defined as the presence of at least one of the following symptoms: fever, chills, cough, shortness of breath, sore throat, diarrhea, muscle or body aches, and change in smell or taste. For nonverbal children, the following symptoms are also included: runny nose, fatigue/being run-down, decreased activity, and irritability/crankiness.

A parent/legal guardian collects the nasal specimen using a flocked nasal swab and places it in a viral transport medium (VTM) for children aged 6 months to 11 years. For children aged 12-17 years, the child has the option to self-collect the nasal specimen or a parent/legal guardian can collect it for them. Parent/legal guardian responses on the collection bag and the results of the reverse transcription-polymerase chain reaction (RT-PCR) tests drive potential survey pathways as described below.

A positive RT-PCR result triggers several study-related activities, starting with reporting the result to the parent/legal guardian and state/local registries. Study staff begin an illness survey (described in Figure 1) and offer parents/legal guardians the opportunity for the participant to provide a COVID-19 convalescent blood draw. Additionally, the study staff ensures that the participant's vaccine information is up to date in REDCap by reminding parents/legal guardians to complete the vaccine update survey and/or accessing vaccine data within electronic medical records (EMRs) or state registries.

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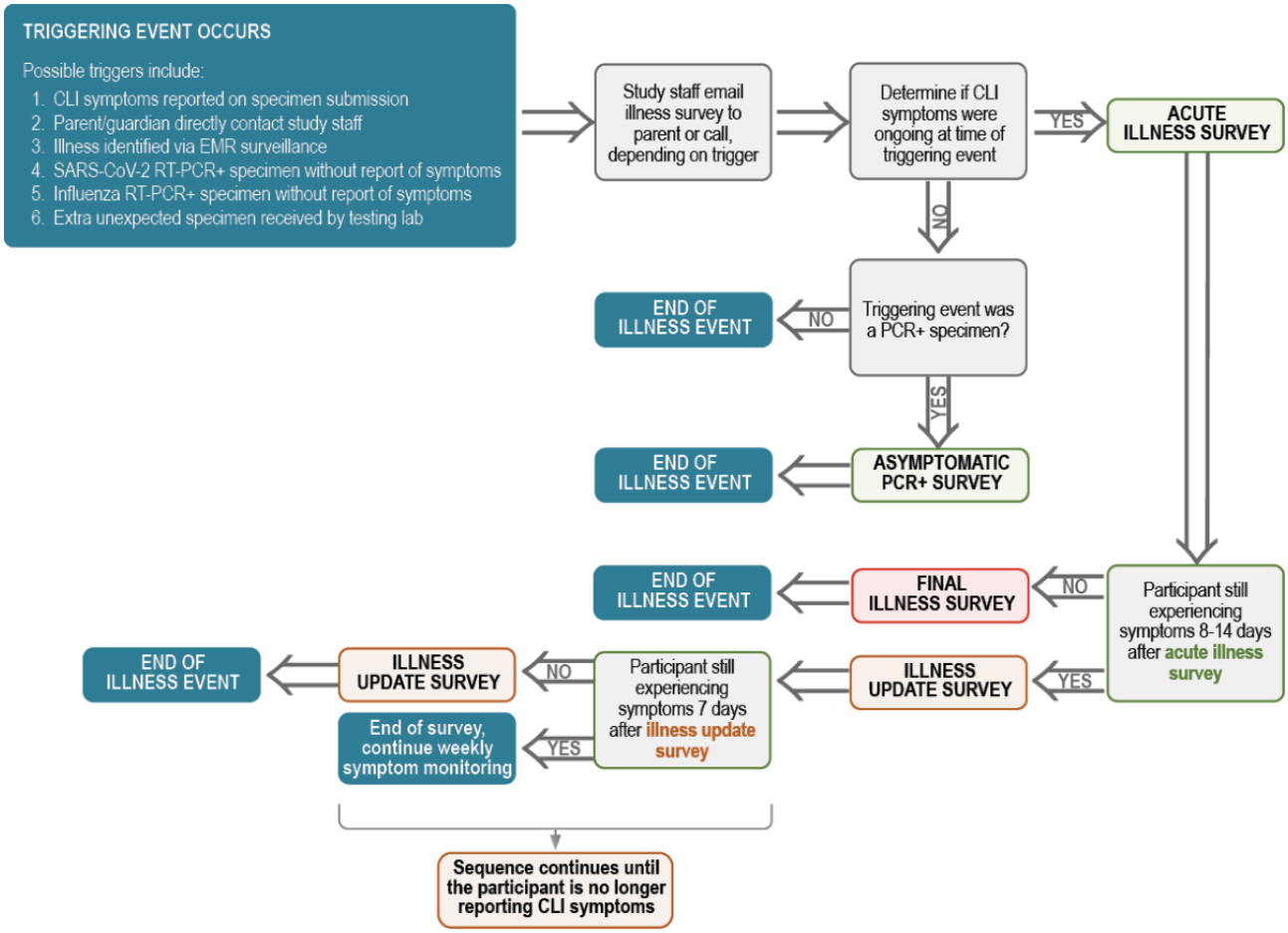
Figure 1. PROTECT active surveillance flowchart. EMR: electronic medical record; CLI: COVID-like illness; RT-PCR: reverse transcription-polymerase chain reaction.



If a specimen has a positive RT-PCR test result for SARS-CoV-2 or influenza A/B, or CLI symptoms are reported on the specimen collection bag, the study staff receives an email alert from REDCap. Likewise, parents/legal guardians may also report a positive COVID-19 test result obtained from outside PROTECT to study staff. If a child is experiencing any CLI symptoms according to the study's case definition on a day other than their predetermined collection day, the parent/legal guardian is directed to collect and submit an additional nasal specimen. Where study sites can access the EMR for research, study staff may also identify acute illness through daily monitoring of medical visits for an acute respiratory illness.

After either a CLI or RT-PCR–positive test result is noted for the child, study staff send the parent/legal guardian an illness survey to complete or the survey is completed with the parent/legal guardian over the phone. In the survey, parents/legal guardians are asked to describe the child's symptoms, subjective illness duration and severity (including missed school/daycare, ability to do normal activities, and days spent in bed), medical utilization, impact on school/daycare/work/extracurricular attendance, and potential exposures. In addition, if the participant is RT-PCR–positive for influenza, parents/legal guardians are asked whether the child has received the flu nasal vaccine, because positive influenza results can occur after recent administration of such vaccines [21,22]. If the child has an RT-PCR–positive result for influenza only, the parent/legal guardian is not asked about direct contact with individuals with COVID-19 at daycare/school or in the community. If the parent/legal guardian reports that the child continues to experience symptoms 7 days after the initial illness survey, they are asked to complete a one-time illness update survey to assess new symptoms, subjective illness severity (including missed school/daycare, ability to do normal activities, and days spent in bed), and medical utilization.

Once symptoms are no longer reported, the parent/legal guardian is asked to complete a final illness survey to assess symptoms experienced throughout the duration of the illness, subjective illness severity (including missed school/daycare, ability to do normal activities, and days spent in bed), whether the child has received the flu nasal vaccine (if RT-PCR–positive for influenza), and whether they used medical care over the course of the entire illness. At this point, the illness event is considered over. If new or additional CLI symptoms are reported (or the child receives a new positive RT-PCR result), a new illness event begins and the parent/legal guardian receives a new series of illness surveys to complete.

This process also occurs if the child experiences a new positive RT-PCR result and does not report CLI symptoms; the parent/legal guardian completes an asymptomatic RT-PCR–positive survey online or over the phone with study staff. This survey, like the acute illness survey, asks the parent/legal guardian if the child has experienced any non-CLI symptoms. If they report symptoms, they describe subjective

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illness severity, duration, medical utilization, impact on school/daycare/work/extracurricular attendance, potential exposures, and whether the child has received the flu nasal vaccine (if RT-PCR–positive for influenza). If the child has an RT-PCR–positive result for influenza only, the parent/legal guardian is not asked about direct contact with individuals with COVID-19 at daycare/school or in the community.

Monthly and Quarterly Surveys

In addition to the weekly active surveillance, parents/legal guardians receive a monthly survey that asks them to provide updated information about their participating child's vaccination status; any COVID-19 vaccine–related side effects; in-person school or daycare attendance; participation in extracurricular, work-related, and social activities; and mask-wearing habits. Quarterly, this survey also asks about their participating child's health status; illnesses not reported in the previous 3 months; the parent/legal guardian's knowledge, attitudes, and perceptions of COVID-19 and COVID-19 vaccination; and any other childhood vaccines received. Parents/legal guardians receive a link to these surveys via email or text message and complete them in REDCap.

Electronic Medical Records

At the Texas site, data from EMRs are abstracted to count medical visits for acute COVID-19 illness, identify influenza and COVID-19 vaccinations, and assess chronic medical conditions for the 12 months before enrollment and through the end of the study. The EMR extraction uses the International Statistical Classification of Diseases and Related Health Problems, 10th revision codes for all ambulatory medical encounters and all hospital admissions.

COVID-19 Vaccine Information

COVID-19 vaccination information is captured in several ways: via data abstracted and extracted from the child's EMR and/or state or municipal vaccine registry, as well as based on parent/legal guardian report. Using multiple methods to collect this information ensures complete and near real-time data capture, which is a critical component of monitoring for receipt of additional doses and allows study staff to cross-check vaccination information received from multiple sources to ensure accuracy. The use of multiple data sources also enables more accurate designation of the child's current vaccination status, particularly for unvaccinated and partially vaccinated children, by ensuring that the study team can correctly track and appropriately designate a change in vaccination status in a timely manner. No COVID-19 vaccines are offered to participants as part of enrolling in PROTECT. The definitions describing a child's COVID-19 vaccination status are provided in Table 3.

All parents/legal guardians of children who are eligible for a COVID-19 vaccine—and do not have vaccination documented from a state or municipal vaccine registry—receive a COVID-19 vaccination update survey asking about the child's COVID-19 vaccination status (as described in Multimedia Appendix 2). If the parent/legal guardian reports that the child has not been vaccinated against COVID-19, they are asked if they expect that the child will receive a vaccine in the next 8 weeks, and, if so, in how many weeks. This timeline is used to inform when the follow-up COVID-19 vaccination update survey is sent; if the parent/legal guardian reports the number of weeks until vaccination, the survey is sent at that time. Otherwise, a follow-up COVID-19 vaccination update survey is sent in 8 weeks. Follow-up COVID-19 vaccination update surveys are sent on this schedule until the parent/legal guardian reports that the child is fully vaccinated against COVID-19.

If the parent/legal guardian reports that the child has been vaccinated, they are asked the child's date of vaccination, number of doses received, vaccine manufacturer, and location of vaccination. They are also asked to upload a copy of the child's vaccine card for study staff to verify the information.

If a child is fully vaccinated and eligible to receive a booster vaccine, the parent/legal guardian is sent a booster survey every 12 weeks as long as the child is eligible to receive a booster vaccine. If the parent/legal guardian reports that the child has received a booster vaccine, they are asked the date of vaccination, vaccine manufacturer, and location of vaccination.

Table 3. COVID-19 vaccination status definitions.

Term	Description
Unvaccinated	No COVID-19 vaccine doses received
Partially vaccinated	≥14 days after the first dose in the primary series
Fully vaccinated	≥14 days after final dose in the primary series of a multidose vaccine or one dose of a single-dose vaccine, if authorized during the study period[a]
Boosted	≥7 days after any booster/additional dose
Indeterminate	<14 days after the first dose in the primary series

[a]At the time of publication, current COVID-19 vaccine recommendations include a primary series and booster doses that vary by age and vaccine product. Currently, Pfizer-BioNTech BNT162b2 primary vaccine series includes 2 doses for children ages 5-17 years and 3 doses for children 6 months to 5 years; a booster dose is recommended at least 5 months after the final dose in the primary series for children aged 12-17 years. Moderna mRNA-1273 primary series includes 2 doses for children 6 months to 17 years; at this time, a booster is not recommended for pediatric Moderna recipients.

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Laboratory Methods

Respiratory Specimens

Each week, children enrolled in PROTECT provide a mid-turbinate nasal specimen collected using a flocked nasal swab, which is placed in VTM and shipped with a cold pack using priority overnight shipping (all specimen collection materials are FDA-approved or authorized for SARS-CoV-2 and influenza RT-PCR testing). Respiratory specimens are sent to Marshfield Clinic Research Laboratories in Marshfield, Wisconsin, for RT-PCR testing for SARS-CoV-2 and influenza A/B using the Thermo Fisher TaqPath COVID-19, FluA, FluB Combo Kit assay, which is authorized for emergency use by the FDA [23]. Testing for influenza is conducted only during periods of relevant viral circulation and is completed using protocols, primers, probes, and reagents approved by the Centers for Disease Control and Prevention (CDC). Test results are returned to study sites via REDCap so they may notify parents/legal guardians of the child's results and flag RT-PCR–positive specimens for follow-up. Each study site complies with the reporting requirements of their state and local public health departments. The remaining aliquots of all study specimens are sent to a CDC-designated facility for additional virus characterization (including but not limited to genetic sequencing and novel severity markers), banking, and storage.

Blood Specimens

Blood draws are not required for participation in the PROTECT study. Participating children, with their parent/legal guardian's permission, may opt into a blood draw at each of the following opportunities: at enrollment, following SARS-CoV-2 infection (if any), following completion of a COVID-19 primary vaccine series, and following each booster dose. They may decline any blood draw at any time. Although at least 5-10 mL of whole blood is preferred, 3 mL may be accepted from infants and young children, with up to 20 mL collected from older children, depending on the study site. In the event of a SARS-CoV-2 infection, the blood sample is requested approximately 4 weeks after illness onset or RT-PCR detection if the child does not develop symptoms. The postvaccination sample is requested 10-60 days after completion of a COVID-19 vaccine primary series and each booster dose (see Table 3 for definitions).

Whole blood is collected and processed by the study site laboratory using CDC guidelines for serum collection [24]. Serum specimens are tested with CDC-approved serologic assays. The CDC laboratory or a CDC-specified reference laboratory will conduct serologic work and report results to the CDC investigators. After testing, any leftover serum will be stored for possible additional testing in the future.

Statistical Considerations

Data Quality

Branching logic, date validation, range checks, and automated skip patterns are used throughout the REDCap project to ensure high-quality data collection. Additionally, study staff perform weekly quality checks for out-of-range values and missing or inconsistent data. Sites review the results of these quality checks and follow up with the parent/legal guardian for verification or correction if necessary.

Power Analysis for VE

Recruitment goals for the minimum necessary sample size were established using Monte Carlo simulation methods that account for time-varying vaccination status, amount of observed person-time at risk for infection in both the vaccinated and unvaccinated groups, the SARS- CoV-2 incidence rate (the "background" rate of infection), and the true underlying effect (VE) size. A time-dependent Cox proportional hazards model was fit to estimate with a hypothetical cohort of 1780 and 9 months of surveillance. Robust standard errors were used to account for the clustering by study location [25]. The simulation accounted for the distribution of participants by site and age group, assumed 15% attrition, and site- and age-specific estimates of SARS-CoV-2 monthly attack rate ranging from 0.25% to 1.2%. The calculation found that the study will have sufficient power to detect at least one breakthrough SARS-CoV-2 infection and calculate VE with a lower confidence interval bound >0. Recruitment/enrollment goals were set higher than this ongoing target sample size to account for expected attrition. Although the power simulation accounted for attrition, an additional count of participants was added to provide the study with the capacity to address unforeseen changes and needs given the pandemic environment. Table 2 illustrates the recruitment goal by site by age.

Depending on the sample size, VE may be calculated by age group, full versus partial vaccination status, by booster or additional dose status, and vaccine type, if multiple products become available to use. The unadjusted incidence of symptomatic or asymptomatic SARS-CoV-2 infections will be calculated as the number of cases in the cohort over the number of person-weeks contributed by children and their associated 95% CIs.

Statistical Analysis

Vaccine Effectiveness

COVID-19 VE among participating children will be estimated using the Andersen-Gill extension of the Cox proportional hazards model. In this model, person-time would be counted according to the times indicated in Table 2 until the end of the follow-up period or SARS-CoV-2 detection. Unadjusted VE will be calculated as 100%×(1–hazard ratio for SARS-CoV-2 infection in vaccinated vs unvaccinated children). An adjusted model will utilize an inverse probability of treatment weighting approach with individual propensities to be vaccinated in each week based on associated characteristics such as sociodemographic characteristics, health information, exposure variables, mask usage, and local viral circulation. These predicted propensities will be used to calculate stabilized weights that are incorporated into a Cox proportional-hazards model.

Incidence

The unadjusted incidence of symptomatic or asymptomatic SARS-CoV-2 infections will be calculated as the number of cases in the cohort over the number of person-weeks contributed

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by participants and 95% CIs, assuming a binomial distribution. The adjusted incidence will be calculated using a negative binomial model, adjusted for age, sex, race, ethnicity, and other potential confounders. The incidence of other respiratory viruses will be calculated as laboratory-confirmed infection data are available.

Ethical Considerations

This study protocol was reviewed and approved by the Abt Associates IRB (which serves as the single IRB of record for the Florida, Texas, and Utah sites and the CDC; approval number 2109), by the University of Arizona IRB for the Arizona site, and the CDC per the US Department of Health and Human Services Policy for Protection of Human Subjects (45 C.F.R. part 46). All parents/legal guardians complete informed consent, with children completing written or verbal assent as appropriate. Study staff verifies that parents/legal guardians, and children, understand the study activities and objectives and are aware of any associated risks before enrollment and study participation.

Results

Enrollment began on July 27, 2021; as of May 13, 2022, 2371 children are enrolled in the PROTECT study, 20% of whom are aged 6 months to 4 years, 59% aged 5-11 years, 16% aged 12-15 years, and 5% aged 16-17 years. Enrollment will continue until the study site targets are met or exceeded, with data collection planned to continue through at least October 2022. This age breakdown reflects COVID-19 vaccine EUA age groups. In December 2021, PROTECT published interim VE estimates among adolescents aged 12-17 years [26].

Discussion

Projected Significance

The PROTECT cohort will provide critical information that allows estimation of SARS-CoV-2 incidence and COVID-19 VE in the real world among children and adolescents with relevance to inform public health policy. PROTECT will prospectively examine VE of authorized COVID-19 vaccines in children aged 6 months to 17 years in real-world conditions, relying on prospective monitoring to capture both symptomatic and asymptomatic SARS-CoV-2 infection. Active surveillance and follow-up are of particular importance for children, who are more likely than adults to experience mild or asymptomatic infections [27].

The study will additionally describe SARS-CoV-2 incidence, severity, and risk factors in children and adolescents, including those with mild, moderate, or no symptoms. While risk factors in pediatric patients are not well characterized, differences in adults by sociodemographic characteristics have been previously established [28,29]. This prospective cohort study addresses this need, while also providing data to estimate and further describe CLI in children and assess the extent of coinfections such as respiratory syncytial virus and influenza.

It is particularly important to understand these factors in the present context of US children's increased exposure to SARS-CoV-2 infection from in-person K-12 schools and daycare settings, especially in the wake of the recent surge in cases due to the emergence of the Omicron variant. The pandemic and responses to it have disrupted US children's education and development [30,31]. Information on sociodemographic and medical characteristics associated with COVID-19 in the pediatric population may influence policy decisions around school closures, quarantine periods, mask mandates, and other preventive measures.

Information gathered from the serial blood sampling component of the study will allow for examinations of immune response to infection and vaccination in children and the presence of antibodies from prior infections. Differences found in immune responses from infection and/or vaccination, as well as analysis of antibody longevity and potential waning protection can help to inform decisions around vaccine recommendations and the booster schedule.

Strengths

PROTECT provides a data-driven platform for contributing to CDC assessments of multiple SARS-CoV-2 and influenza research objectives in a pediatric population across multiple age groups and sociodemographic characteristics in multiple geographic settings. Moreover, PROTECT's verification of vaccines with state registries, and EMR where available, promote data quality.

The multisite cohort design can account for the heterogeneity of SARS-CoV-2 incidence as well as other factors related to geographic variability. Another strength is the inclusion of children and adolescents with potentially high exposure to SARS-CoV-2 through school, daycare, extracurricular activities, and the community. The longitudinal cohort study design allows for continuous and consistent assessment of symptoms, CLI, exposure, and SARS-CoV-2 infection and VE. Depending on sample size, VE may be calculated by age group, full versus partial vaccination status, by booster or additional dose status, and vaccine type, if multiple products become available to use. Finally, because one of the primary recruitment pools is the existing HEROES-RECOVER network, a high percentage of children come from households with health care personnel, first responders, and other essential frontline workers, making this study an important contributor to understanding COVID-19 VE and incidence in children of workers who are at risk for high exposure.

Limitations

This study is subject to several limitations. First, the ability to generalize trends in SARS-CoV-2 infection, disease severity, and immunological response in children may be biased based on enrollment, as those who participate in this type of study may be more likely to immunize their children. Moreover, PROTECT is recruiting in part directly from the HEROES-RECOVER network, which is likely biased by the healthy worker effect [32]. Adults who choose to participate in the HEROES-RECOVER network are required to meet a baseline level of health (eg, physical examinations to qualify for employment as first responders) or have specialized health care knowledge for their professions, which may potentially lead to differences in knowledge, attitudes, and practices around

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vaccinating children in their household against COVID-19 that differ from those of the general population. Second, the information received from children is self-reported, which can introduce error if the parents/legal guardians of children are not able to provide consistent information related to specimen collection, COVID-19, or influenza vaccination, and potential CLI via illness surveys. Third, there may be selection bias due to the requirement of phone and internet access to complete surveys and the requirement for children to reside at a permanent address. Fourth, nasal specimens are collected by parents/legal guardians or participants, and therefore may have a higher rate of error than if the specimens were collected by trained health care professionals. Additionally, because the PROTECT cohort includes select study sites in multiple states and is not nationally representative, the generalizability of study findings and results may be limited. Further limitations of PROTECT include relatively low enrollment and difficulty of participants adhering to the study activities. Because of experience with the HEROES-RECOVER adult cohorts, the study team predicted that adherence and retention were likely challenges. Currently, adherence of weekly nasal specimens is approximately 85%, and a total of 169 participants have withdrawn.

Conclusions

The study design, recruitment strategies, research activities, and pediatric population of the PROTECT study create a unique opportunity to further understand SARS-CoV-2 infection, illness, and VE in children and adolescents residing in multiple geographic areas throughout the United States. Ongoing monitoring of symptoms may allow researchers to further refine the characterization of CLI in children. This study also examines the knowledge, attitudes, and practices of parents as they relate to the COVID-19 vaccines in children and adolescents. Finally, the study is designed to explore possible risk factors associated with both symptomatic and asymptomatic illness and disease severity in both vaccinated and unvaccinated children, which are of interest to public health, child development, and education policymakers.

Acknowledgments

The authors would like to thank the multiple staff members who conduct study activities, as well as the research participants, without whom this research would not be possible.

Authors' Contributions

Authors ALF, JB, and LBL are all corresponding authors of this manuscript and contributed equally.

Conflicts of Interest

JB, LBL, RPR, LJE, HMW, ALP, BES, KBJ, DRH, MGW, MKH, JLB, LEWO, and MG are employees of or work for subcontractors of Abt Associates who received funds for this work through a contract awarded by the Centers for Disease Control and Prevention (CDC), National Center for Immunization and Respiratory Diseases (75D30120C08150). ALN has received research funding from Pfizer and Vir Biotechnology for unrelated studies. MG reports grants from CDC, CDC-Abt Associates, CDC-Westat, CDC-Vanderbilt, and Janssen for unrelated work. The other authors have no conflicts of interest to declare.

Multimedia Appendix 1
Incentives for PROTECT (Pediatric Research Observing Trends and Exposures in COVID-19 Timelines).
[DOCX File , 16 KB - resprot_v11i7e37929_app1.docx]

Multimedia Appendix 2
PROTECT (Pediatric Research Observing Trends and Exposures in COVID-19 Timelines) study data collection activities.
[XLSX File (Microsoft Excel File), 20 KB - resprot_v11i7e37929_app2.xlsx]

References

1. American Academy of Pediatrics. Children and COVID-19: State-Level Data Report. URL: https://www.aap.org/en/pages/2019-novel-coronavirus-covid-19-infections/children-and-covid-19-state-level-data-report/ [accessed 2022-06-09]
2. Kim L, Whitaker M, O'Halloran A, Kambhampati A, Chai SJ, Reingold A, COVID-NET Surveillance Team. Hospitalization Rates and Characteristics of Children Aged <18 Years Hospitalized with Laboratory-Confirmed COVID-19 - COVID-NET, 14 States, March 1-July 25, 2020. MMWR Morb Mortal Wkly Rep 2020 Aug 14;69(32):1081-1088. [doi: 10.15585/mmwr.mm6932e3] [Medline: 32790664]
3. Havers FP, Whitaker M, Self JL, Chai SJ, Kirley PD, Alden NB, COVID-NET Surveillance Team. Hospitalization of Adolescents Aged 12-17 Years with Laboratory-Confirmed COVID-19 - COVID-NET, 14 States, March 1, 2020-April 24, 2021. MMWR Morb Mortal Wkly Rep 2021 Jun 11;70(23):851-857 [FREE Full text] [doi: 10.15585/mmwr.mm7023e1] [Medline: 34111061]
4. CDC COVID-19 Response Team. Coronavirus Disease 2019 in Children - United States, February 12-April 2, 2020. MMWR Morb Mortal Wkly Rep 2020 Apr 10;69(14):422-426. [doi: 10.15585/mmwr.mm6914e4] [Medline: 32271728]

XSL•FO
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5. American Academy of Pediatrics. Summary of data publicly reported by the Centers for Disease Control and Prevention. 2022. URL: https://www.aap.org/en/pages/2019-novel-coronavirus-covid-19-infections/children-and-covid-19-vaccination-trends/ [accessed 2022-03-02]
6. Pfizer and BioNTech Initiate Rolling Submission for Emergency Use Authorization of Their COVID-19 Vaccine in Children 6 Months Through 4 Years of Age Following Request From U.S. FDA. Pfizer Inc. 2022. URL: https://www.pfizer.com/news/press-release/press-release-detail/pfizer-and-biontech-initiate-rolling-submission-emergency [accessed 2022-06-09]
7. Delahoy MJ, Ujamaa D, Whitaker M, O'Halloran A, Anglin O, Burns E, COVID-NET Surveillance Team, COVID-NET Surveillance Team. Hospitalizations associated with COVID-19 among children and adolescents - COVID-NET, 14 States, March 1, 2020-August 14, 2021. MMWR Morb Mortal Wkly Rep 2021 Sep 10;70(36):1255-1260. [doi: 10.15585/mmwr.mm7036e2] [Medline: 34499627]
8. Polack FP, Thomas SJ, Kitchin N, Absalon J, Gurtman A, Lockhart S, C4591001 Clinical Trial Group. Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine. N Engl J Med 2020 Dec 31;383(27):2603-2615 [FREE Full text] [doi: 10.1056/NEJMoa2034577] [Medline: 33301246]
9. Frenck RW, Klein NP, Kitchin N, Gurtman A, Absalon J, Lockhart S, C4591001 Clinical Trial Group. Safety, immunogenicity, and efficacy of the BNT162b2 Covid-19 vaccine in adolescents. N Engl J Med 2021 Jul 15;385(3):239-250 [FREE Full text] [doi: 10.1056/NEJMoa2107456] [Medline: 34043894]
10. Walter EB, Talaat KR, Sabharwal C, Gurtman A, Lockhart S, Paulsen GC, C4591007 Clinical Trial Group. Evaluation of the BNT162b2 Covid-19 vaccine in children 5 to 11 years of age. N Engl J Med 2022 Jan 06;386(1):35-46 [FREE Full text] [doi: 10.1056/NEJMoa2116298] [Medline: 34752019]
11. Woodruff RC, Campbell AP, Taylor CA, Chai SJ, Kawasaki B, Meek J, et al. Risk factors for severe COVID-19 in children. Pediatrics 2021 Dec 22:e2021053418. [doi: 10.1542/peds.2021-053418] [Medline: 34935038]
12. Edwards LJ, Fowlkes AL, Wesley MG, Kuntz JL, Odean MJ, Caban-Martinez AJ, et al. Research on the epidemiology of SARS-CoV-2 in essential response personnel (RECOVER): protocol for a multisite longitudinal cohort study. JMIR Res Protoc 2021 Dec 03;10(12):e31574 [FREE Full text] [doi: 10.2196/31574] [Medline: 34662287]
13. Thompson MG, Burgess JL, Naleway AL, Tyner H, Yoon SK, Meece J, et al. Prevention and attenuation of Covid-19 with the BNT162b2 and mRNA-1273 vaccines. N Engl J Med 2021 Jul 22;385(4):320-329 [FREE Full text] [doi: 10.1056/NEJMoa2107058] [Medline: 34192428]
14. Fowlkes A, Gaglani M, Groover K, Thiese MS, Tyner H, Ellingson K, HEROES-RECOVER Cohorts. Effectiveness of COVID-19 vaccines in preventing SARS-CoV-2 infection among frontline workers before and during B.1.617.2 (Delta) variant predominance - eight U.S. locations, December 2020-August 2021. MMWR Morb Mortal Wkly Rep 2021 Aug 27;70(34):1167-1169. [doi: 10.15585/mmwr.mm7034e4] [Medline: 34437521]
15. Lutrick K, Ellingson KD, Baccam Z, Rivers P, Beitel S, Parker J, et al. COVID-19 infection, reinfection, and vaccine effectiveness in a prospective cohort of Arizona frontline/essential workers: The AZ HEROES research protocol. JMIR Res Protoc 2021 May 26;10(6):e28925 [FREE Full text] [doi: 10.2196/28925] [Medline: 34057904]
16. U.S. Census Bureau QuickFacts. United States Census Bureau. URL: https://www.census.gov/quickfacts/fact/table/US/PST045221 [accessed 2022-02-01]
17. Harris PA, Taylor R, Minor BL, Elliott V, Fernandez M, O'Neal L, REDCap Consortium. The REDCap consortium: building an international community of software platform partners. J Biomed Inform 2019 Jul;95:103208 [FREE Full text] [doi: 10.1016/j.jbi.2019.103208] [Medline: 31078660]
18. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)--a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform 2009 Apr;42(2):377-381 [FREE Full text] [doi: 10.1016/j.jbi.2008.08.010] [Medline: 18929686]
19. Weinstein G. What is Twilio? An introduction to the leading customer engagement platform. The Current. URL: https://www.twilio.com/the-current/what-is-twilio-how-does-it-work [accessed 2021-02-15]
20. About Us. Mosio. URL: https://www.mosio.com/about-us/ [accessed 2022-01-21]
21. Vesikari T, Karvonen A, Korhonen T, Edelman K, Vainionpää R, Salmi A, CAIV-T Transmission Study Group. A randomized, double-blind study of the safety, transmissibility and phenotypic and genotypic stability of cold-adapted influenza virus vaccine. Pediatr Infect Dis J 2006 Jul;25(7):590-595. [doi: 10.1097/01.inf.0000220229.51531.47] [Medline: 16804427]
22. Jackson D, Pitcher M, Hudson C, Andrews N, Southern J, Ellis J, et al. Viral shedding in recipients of live attenuated influenza vaccine in the 2016-2017 and 2017-2018 influenza seasons in the United Kingdom. Clin Infect Dis 2020 Jun 10;70(12):2505-2513 [FREE Full text] [doi: 10.1093/cid/ciz719] [Medline: 31642899]
23. Fact Sheet for Healthcare Providers - Thermo Fisher Scientific TaqPath COVID-19, Flu A, Flu B Combo Kit. Food and Drug Administration. 2021. URL: https://www.fda.gov/media/145929/download [accessed 2022-02-03]
24. Interim Guidelines for Collecting and Handling of Clinical Specimens for COVID-19 Testing. Centers for Disease Control and Prevention. 2020. URL: https://www.cdc.gov/coronavirus/2019-ncov/lab/guidelines-clinical-specimens.html [accessed 2020-10-12]

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25. Simoes E, Cherian T, Chow J, Shaid-Salles S, Laxminarayan R, John T. Acute respiratory infections in children. In: Jamison DT, Breman JG, Measham AR, Alleyne G, Claeson M, Evans DB, editors. Disease control priorities in developing countries. 2 edition. New York: Oxford University Press; 2006.
26. Lutrick K, Rivers P, Yoo YM, Grant L, Hollister J, Jovel K, et al. Interim estimate of vaccine effectiveness of BNT162b2 (Pfizer-BioNTech) vaccine in preventing SARS-CoV-2 infection among adolescents aged 12-17 years - Arizona, July-December 2021. MMWR Morb Mortal Wkly Rep 2021 Dec 31;70(5152):1761-1765. [doi: 10.15585/mmwr.mm705152a2] [Medline: 34968373]
27. Assaker R, Colas A, Julien-Marsollier F, Bruneau B, Marsac L, Greff B, et al. Presenting symptoms of COVID-19 in children: a meta-analysis of published studies. Br J Anaesth 2020 Sep;125(3):e330-e332 [FREE Full text] [doi: 10.1016/j.bja.2020.05.026] [Medline: 32534738]
28. Graff K, Smith C, Silveira L, Jung S, Curran-Hays S, Jarjour J, et al. Risk factors for severe COVID-19 in children. Pediatr Infect Dis J 2021 Apr 01;40(4):e137-e145. [doi: 10.1097/INF.0000000000003043] [Medline: 33538539]
29. Moreira A, Chorath K, Rajasekaran K, Burmeister F, Ahmed M, Moreira A. Demographic predictors of hospitalization and mortality in US children with COVID-19. Eur J Pediatr 2021 May;180(5):1659-1663 [FREE Full text] [doi: 10.1007/s00431-021-03955-x] [Medline: 33474580]
30. Panda PK, Gupta J, Chowdhury SR, Kumar R, Meena AK, Madaan P, et al. Psychological and behavioral impact of lockdown and quarantine measures for COVID-19 pandemic on children, adolescents and caregivers: a systematic review and meta-analysis. J Trop Pediatr 2021 Jan 29;67(1):fmaa122 [FREE Full text] [doi: 10.1093/tropej/fmaa122] [Medline: 33367907]
31. Engzell P, Frey A, Verhagen MD. Learning loss due to school closures during the COVID-19 pandemic. Proc Natl Acad Sci U S A 2021 Apr 27;118(17):e2022376118 [FREE Full text] [doi: 10.1073/pnas.2022376118] [Medline: 33827987]
32. Chowdhury R, Shah D, Payal AR. Healthy worker effect phenomenon: revisited with emphasis on statistical methods - a review. Indian J Occup Environ Med 2017;21(1):2-8 [FREE Full text] [doi: 10.4103/ijoem.IJOEM_53_16] [Medline: 29391741]

Abbreviations

CDC: Centers for Disease Control and Prevention
CLI: COVID-like illness
EMR: electronic medical record
EUA: emergency use authorization
FDA: Food and Drug Administration
HEROES: Healthcare, Emergency Response, and Other Essential Workers Surveillance
IRB: Institutional Review Board
PROTECT: Pediatric Research Observing Trends and Exposures in COVID-19 Timelines
RECOVER: Research on the Epidemiology of SARS-CoV-2 in Essential Response Personnel
REDCap: Research Electronic Data Capture
RT-PCR: reverse transcription-polymerase chain reaction
VE: vaccine effectiveness
VTM: viral transport medium

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Corrigenda and Addenda

Correction: The Need for Standards Unification in Forensic Laboratory Practices: Protocol for Setting Up the Arab Forensic Laboratories Accreditation Center

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Related Article:

Correction of: https://www.researchprotocols.org/2022/6/e36778

(JMIR Res Protoc 2022;11(7):e40863) doi:10.2196/40863

In "The Need for Standards Unification in Forensic Laboratory Practices: Protocol for Setting Up the Arab Forensic Laboratories Accreditation Center" (JMIR Res Protoc 2022;11(6):e36778) the authors noted one error.

In the originally published article, Reference 6 was incorrectly published as follows:

Naglaa F. The Prevalence of Illicit Drugs and Alcohol in Road Traffic Accident Fatalities in the Eastern Region of Saudi Arabia. IJFMT 2020 Oct 7 [doi: 10.37506/ijfmt.v14i4.12122]

This reference is now corrected as follows:

Mahmoud NF, Al-Mazroua MK, Afify MM. The Prevalence of Illicit Drugs and Alcohol in Road Traffic Accident Fatalities in the Eastern Region of Saudi Arabia. Indian Journal of Forensic Medicine & Toxicology 2020;14(4): 3219-3225. [doi: 10.37506/ijfmt.v14i4.12122]

The correction will appear in the online version of the paper on the JMIR Publications website on July 14, 2022, together with the publication of this correction notice. Because this was made after submission to PubMed, PubMed Central, and other full-text repositories, the corrected article has also been resubmitted to those repositories.

Reference

1. Mahmoud NF, Al-Mazroua MK, Afify MM. The Prevalence of Illicit Drugs and Alcohol in Road Traffic Accident Fatalities in the Eastern Region of Saudi Arabia. Indian Journal of Forensic Medicine & Toxicology 2020;14(4):3219-3225. [doi: 10.37506/ijfmt.v14i4.12122]

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Corrigenda and Addenda

Correction: Assessing the Efficacy of an Individualized Psychological Flexibility Skills Training Intervention App for Medical Student Burnout and Well-being: Protocol for a Randomized Controlled Trial

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Related Article:

Correction of: https://www.researchprotocols.org/2022/2/e32992

(JMIR Res Protoc 2022;11(7):e40684) doi:10.2196/40684

In "Assessing the Efficacy of an Individualized Psychological Flexibility Skills Training Intervention App for Medical Student Burnout and Well-being: Protocol for a Randomized Controlled Trial" (JMIR Res Protoc 2022;11(2):e32992), the authors made the following update.

On March 17, 2022, the authors had published a corrigendum [1] to change the reported intervention duration from 5 weeks to 8 weeks. However, the intervention duration reported in the originally published article was correct. The current corrigendum restores the reported intervention duration to 5 weeks with the following changes:

1. In the *Methods* section of the *Abstract*, a statement appeared as follows:

> *Participants in the individualized and nonindividualized intervention arms will have 8 weeks to access the app, which includes a PF concepts training session (stage 1) and access to short PF skill activities on demand (stage 2).*

This has been corrected as follows:

> *Participants in the individualized and nonindividualized intervention arms will have 5 weeks to access the app, which includes a PF concepts training session (stage 1) and access to short PF skill activities on demand (stage 2).*

2. In the *Data Collection Tools and Procedures* section of *Methods*, a statement appeared as follows:

> *Data will be collected at two time points: T1 (baseline) and T2 (following the completion of the app-based intervention, commencing 8 weeks after baseline).*

This has been corrected as follows:

> *Data will be collected at two time points: T1 (baseline) and T2 (following the completion of the app-based intervention, commencing 5 weeks after baseline).*

3. In the *Intervention Stages* section of *Methods*, a statement appeared as follows:

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Participants who are allocated to the individualized and nonindividualized groups will have access to the 2-stage app for 8 weeks.

This has been corrected as follows:

Participants who are allocated to the individualized and nonindividualized groups will have access to the 2-stage app for 5 weeks.

4. In the *Intervention Stages* section of *Methods*, a statement appeared as follows:

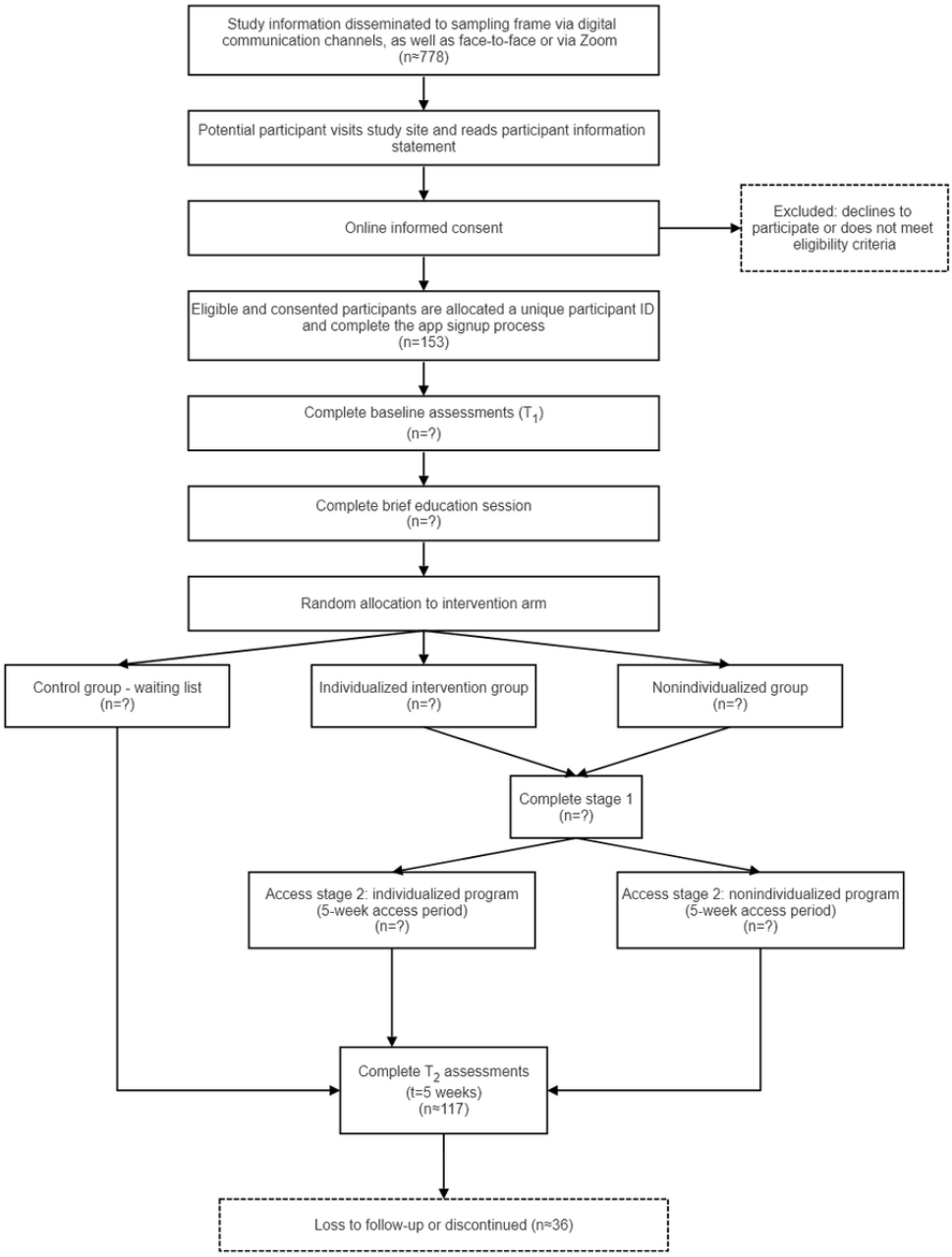
Participants may complete as many activities as they choose, but will be asked to complete at least four stage 2 skill activities during their 8-week period of access to the app.

This has been corrected as follows:

Participants may complete as many activities as they choose, but will be asked to complete at least four stage 2 skill activities during their 5-week period of access to the app.

5. Following the previous corrigendum [1], Figure 1 was altered to reflect the intervention duration of 8 weeks. The present corrigendum updated Figure 1 as follows:

Figure 1. Participant timeline.



The correction will appear in the online version of the paper on the JMIR Publications website on July 11, 2022, together with the publication of this correction notice. Because this was made after submission to PubMed, PubMed Central, and other full-text repositories, the corrected article has also been resubmitted to those repositories.

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Reference

1. Ditton E, Knott B, Hodyl N, Horton G, Walker FR, Nilsson M. Correction: Assessing the Efficacy of an Individualized Psychological Flexibility Skills Training Intervention App for Medical Student Burnout and Well-being: Protocol for a Randomized Controlled Trial. JMIR Res Protoc 2022 Mar 16;11(3):e37798 [FREE Full text] [doi: 10.2196/37798] [Medline: 35294370]

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Corrigenda and Addenda

Correction: The Hip Instructional Prehabilitation Program for Enhanced Recovery (HIPPER) as an eHealth Approach to Presurgical Hip Replacement Education: Protocol for a Randomized Controlled Trial

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Related Article:

Correction of: https://www.researchprotocols.org/2021/7/e29322

(JMIR Res Protoc 2022;11(7):e39745) doi:10.2196/39745

In "The Hip Instructional Prehabilitation Program for Enhanced Recovery (HIPPER) as an eHealth Approach to Presurgical Hip Replacement Education: Protocol for a Randomized Controlled Trial" (JMIR Res Protoc 2021;10(7):e29322) the authors noted the following errors:

The fourth timepoint (T4) was not recorded as a part of the study and was inadvertently included in the paper. As a result, the following 17 corrections have been made:

1. In the originally published article, the following indicator appeared in "Table 1. Feasibility Indicators" as a retention rate process indicator:

> *% of participants with T4[a] data*

This has been corrected to:

> *% of participants with T3[a] data*

2. In the originally published article, the following indicator appeared in "Table 1. Feasibility Indicators" as a perceived benefit process indicator:

> *Posttreatment participant questionnaire; qualitative interviews at T4*

This has been corrected to:

> *Posttreatment participant questionnaire; qualitative interviews at T3*

3. In the originally published article, the following indicator appeared in "Table 1. Feasibility Indicators" as a data collection (T): participant & assessor burden resources indicator:

> *T1 duration; T2, T3, & T4 durations*

This has been corrected to:

> *T1 duration; T2, & T3 durations*

4. In the originally published article, the following footnote appeared in "Table 1. Feasibility Indicators":

> *[a]Fourth measurement timepoint.*

This has been corrected to:

> *[a]Third measurement timepoint.*

5. In the originally published article, the following sentence was included in the "Secondary Outcomes" section regarding the Oxford Hip Score:

> *Participants will complete this measure at all time points (T1-T4).*

This sentence has been corrected to:

> *Participants will complete this measure at all time points (T1-T3).*

6. In the originally published article, the following sentence was included in the "Secondary Outcomes" section regarding the 30-second Chair Stand Test:

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Participants will be asked to complete this test at T1, T2, and T4.

This sentence has been corrected to:

Participants will be asked to complete this test at T1 and T2.

7. In the originally published article, the following sentence was included in the “Secondary Outcomes” section regarding the Physical Activity Scale for the Elderly:

Participants will complete this measure at T1-T4.

This sentence has been corrected to:

Participants will complete this measure at T1-T3.

8. In the originally published article, the following sentence was included in the “Secondary Outcomes” section regarding the Self-Efficacy for Rehabilitation Outcome Scale:

Participants will complete this measure at T1-T4.

This sentence has been corrected to:

Participants will complete this measure at T1-T3.

9. In the originally published article, the following sentences were included in the “Secondary Outcomes” section regarding the equipment checklist:

Patients will use the checklist at T2-T4 to record the number and type of equipment items they have used and how often they have used each (eg, dressing equipment). Participants will complete this measure at T2-T4.

These sentences have been corrected to:

Patients will use the checklist at T2 and T3 to record the number and type of equipment items they have used and how often they have used each (eg, dressing equipment). Participants will complete this measure at T2-T3.

10. In the originally published article, the following sentence was included in the “Secondary Outcomes” section regarding the EuroQoL-5 Dimension, 5 Level:

Participants will complete this measure at T1-T4.

This sentence has been corrected to:

Participants will complete this measure at T1-T3.

11. In the originally published article, the following sentence was included in the “Secondary Outcomes” section regarding the System Usability Scale:

Participants will complete this measure at T2-T4 (if randomized to the treatment group).

This sentence has been corrected to:

Participants will complete this measure at T2 and T3 (if randomized to the treatment group).

12. In the originally published article, the following sentence was included in the “Participant Timeline” section:

Follow-up data will be collected 7-10 days prior to surgery (T2), 30 days (T3) postsurgery, and 90 days (T4) postsurgery.

This sentence has been corrected to:

Follow-up data will be collected 7-10 days prior to surgery (T2), 30 days and (T3) postsurgery.

13. In the originally published article, the following sentences were included in the ”Data Collection Method and Data Management“ section:

To collect the data at T2, T3, and T4, the assessor will send a link to the participants to complete the questionnaires in Qualtrics. In addition, at T2 and T4, the assessor will contact the participants to schedule a short online meeting during which the participants will be asked to do the 30-sec CST via videoconference.

These sentences have been corrected to:

To collect the data at T2 and T3, the assessor will send a link to the participants to complete the questionnaires in Qualtrics. In addition, at T2 the assessor will contact the participants to schedule a short online meeting during which the participants will be asked to do the 30-sec CST via videoconference.

14. In the originally published article, Multimedia Appendix 1 indicated ”Retention rate“ process indicator indicated:

% of participants with T4 data

This has been corrected to:

% of participants with T3 data

15. In the originally published article, Multimedia Appendix 1 indicated “Perceived benefit” process indicator indicated:

*Qualitative Interviews at T4**

This has been corrected to:

*Qualitative Interviews at T3**

16. In the originally published article, Multimedia Appendix 1 indicated “Data collection (T): Participant & Assessor burden” resources indicator indicated:

T2, 3 & 4 duration

This has been corrected to:

T2 & 3 duration

The revised version of the appendix is in Multimedia Appendix 1.

17. In the originally published article, Figure 1 contained a box indicating “T4 Data Collection 90 days post surgery” (see Multimedia Appendix 2).

In the corrected article, Figure 1 has been corrected by removing this box as follows:

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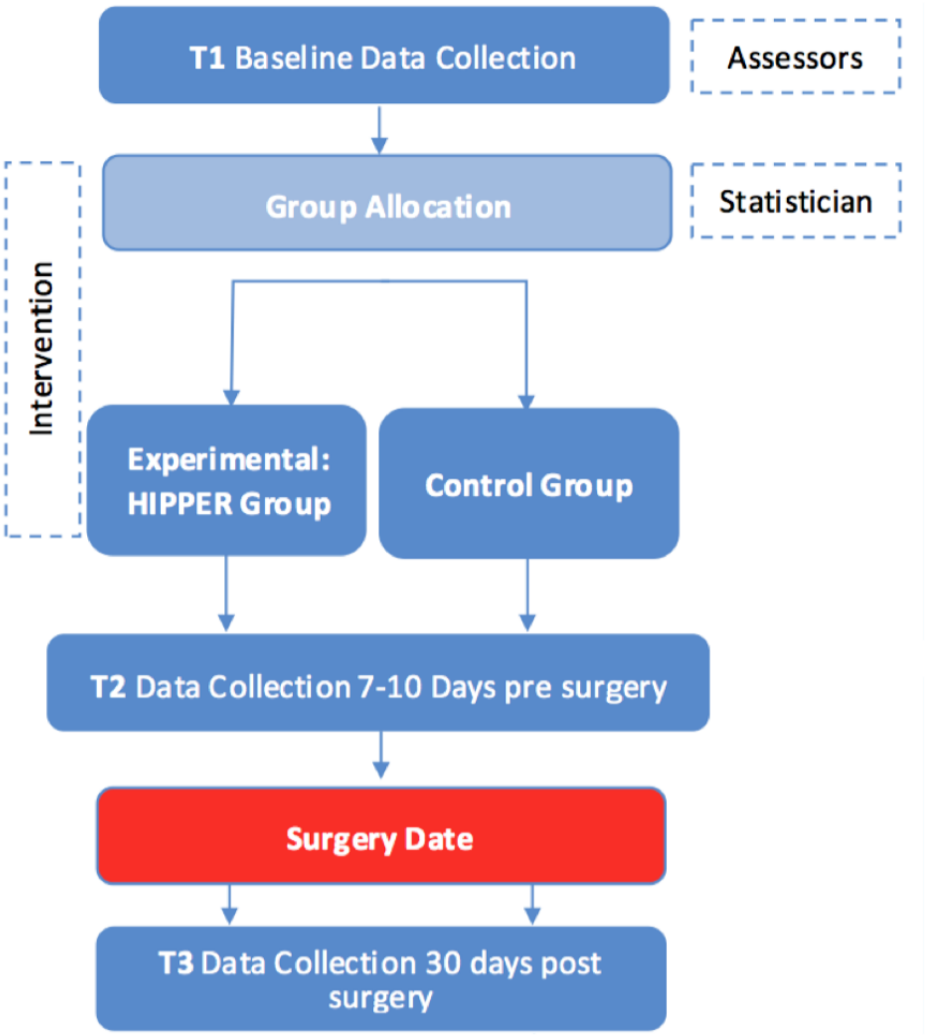
Figure 1. Data collection procedure for the randomized controlled trial. HIPPER: Hip Instructional Prehabilitation Program for Enhanced Recovery.



The correction will appear in the online version of the paper on the JMIR Publications website on July 14, 2022, together with the publication of this correction notice. Because this was made after submission to PubMed, PubMed Central, and other full-text repositories, the corrected article has also been resubmitted to those repositories.

Multimedia Appendix 1
Feasibility indicators.
[DOCX File , 16 KB - resprot_v11i7e39745_app1.docx]

Multimedia Appendix 2
Originally published version of Figure 1.
[PNG File , 65 KB - resprot_v11i7e39745_app2.png]

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Protocol

Implementation of Virtual Reality in Health Professional Higher Education: Protocol for a Scoping Review

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Abstract

Background: The use of virtual reality in higher education show great potential to promote novel and innovative learning experiences. Until recently, virtual reality has mostly been used in technical higher education, but lately medical education programs have begun using virtual reality. Virtual reality for health professional education improves the knowledge and skills of health professionals compared with traditional or other digital education initiatives. However, the implementation of technology in higher education is slow because of barriers to technology use and innovative and successful practices are not shared. It is, therefore, of great interest to explore how virtual reality is implemented in higher health professional and continuing education.

Objective: The aim of this scoping review is to identify studies that reported implementation of virtual reality in higher health professional education, to identify barriers and facilitators for implementation, and to highlight research gaps in this area.

Methods: The scoping review will be conducted according to JBI Evidence Synthesis methodologies. CINAHL, the Academic Search Elite and Education Source electronic databases, and Google Scholar will be searched for studies published between 2017 and 2022. In addition, manual searching of key items, reference tracking, and citation tracking will be performed. Searches for white papers will also be manually conducted. All authors will independently extract data from full-text papers. We will use qualitative content analysis to abstract the findings.

Results: The literature searches were conducted in January and February 2022. The review is expected to be completed by fall 2022, after which time it will be submitted for publication.

Conclusions: We anticipate that, from the review, we will be able to coordinate recommendations for and present the challenges of virtual reality initiatives in health professional education programs. We will present recommendations for future research.

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KEYWORDS

virtual reality; higher education; medical education; health care professional education; continuing education; implementation; technology; scoping review; Google Scholar; health professional

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Introduction

Background

Virtual reality is defined as a digital representation of a 3D environment [1]. Immersive virtual reality, wherein head-mounted displays are used to block out the real world, is now the general understanding of what constitutes virtual reality [2]. In higher education, the use of virtual reality shows great potential to promote novel and innovative learning experiences [3]. Virtual reality offers students and health care professionals a platform with which they can experience and learn how to master situations without putting patients or themselves in any risk of harm [4]. Until recently virtual reality has mostly been used in technical higher education programs, such as engineering, computer science, and astronomy [5], but lately, there has been growth in interest and the use of virtual reality in medical education programs [6]. A review [7] on virtual reality for health professional education found that, in comparison with traditional or other digital education initiatives, virtual reality initiatives improved health professionals' knowledge and skills [7]. However, the implementation of technology in higher education is slow because of barriers to technology use and innovative and successful practices are not shared [8].

Preliminary Search and Review

Preliminary searches of PROSPERO, the Cochrane Database of Systematic Reviews, JBI Evidence Synthesis, and the Journal of Medical Internet Research, using the search string "implement* virtual reality" were conducted to gain an overview of in-progress reviews. No current or in-progress scoping reviews or systematic reviews on the implementation of virtual reality in health professional education were identified; however, a protocol [9] for a scoping review of virtual reality education for dementia care was identified. In December 2021, a preliminary search of Google Scholar, limited to papers published after 2017, using the search string *implement* virtual reality in higher education* was also conducted. The preliminary search yielded a total of 17,200 hits. We screened the first 50 hits to identify papers on the implementation of virtual reality in higher education, and 9 articles were considered relevant for full-text reading.

We identified 3 reviews on virtual reality in higher education, one of which reported on virtual reality in higher health professional education [7], which included studies from 1990 to 2017 and found that most assessed the effectiveness of nonimmersive virtual reality. Virtual reality interventions with greater interactivity seemed to improve students' competencies more than interventions with less interactivity. The review [7] concludes that immersive scenarios could make education programs more efficient and attractive. A review [1] of virtual reality in science and technology education found that there are problems pertaining to training programs, such as students finding virtual reality implementations to be unrealistic, due to the limited time and resources available to the students. Moreover, most virtual reality projects included in the review [1] were at experimental stages. A more recent review [5] of virtual reality in general higher education found that there were few design-oriented studies wherein the virtual reality apps were constructed based on a specific learning theory. Moreover, few papers included in the review [5] thoroughly described how virtual reality–based teaching can be adopted in the teaching curriculum, which is a central aspect of implementation of virtual reality in higher education. Fernandez [10] suggests that teacher technological competency is a barrier to successful implementation of virtual reality in education, and training in the use of the technology and in the pedagogical purposes of virtual reality are equally important [10].

Our preliminary findings—virtual reality's rapidly changing technology nature and continued interest in virtual reality—indicate that a review on the implementation of virtual reality in higher health professional education would be timely. Because the use of virtual reality is still a novelty in higher education, descriptions and evaluations of their implementation in this setting are also likely to be few in number; therefore, a scoping review was considered the most appropriate review methodology because its purpose is to provide an overview of available evidence [11].

Aim

The aim of this scoping review is to identify studies reporting on implementation of virtual reality in higher health professional education, to identify barriers and facilitators for implementation, and to highlight research gaps in this area.

Methods

Overview

The scoping review will be conducted according to JBI Evidence Synthesis methodologies [11-13] and reported according to the PRISMA-ScR (Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews) checklist [14].

Search Strategy

CINAHL, Academic Search Elite, Education Source, and Google Scholar will be searched. Manual searching of key items, reference tracking, and citation tracking will also be performed. We will also search for white papers manually.

Initial searches were conducted by SSL and a university librarian in November and December 2021 to refine the search string for electronic databases (Table 1). Search terms, such as *Virtual reality*, *Higher Education (health)*, and *Implementation*, as well as several synonyms, were chosen (Table 1). The search words will be combined with the operator *AND*. Search criteria will be papers published from 2017 to 2022 and papers written in English (on higher education or health professional education, including medicine and continuing education with individuals over 18 years and on virtual reality or computer simulation).

Forward and backward citation searching will be conducted on papers that meet search criteria. We will also conduct manual searches on Norwegian government webpages to identify government reports, policy documents, and other material relevant to this scoping study.

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Table 1. Search strategy development for Academic Search Elite.

Search string number	Query	Results
S10	S3 AND S6 AND S9 (Limiters - Published Date: 20170101-20221231. Narrow by Language: - english)	48
S9	S7 OR S8	950,876
S8	Implementation OR "program implementation"	437,365
S7	implement* or "implementation science" or "implementation method" or "implementation strateg*" or "program implementation" or "training programs"	950,876
S6	S4 OR S5	502,010
S5	"Medical education" or "higher education"	474,913
S4	"higher education (health)" or "nursing school" or "health scienc* educat*" or "allied health education" or "medical educat*", "social science* educat*" or "healthcare education" or "health occupation students"	31,052
S3	S1 OR S2	21,497
S2	TI "virtual reality" OR AB "virtual reality" OR TI "VR" OR AB "VR"	21,436
S1	"Virtual reality in higher education" or "simulation methods and models"	79

Study Selection Criteria

Participants

Studies with faculty or students in health-related fields (such as medicine, nursing, physiotherapy, occupational therapy, social education, disability nursing, dental care, pharmacy, and psychology) will be included.

Concept

The primary concept under investigation in this review is the implementation of virtual reality, with implementation defined as "the act of putting a plan into action or starting to use something" [15]. We will explore barriers and facilitators for the implementation of virtual reality. We define virtual reality as a digital representation of a 3D environment, presented in a head-mounted display for a fully immersive experience [1,2]. Based on the above, papers addressing virtual reality implementation will be included.

Context

Only papers on virtual reality implementation in higher health professional education (Bachelor's and Master's programs) or continuing education for health care professionals will be included. Continuing education was deemed to be relevant because its aim is to provide secure lifelong learning for health care professionals [16].

Types of Sources

We will consider quantitative, qualitative, and mixed methods study designs for inclusion. In addition, reviews, background papers, and white papers will be considered for inclusion to gain a broad understanding of the topic at hand.

Exclusions

Papers describing the implementation of virtual reality in clinical use for patients or children will also be excluded.

Study Selection Process

Identified records will be uploaded into EndNote (version 20; Clarivate Analytics), and duplicates will be removed. Titles and abstracts will be screened by 4 independent reviewers using Rayyan's (Qatar Computing Research Institute) [17] blinded screening functionality. We will meet and discuss the screening process several times to ensure consistency. For studies that meet selection criteria, the full-text papers will be assessed by all 5 reviewers. Reasons for the exclusion of full-text papers will be recorded and reported. Disagreements between the reviewers at any stage of the selection process will be resolved by discussion within the research group.

Data Extraction and Analysis

Data will be extracted from papers selected for inclusion in the scoping review independently by all authors. We will use an extraction instrument (Figure 1) adapted from JBI guidelines [11]. The draft was piloted on 1 paper that met selection criteria to ensure that all members of the research team had a similar understanding of the items. This resulted in the team choosing to focus on only the 3 factors under the heading *Results extracted from source of evidence*.

The data extraction tool may be further modified and revised as necessary during the process of extracting data from each paper; such modifications will be recorded and reported. Given that the aim is to map available evidence, critical quality appraisal of the papers will not be performed [11]. Qualitative content analysis will be used to identify key themes.

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Figure 1. Data extraction tool. VR: virtual reality.

Data extraction point	Response
Date	
Reviewer	
Citation details	
Author, date, title, journal, volume, issue, pages	
Language	
Country evidence collected from	
Concept	
Implementation of VR	
Context	
Higher health professional education	
Educational institutions	
Health care institutions	
Participants (population)	
Students in higher health professional education	
Faculty in higher health professional education	
Health care professionals	
N=	
Age	
Sex	
Type of evidence source	
Methods	
Study aims	
Study design	
Results extracted from source of evidence	
Facilitators for VR implementation	
Barriers to VR implementation	
Recommendations for implementing VR	

Results

The project is ongoing. Searches were conducted in January 2022 in Academic Search Elite, Education Source, CINAHL, and Google Scholar. The review is expected to be completed by fall 2022, after which time it will be submitted for publication.

Discussion

We expect to abstract 5 to 8 themes that present the challenges of and recommendations for implementation of virtual reality initiatives in health professional education programs; and recommendations for future research. We will discuss principal findings, prior work, strengths and limitations, and future directions. In part, the findings of the review will be used to inform the implementation of a virtual reality–based educational program that is currently being developed in a private higher educational institution in Norway for undergraduate programs in nursing, occupational therapy, social education, and social work.

Limitations of this scoping review protocol are that relevant sources of information may be omitted by our choice of search words and our choice of languages. Moreover, we will not rate the quality of evidence, and therefore, implications for practice cannot be assessed [11]. Since use of virtual reality in health professional education is a novelty, we may face some challenges in the literature search process in identifying literature specifically on implementation. However, since our preliminary searches yielded papers on virtual reality in health professional education, we believe that this scoping review is timely and relevant.

Acknowledgments

We thank Gunn Alice Brekke Valskår, university librarian, for her assistance and feedback with initial literature searches and the development of the initial search strategy.

Conflicts of Interest

None declared.

References

1. Kavanagh S, Luxton-Reilly A, Wuensche B, Plimmer B. A systematic review of virtual reality in education. Theme Sci Technol Educ 2017;10:85-119 [FREE Full text]
2. Pottle J. Virtual reality and the transformation of medical education. Future Healthc J 2019 Oct 11;6(3):181-185 [FREE Full text] [doi: 10.7861/fhj.2019-0036] [Medline: 31660522]
3. Allcoat D, von Mühlenen A. Learning in virtual reality: effects on performance, emotion and engagement. Res Learn Technol 2018 Nov 27;26:2140 [FREE Full text] [doi: 10.25304/rlt.v26.2140]

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4. Vesisenaho M, Juntunen M, Häkkinen P, Pöysä-Tarhonen J, Fagerlund J, Miakush I, et al. Virtual reality in education: focus on the role of emotions and physiological reactivity. J Virtual Worlds Res 2019 Feb 06;12(1):1-15. [doi: 10.4101/jvwr.v12i1.7329]
5. Radianti J, Majchrzak TA, Fromm J, Wohlgenannt I. A systematic review of immersive virtual reality applications for higher education: design elements, lessons learned, and research agenda. Comput Educ 2020 Apr 01;147:103778 [FREE Full text] [doi: 10.1016/j.compedu.2019.103778]
6. Plotzky C, Lindwedel U, Sorber M, Loessl B, König P, Kunze C, et al. Virtual reality simulations in nurse education: a systematic mapping review. Nurse Educ Today 2021 Jun 23;101:104868. [doi: 10.1016/j.nedt.2021.104868] [Medline: 33798987]
7. Kyaw BM, Saxena N, Posadzki P, Vseteckova J, Nikolaou CK, George PP, et al. Virtual reality for health professions education: systematic review and meta-analysis by the digital health education collaboration. J Med Internet Res 2019 Jan 22;21(1):e12959 [FREE Full text] [doi: 10.2196/12959] [Medline: 30668519]
8. Lillejord S, Ruud E, Børte K, Nesje K. Learning and teaching with technology in higher education - a systematic review. Universitetet i Stavanger. 2018. URL: https://www.uis.no/nb/kunnskapssenter-for-utdanning/ressurser/learning-and-teaching-with-technology-in-higher-education [accessed 2022-06-07]
9. Yamakawa M, Sung HC, Tungpunkom P. Virtual reality education for dementia care: a scoping review protocol. JBI Evid Synth 2020 Sep;18(9):2075-2081. [doi: 10.11124/JBISRIR-D-19-00230] [Medline: 32813416]
10. Fernandez M. Augmented-virtual reality: how to improve education systems. High Learn Res Commun 2017 Jun 30;7(1):1-15. [doi: 10.18870/hlrc.v7i1.373]
11. Peters M, Godfrey C, McInerney P, Munn Z, Tricco A, Khalil H. Scoping reviews (2020 version). In: Aromataris E, Munn Z, editors. JBI Manual for Evidence Synthesis. Australia: JBI; 2020.
12. Peters M, Godfrey C, Khalil H, McInerney P, Parker D, Soares C. Guidance for conducting systematic scoping reviews. Int J Evid Based Healthc 2015 Sep;13(3):141-146. [doi: 10.1097/XEB.0000000000000050] [Medline: 26134548]
13. Peters M, Marnie C, Tricco A, Pollock D, Munn Z, Alexander L, et al. Updated methodological guidance for the conduct of scoping reviews. JBI Evid Synth 2020 Oct;18(10):2119-2126. [doi: 10.11124/JBIES-20-00167] [Medline: 33038124]
14. Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, et al. PRISMA extension for scoping reviews (PRISMA-ScR): checklist and explanation. Ann Intern Med 2018 Oct 02;169(7):467-473 [FREE Full text] [doi: 10.7326/M18-0850] [Medline: 30178033]
15. Implementation. Cambridge Dictionary. URL: https://dictionary.cambridge.org/dictionary/english/implementation [accessed 2022-06-07]
16. Meld. St. 14 (2019-2020). Kunnskapsreformen - lære hele livet. Kunnskapsdepartementet. 2019. URL: https://www.regjeringen.no/contentassets/afb66fbbcdfb47749f1b7007b559d145/no/pdfs/stm201920200014000dddpdfs.pdf [accessed 2022-06-07]
17. Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan-a web and mobile app for systematic reviews. Syst Rev 2016 Dec 05;5(1):210 [FREE Full text] [doi: 10.1186/s13643-016-0384-4] [Medline: 27919275]

Abbreviations

PRISMA-ScR: Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews

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Protocol

Organizations' Strategies to Improve Implementation of Universal Accessibility Principles: Protocol for a Scoping Review

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Abstract

Background: Since the publication of the Convention on the Rights of Persons with Disabilities, several countries have adopted laws, policies, and action plans to improve the universal accessibility of environments to improve inclusion and social participation of all citizens. Different organizations are involved in the application of these measures.

Objective: The aim of this study is to identify strategies that are contextually appropriate and provide guidelines for organizations to promote successful implementation of universal accessibility.

Methods: We will conduct a scoping review identifying implementation strategies of universal accessibility measures in local organizations using the Arksey and O'Malley framework. We will search in Medline, CINHAL, Urban Studies Abstracts, ABI Inform, and Social Sciences Full Text from 2006 until today, following the adoption of the Convention on the Rights of Persons with Disabilities. Two reviewers will independently select studies for inclusion and will extract the data. A descriptive and thematic analysis of the characteristics of the identified implementation strategies will be performed.

Results: Implementation strategies will be summarized in tables. They will then be linked to various constructs and domains listed in the Theoretical Domain Framework to identify barriers and facilitators of organizations' uptake of evidence-based strategies of implementation.

Conclusions: We will tabulate the characteristics of the included studies and the outcomes of implementation strategies in them. The results of this scoping review are expected to help the research community in various fields, local organizations, and stakeholders to identify better ways to improve implementation strategies of universal accessibility practices.

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KEYWORDS

universal accessibility; universal design; public organizations; implementation strategies; disability; person with disability; human rights; thematic analysis; occupational health; workplace

Introduction

Background

Universal accessibility is defined as the character of an environmental design that allows all individuals to carry out their activities independently, with equity and in an inclusive approach [1]. It aims to create better and adapted environments and to provide equal access to buildings, services, resources, and activities for the population [2,3]. The Convention on the Rights of Persons with Disabilities (CRPD), adopted in 2006 by the United Nations (UN), put forward the importance of this

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concept [4]. The general objective of this convention is to improve the life of people with disabilities and to promote a significant change in social development in several spheres of life (health and mental health, accessibility, independence and autonomy, education, employment, housing, etc) to facilitate the inclusion of these people [4-7]. The recognition of the importance of universal accessibility is even more relevant today. Indeed, the global social context of modern societies, demographic changes, and the aging population are leading to a greater proportion of people with disabilities living in urban areas [8]. Since the adoption of the CRPD, several countries have stepped in to create more accessible environments for all individuals [9]. Universal accessibility is an important catalyst for the social and economic participation of every individual. It touches several aspects of citizens' lives, such as quality of life, sense of belonging, health, social inclusion and participation, and employment [9-11]. For this scoping review, the concept of universal accessibility includes a built environment. Accessibility for all to build an environment helps to reduce risks of social exclusion by providing opportunities for activities and reducing isolation and loneliness [12,13]. It helps to promote social participation by facilitating access to employment, decision-making, and various activities. These benefits also contribute to meet the important sociopolitical objective to improve the quality of life of communities [10].

Although the CRPD is an initiative of the UN grouping of countries, in many cases, local jurisdictions are more involved in implementing the various recommendations, since a built environment is generally the responsibility of local governments. For example, Canada, a member of the UN, responds to the CRPD by creating the Accessible Canada Act [14] as the province of Quebec proposes the act to secure handicapped persons in the exercise of their rights with a view to achieving social, school, and workplace integration [15]. The creation of accessible environments is regulated in the various action plans established by local governments that are themselves governed by the provincial law. Thus, municipalities are directly concerned and responsible for the implementation of measures that will allow the creation of accessible environments. The United States created the American with Disabilities Act [16], which prohibits discrimination against people with disabilities in several areas. Each state must then individually set up their laws so local governments can implement policies that propose measures to create accessible environments. In the literature, the involvement of local governments in conventions about international issues (climate change, racial discrimination, cultural heritage, tobacco control, child welfare, etc) is demonstrated. From these conventions, provinces and municipal governments develop their own legislation, as seen in Canada. The literature also shows that municipalities have a key role to play in addressing the social and global issues, given their proximity to citizens [17-19]. For example, the UNESCO (United Nations Educational, Scientific and Cultural Organization) 2003 convention about cultural heritage highlights the role of local governments worldwide to actively participate in the safeguarding and the promotion of their culture [20]. Pineda et al [19] also argue that "addressing accessibility will require assessing and addressing gaps in infrastructure management, municipal codes land use, transportation planning, housing and community development, mobility, social services, and broader monitoring of human rights at the local level."

Prior Work

While the implementation of universal accessibility measures, as the design of environments and services usable for all people [4], has an important impact on the social participation and quality of life of people living with disabilities [2,9,21-23], it also benefits all populations, regardless of disability, by facilitating access to environments for all [2,24,25]. An accessible environment allows everyone, with or without disability, to use it equitably and provides added value to the entire population, such as the elderly experiencing loss of mobility, parents with children in strollers, tourists with their suitcases, etc. Universal accessibility is important in many areas of the citizens' lives, such as public services, educational institutions, housing policies, leisure, health care, cultural, social, and political participation, transportation, information, built environment, territory development, and others [10]. However, this scoping review will focus on the built environment involving the local government, as several stakeholders are consequently involved in the implementation such as governments, municipalities, community-based organizations, or researchers. It is especially common for local governments to adopt a set of measures to follow the guidelines for accessible design of the physical environment [26,27], making the implementation of universal accessibility principles a purview of employees of these organizations.

The implementation of universal accessibility principles is, however, a complex initiative [28]. While implementation is often perceived as linear and easy, implementation scientists suggest that implementation strategies should be tailored to a specific context and be carefully designed to allow the actualization of the innovation, such as universal accessibility principles [29-31]. It is also well established that the implementation of a given innovation is influenced simultaneously by various determinants [31,32]. The level of knowledge, beliefs of the actors involved, or the availability of resources are some examples of determinants influencing implementation strategies and behaviors [33]. Knowing what determinants influence the implementation of principles can help guide decisions about what strategies to adopt on the basis of how well they address the key determinants that can facilitate the implementation of universal accessibility measures [34]. However, little is known about how local governments have adopted implementation strategies to address the various determinants and environmental barriers in the application of universal accessibility principles. Otherwise, we do not know much about municipal perspectives or evaluation toward accessibility practices, or about the nature, targets, and effectiveness of the various strategies chosen by organizations to improve the implementation of universal accessibility principles. Such knowledge is crucial to a better implementation and use of universal accessibility principles in organizations, including, but not limited to, municipalities. Thus, the objectives are to describe the strategies that are used by municipalities to implement better universal accessibility measures.

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Identifying the Research Question

To identify the appropriate research question, the authors, specialized in the accessibility field or in implementation sciences (MC, MEL, and FR), consulted each other to identify relevant questions that address a gap in scientific and organizational knowledge. This scoping review aims to answer the research question, "What are the implementation strategies used by public organizations to apply universal accessibility measure?" The identification of the question is based on gaps in the literature specifically related to implementation strategies in local organizations, the effectiveness of strategies in implementing universal accessibility measures, and to address the needs of organizations to better document these strategies for improvement of universal accessibility. This scoping review will focus on implementation strategies used only by the local government and municipalities. This choice is justified by the fact that they are directly concerned within the implementation of universal accessibility measures, not only because of their duty and legal responsibility to create laws and policies in this sense, but also because they have the direct and proximal impact on the creation of infrastructures, etc, on the daily life of citizens.

Aim of This Study

The aim of the proposed study is to explore the implementation strategies used by local governments to implement universal accessibility measures. The specific objectives are to (1) identify the different strategies implemented by local governments in relation to the principles of universal accessibility, (2) understand how effective these strategies are, and (3) identify the facilitators and barriers to the implementation of the principles of universal accessibility.

Methods

Overview

This knowledge synthesis will take the form of a scoping review. This type of knowledge synthesis is adapted to the needs of the subject since it will allow us to (1) examine the extent, range, and nature of research activity; (2) determine the value for undertaking a full systematic review; (3) summarize and disseminate research findings; and (4) identify research gaps in the existing literature [35-37]. This seems appropriate given the innovative character of the research topic and the limited knowledge available, as it will help to determine the scope of the literature on the topic and provide a clear indication of the volume of literature and studies available [1]. We will use the framework described by Arksey and O'Malley [36], which involves 5 different stages: (1) identifying the research question, (2) identifying relevant studies, (3) selecting studies, (4) charting the data, and (5) collating, summarizing, and reporting the results. Step 1 is described in the *Introduction*, while step 5 is described in the *Results*. The method will be reported in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) extension guidelines for scoping reviews [38].

Identifying Relevant Studies

A consultation with research librarians (EPR and MG) specialized in databases relevant to both fields—environment and implementation—is supporting the definition of the parameters of the strategy. For the purposes of this scoping review, academic and gray literature will be consulted to identify all relevant information about the subject. As the creation of accessible environments is addressed in several disciplines and fields of research (social sciences, medicine and rehabilitation, psychology, public health, geography, urban studies, environment, and engineering), interdisciplinary electronic databases will be consulted: Medline (EBSCO), Urban studies abstract (EBSCO), CINHAL plus full text (EBSCO), ABI Inform (Proquest), and Social Sciences Full Text (EBSCO). Telecommunications-related studies will be excluded since the scoping review subject is about the built environments. All empirical study designs will be considered in this scoping review, including quantitative and qualitative methods and mixed methods studies. Gray literature sources such as local organizations' or municipalities' reports in local governments' websites or those in Google Scholar will also be searched with the key words "universal design" or "universal accessibility." Through controlled vocabulary, various keywords and related terms will be included: (1) "Universal access*" OR "architectural design" OR "universal design," (2) "Local govern*" OR "Municipalit*." The following is an example of the search strategy used in Medline: *((Universal access* OR "universal design" OR "design for all") OR (MH "Universal Design+") OR (MH "Facility Design and Construction+")) AND (("Local govern*" OR City OR Cities OR municipal*) OR ((MH "Cities") OR (MH "Local Government"))*. Articles will have to be published since 2006 to the day of this writing; that is, at the time of the establishment of the UN CRPD. Search results will be imported into the Covidence platform, where the duplicates will be automatically removed.

Study Selection

To be included, the studies will need to adhere to the following inclusion criteria: (1) having been published after 2006, (2) be an empirical study (qualitative, quantitative, or mixed methods), (3) be relevant to local governments or municipalities, and (4) be written in French or English. The exclusion criteria are as follows: (1) telecommunications accessibility studies (websites, media, TV, etc) and (2) studies evaluating accessibility. Studies on the implementation of accessibility of built environments for people with disabilities (including seniors). The study selection will consist of 2 steps: (1) screening of title and abstract and (2) review of the full text will be done on the Covidence platform. At first, 2 doctoral students (MC and CRM) will independently screen the titles and abstracts. Conflicts will be resolved through discussion and a third reviewer (AB) will be involved if a consensus cannot be reached. In the second selection step, all full-text versions of the articles will be obtained and read. MC and CRM will decide independently of the final inclusion of the article in the review. The reasons of exclusion for each article will be noted. Occurring disagreements will be discussed with a third reviewer (AB) and consensus will be reached.

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Charting the Data

The selected articles and the Endnote references with attached files will be imported in the NVivo software. Sources will be classified using attributes such as author name or publication date. Each article will be read, annotated, and coded with emerging themes. Because of its relevance in the implementation field, the coding tree will be inspired by the one used in the implementation review study of Aregbesola [39] (see Textbox 1) and will be composed of 2 main codes: the study details and the intervention described. The subcodes will be broken down as follows: the study details will include the name of the first author, year of publication, country, study design, study period, study objective (what is being implemented), and area of study. The use of any of the implementation strategies, dissemination strategies (developing messages and materials and distribution of evidence-based information), implementation process strategies, integration strategies, capacity building, and the numbers and types of implementation strategies used will be extracted in the intervention code. Textbox 1 shows the extraction chart categories, which will be imported in NVivo software. A pilot of this coding tree will be carried out on 5 studies to determine whether other themes are emerging. A word frequency query or a matrix coding query could be used to determine which themes are most and least represented within the implementation strategies and to verify the accuracy of the information extracted.

Textbox 1. Coding tree for analysis of implementation strategies.

Study details:

- First author
- Year of publication
- Country
- Study period
- Study objective (what is being implemented)
- Area of study

Interventions, policies, or strategies:

- Use of any of the implementation strategies
- Dissemination strategies (messages, materials, distribution, or evidence-based interventions)
- Implementation process strategies
- Integration strategies

Results

The results of the studies will be reported in tables. Specific characteristics and outcome measures of included studies will be presented in a table. Each type of implementation strategy will be summarized, along with the study designs and the effects produced, in the table. The strategies used by the organizations will be linked to various constructs and domains listed in the Theoretical Domain Framework [40]. This implementation sciences framework will allow us to identify barriers and facilitators of organizations' uptake of evidence-based strategies of implementation [41]. The impact of each construct on the implementation of universal accessibility measures will be described in the table form. These different steps will allow us to answer the research question by identifying the implementation strategies used by organizations to improve the universal accessibility of environments. A participatory process is planned during the analysis of the scoping review by soliciting representatives of local organizations to ensure that the scoping review meets the needs of municipalities and citizens. Three meetings with the research team and the representatives of local organizations will be planned. They will be held in person or on Zoom (Zoom Video Communications), depending on the state of the pandemic at the time. Representatives of local organizations will be contacted initially to present them the project, the objectives, and the analysis process that will be conducted. The first 10 articles will be analyzed, and the second meeting will be used to discuss this preanalysis and adjust it as needed, based on comments and suggestions from the representatives. Once all parties have agreed on the analysis process, an analysis of all articles will be conducted. Finally, a last meeting will be scheduled to validate the results of the analysis and ensure that they meet the needs of local organizations. We expect the scoping review to be completed by December 2022.

Discussion

Principal Findings

In summary, this scoping review will empirically identify the nature, scope, and effectiveness of implementation strategies in municipal settings to improve environmental accessibility. In a world with an increasing aging and a disabled population, it is essential to address the issue of accessible environments for all [42-45]. Public organizations, from a local to national level, have an essential role to play in improving universal accessibility services and practices and in developing better implementation strategies [27,46].

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Comparison to Prior Work

To the best of our knowledge, little research has documented the effectiveness and nature of implementation strategies used specifically by public organizations in creating accessible environments [9,12,34,47,48]. Therefore, this scoping review will provide evidence-based information on the different implementation strategies that have been used to date in the field of universal accessibility by public organizations and will characterize domains influencing the implementation of such an innovation. It will also contribute to literature and research advancement by identifying implementation strategies that could possibly be applicable in other contexts. It will help reduce the gap between knowledge owners and knowledge users for the implementation of universal accessibility measures [9]. This will potentially influence future research in the social sciences, urban and environmental studies, rehabilitation, or public health research by providing new knowledge in implementation science and in universal accessibility within organizations.

This scoping review could also influence the important need of better coordination in practices and policies in regard to the implementation of accessibility practices within organizations [49]. The use of relevant implementation strategies by organizations could bring the stakeholders to improve their capacity to establish better initiatives and strategies of the implementation of universal accessibility principles [34]. It will likely help them overcome barriers to the implementation of such measures. Organizational practices toward universal accessibility are crucial to the elaboration of quality interventions and to improve the accessibility of environments and the quality of life of people living with disabilities as well as those of their cocitizens without disabilities. This will help increase social participation and inclusion of people living with disabilities [10]. It may also impact economic, social, and overall health dimensions of populations [50]. Better accessibility to services and infrastructures could ultimately reduce exclusion and various risk factors associated with health and lack of employment and will improve general mobility for the entire population [12,13,51]. It will allow every citizen to participate fully in different aspects of society.

Future Directions

Conducting a scoping review of the knowledge available across many fields will assist all city employees, whether they are managers, civil servants, professionals, blue collar, or seasonal employees, to develop better implementation strategies of universal accessibility measures [51]. It will also be beneficial for publishers, policy makers, researchers, teachers, and students to be more informed on the various component of appropriate practices in the field of implementation strategies toward universal accessibility practices [8].

Dissemination Plan

To share the knowledge gained from this scoping review, a dissemination plan has been developed. The results of the scoping review will be published in a scientific paper by December 2022. They will also be presented at a provincial and an international conference. Finally, the results will be communicated to the City of Quebec, to pursue the objectives of the partnership, to find innovative solutions in knowledge mobilization, and to facilitate the implementation of universal accessibility measures within the municipality.

Conclusions

The fact that the research question for this scoping review was refined through rigorous questioning by specialized researchers and that a participatory process involving local organizations representatives is planned to analyze and report the results, demonstrates the concern to respond to a real need felt by local organizations and the research community in the field of universal accessibility. The complex and challenging aspects of implementation science, particularly of the implementation of universal accessibility measures and its success depending on the effectiveness of the strategies used and the various domains, justify the relevance of conducting this scoping review. The identification of robust implementation strategies, processes, and outcomes is essential to the creation of accessible environments that enable inclusion and social participation for all, regardless of disability. Given the growing need of disabled populations and the importance of the sociopolitical objective to improve the quality of life of communities, addressing ways to reduce environmental barriers, better implementation strategies initiatives within public organizations will contribute to future practices in this field.

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Authors' Contributions

MC conceptualized the study and was the lead author of the manuscript. MEL and FR contributed to concept development, protocol development, and manuscript writing. EPR and MG, from the library, assisted and reviewed the concept definition and research strategy. AB and CM reviewed the manuscript and provided comments and suggestions to enhance the development of the protocol. All authors read and approved the final manuscript.

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Conflicts of Interest

None declared.

References

1. Fougeyrollas P, Boucher N, Fiset D, Grenier Y, Noreau L, Philibert M, et al. Handicap, environnement, participation sociale et droits humains : du concept d'accès à sa mesure. Développement Humain, Handicap et Changement Social 2015:5-28. [doi: 10.7202/1086792ar]
2. Larkin H, Hitch D, Watchorn V, Ang S. Working with policy and regulatory factors to implement universal design in the built environment: the Australian experience. Int J Environ Res Public Health 2015 Jul 15;12(7):8157-8171 [FREE Full text] [doi: 10.3390/ijerph120708157] [Medline: 26184278]
3. Folcher V, Lompré M. Accessibilité pour et dans l'usage : concevoir des situations d'activité adaptées à tous et à chacun. Le travail humain 2012;75:89-120 [FREE Full text] [doi: 10.3917/th.751.0089]
4. United Nations. Convention on the rights of persons with disabilities. In: The Core International Human Rights Treaties. New York, NY: United Nations; 2014:267-302.
5. Groce N. Global disability: an emerging issue. The Lancet Global Health 2018 Jul;6(7):e724-e725. [doi: 10.1016/s2214-109x(18)30265-1]
6. Steinert C, Steinert T, Flammer E, Jaeger S. Impact of the UN convention on the rights of persons with disabilities (UN-CRPD) on mental health care research - a systematic review. BMC Psychiatry 2016 May 26;16(1):166 [FREE Full text] [doi: 10.1186/s12888-016-0862-1] [Medline: 27387916]
7. Szmukler G. UN CRPD: equal recognition before the law. Lancet Psychiatry 2015 Nov;2(11):e29. [doi: 10.1016/S2215-0366(15)00369-7] [Medline: 26544753]
8. Heylighen A, Van der Linden V, Van Steenwinkel I. Ten questions concerning inclusive design of the built environment. Build Environ 2017 Mar;114:507-517. [doi: 10.1016/j.buildenv.2016.12.008]
9. Eisenberg Y, Heider A, Gould R, Jones R. Are communities in the United States planning for pedestrians with disabilities? Findings from a systematic evaluation of local government barrier removal plans. Cities 2020 Jul;102:102720. [doi: 10.1016/j.cities.2020.102720]
10. Eckhardt J, Kaletka C, Pelka B. Monitoring inclusive urban development alongside a human rights approach on participation opportunities. Eur Plan Stud 2020 Jan 17;28(5):991-1009. [doi: 10.1080/09654313.2020.1713995]
11. Gamache S, Routhier F, Morales E, Vandersmissen M, Boucher N, McFadyen BJ, et al. Methodological insights into the scientific development of design guidelines for accessible urban pedestrian infrastructure. Journal of Urban Technology 2019 Jul 22;27(1):87-105. [doi: 10.1080/10630732.2019.1632677]
12. Heitor T, Medeiros V, Nascimento R, Tomé A. Investigating accessibility to achieve inclusive environments: the spatial experience of disability at a university precinct in Lisbon. In: Inclusive Designing. Cham: Springer; 2014:93-103.
13. Hästbacka E, Nygård N, Nyqvist F. Barriers and facilitators to societal participation of people with disabilities: A scoping review of studies concerning European countries. Alter 2016 Jul;10(3):201-220. [doi: 10.1016/j.alter.2016.02.002]
14. Accessible Canada Act (S.C. 2019, c. 10). Justice Laws Website. Government of Canada. URL: https://laws-lois.justice.gc.ca/eng/acts/A-0.6/ [accessed 2022-06-17]
15. Chapter E-20.1: Act to Secure Handicapped Persons in the exercise of their rights With a View to Achieving Social, School and Workplace Integration. Gouvernement du Québec. 2004. URL: https://www.legisquebec.gouv.qc.ca/en/document/cs/e-20.1 [accessed 2022-06-17]
16. Americans with disabilities act of 1990, as amended. United Nations. URL: https://www.un.org/development/desa/disabilities/wp-content/uploads/sites/15/2019/11/US_American-Disability-Act.pdf [accessed 2022-06-17]
17. Mohan S, Mini G, Thankappan KR. High knowledge of Framework Convention on Tobacco Control provisions among local government representatives does not translate into effective implementation: findings from Kerala, India. Public Health 2013 Feb;127(2):178-181. [doi: 10.1016/j.puhe.2012.11.018] [Medline: 23298574]
18. Baker I, Peterson A, Brown G, McAlpine C. Local government response to the impacts of climate change: An evaluation of local climate adaptation plans. Landscape and Urban Planning 2012 Aug;107(2):127-136. [doi: 10.1016/j.landurbplan.2012.05.009]
19. Pineda VS, Meyer S, Cruz JP. The inclusion imperative. Forging an inclusive new urban agenda. JPS 2017 Dec 31;2(4):1. [doi: 10.5204/jps.v2i4.138]
20. Choi H, Nam S. Why local governments matters in implementing the UNESCO 2003 Convention: the case for ICCN. Int J Intang Herit 2015 [FREE Full text]
21. Gossett A, Mirza M, Barnds AK, Feidt D. Beyond access: a case study on the intersection between accessibility, sustainability, and universal design. Disabil Rehabil Assist Technol 2009 Nov;4(6):439-450. [doi: 10.3109/17483100903100301] [Medline: 19817658]
22. Mayordomo-Martínez D, Carrillo-de-Gea JM, García-Mateos G, García-Berná JA, Fernández-Alemán JL, Rosero-López S, et al. Sustainable accessibility: a mobile app for helping people with disabilities to search accessible shops. Int J Environ Res Public Health 2019 Feb 20;16(4):A [FREE Full text] [doi: 10.3390/ijerph16040620] [Medline: 30791577]

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23. Imrie R, Luck R. Designing inclusive environments: rehabilitating the body and the relevance of universal design. Disabil Rehabil 2014;36(16):1315-1319 [FREE Full text] [doi: 10.3109/09638288.2014.936191] [Medline: 24989068]
24. Gamache S, Routhier F, Morales E, Vandersmissen M, Boucher N. Mapping review of accessible pedestrian infrastructures for individuals with physical disabilities. Disabil Rehabil Assist Technol 2019 May 14;14(4):410-422. [doi: 10.1080/17483107.2018.1449018] [Medline: 29537329]
25. Hammel J, Magasi S, Heinemann A, Gray DB, Stark S, Kisala P, et al. Environmental barriers and supports to everyday participation: a qualitative insider perspective from people with disabilities. Arch Phys Med Rehabil 2015 Apr;96(4):578-588. [doi: 10.1016/j.apmr.2014.12.008] [Medline: 25813890]
26. Boucher N, Dumont I, Fougeyrollas P, Ruel J, Moreau A, Duplessis A. Perspective d'analyse comparée des effets des plans d'action à l'égard des personnes handicapées sur les territoires des villes de Sherbrooke, de TroisRivières, Victoriaville et de Cowansville, 2011-2015. Office des personnes handicapées du Québec. URL: https://www.ophq.gouv.qc.ca/fileadmin/centre_documentaire/Etudes__analyses_et_rapports/RAP_N.Boucher_et_al.pdf [accessed 2022-06-17]
27. Imrie R. Disabling environments and the geography of access policies and practices. Disabil Soc 2000 Jan;15(1):5-24. [doi: 10.1080/09687590025748]
28. Phillips C, Marshall AP, Chaves NJ, Jankelowitz SK, Lin IB, Loy CT, et al. Experiences of using the Theoretical Domains Framework across diverse clinical environments: a qualitative study. J Multidiscip Healthc 2015;8:139-146 [FREE Full text] [doi: 10.2147/JMDH.S78458] [Medline: 25834455]
29. Damschroder LJ, Aron DC, Keith RE, Kirsh SR, Alexander JA, Lowery JC. Fostering implementation of health services research findings into practice: a consolidated framework for advancing implementation science. Implement Sci 2009 Aug 07;4:50 [FREE Full text] [doi: 10.1186/1748-5908-4-50] [Medline: 19664226]
30. Atkins L, Francis J, Islam R, O'Connor D, Patey A, Ivers N, et al. A guide to using the Theoretical Domains Framework of behaviour change to investigate implementation problems. Implement Sci 2017 Jun 21;12(1):77 [FREE Full text] [doi: 10.1186/s13012-017-0605-9] [Medline: 28637486]
31. Birken S, Powell BJ, Presseau J, Kirk MA, Lorencatto F, Gould NJ, et al. Combined use of the Consolidated Framework for Implementation Research (CFIR) and the Theoretical Domains Framework (TDF): a systematic review. Implement Sci 2017 Jan 05;12(1):2 [FREE Full text] [doi: 10.1186/s13012-016-0534-z] [Medline: 28057049]
32. Lewis CC, Scott K, Marriott BR. A methodology for generating a tailored implementation blueprint: an exemplar from a youth residential setting. Implement Sci 2018 May 16;13(1):68 [FREE Full text] [doi: 10.1186/s13012-018-0761-6] [Medline: 29769096]
33. Michie S, Johnston M, Abraham C, Lawton R, Parker D, Walker A, "Psychological Theory" Group. Making psychological theory useful for implementing evidence based practice: a consensus approach. Qual Saf Health Care 2005 Feb;14(1):26-33 [FREE Full text] [doi: 10.1136/qshc.2004.011155] [Medline: 15692000]
34. Aarons GA, Hurlburt M, Horwitz SM. Advancing a conceptual model of evidence-based practice implementation in public service sectors. Adm Policy Ment Health 2011 Jan;38(1):4-23 [FREE Full text] [doi: 10.1007/s10488-010-0327-7] [Medline: 21197565]
35. Grant M, Booth A. A typology of reviews: an analysis of 14 review types and associated methodologies. Health Info Libr J 2009 Jun;26(2):91-108 [FREE Full text] [doi: 10.1111/j.1471-1842.2009.00848.x] [Medline: 19490148]
36. Arksey H, O'Malley L. Scoping studies: towards a methodological framework. Int J Soc Res Methodol 2005 Feb;8(1):19-32. [doi: 10.1080/1364557032000119616]
37. Levac D, Colquhoun H, O'Brien KK. Scoping studies: advancing the methodology. Implement Sci 2010 Sep 20;5:69 [FREE Full text] [doi: 10.1186/1748-5908-5-69] [Medline: 20854677]
38. PRISMA for Scoping Reviews. URL: http://www.prisma-statement.org/Extensions/ScopingReviews [accessed 2022-06-17]
39. Aregbesola A, Abou-Setta AM, Jeyaraman MM, Okoli G, Lam O, Sibley KM, et al. Implementation strategies in emergency management of children: a scoping review protocol. Syst Rev 2020 Mar 03;9(1):46 [FREE Full text] [doi: 10.1186/s13643-020-01310-z] [Medline: 32127032]
40. Michie S, Johnston M, Francis J, Hardeman W, Eccles M. From theory to intervention: mapping theoretically derived behavioural determinants to behaviour change techniques. Appl Psychol 2008;57(4):660-680. [doi: 10.1111/j.1464-0597.2008.00341.x]
41. Flottorp SA, Oxman AD, Krause J, Musila NR, Wensing M, Godycki-Cwirko M, et al. A checklist for identifying determinants of practice: a systematic review and synthesis of frameworks and taxonomies of factors that prevent or enable improvements in healthcare professional practice. Implement Sci 2013 Mar 23;8(1):35 [FREE Full text] [doi: 10.1186/1748-5908-8-35] [Medline: 23522377]
42. Kadir SA, Jamaludin M, Rahim AA. Building managers' perception in regards to accessibility and universal design implementation in public buildings: Putrajaya case studies. Procedia - Social and Behavioral Sciences 2012:129-136. [doi: 10.1016/j.sbspro.2012.02.071]
43. Labbé D, Mahmood A, Miller WC, Mortenson WB. Examining the impact of knowledge mobilization strategies to inform urban stakeholders on accessibility: a mixed-methods study. Int J Environ Res Public Health 2020 Feb 28;17(5) [FREE Full text] [doi: 10.3390/ijerph17051561] [Medline: 32121293]

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44. Morris S, Fawcett G, Brisebois L, Hughes J. A demographic, employment and income profile of Canadians with disabilities aged 15 years and over, 2017. Statistique Canada. 2018. URL: https://www150.statcan.gc.ca/n1/pub/89-654-x/89-654-x2018002-eng.htm [accessed 2022-06-17]
45. Population size and growth in Canada: Key results from the 2016 Census. Statistics Canada. 2016. URL: https://www150.statcan.gc.ca/n1/daily-quotidien/170208/dq170208a-eng.htm [accessed 2022-06-17]
46. Ncoyini S, Cilliers L. Factors that influence knowledge management systems to improve knowledge transfer in local government: A case study of Buffalo City Metropolitan Municipality, Eastern Cape, South Africa. SA J Hum Resour Manag 2020 Jul 22;18:A. [doi: 10.4102/sajhrm.v18i0.1147]
47. Milligan N, Nieuwenhuijsen EC, Grawi CL. Using a participatory action strategic approach to enhance accessibility and participation in arts and cultural events: results of four focus groups. Disabil Health J 2014 Jan;7(1):105-113. [doi: 10.1016/j.dhjo.2013.09.001] [Medline: 24411514]
48. Van der Linden V, Dong H, Heylighen A. From accessibility to experience: Opportunities for inclusive design in architectural practice. Nordic Journal of Architectural Research 2016:33-58 [FREE Full text]
49. Frías-López E, Queipo-de-Llano J. Methodology for 'reasonable adjustment' characterisation in small establishments to meet accessibility requirements: A challenge for active ageing and inclusive cities. Case study of Madrid. Cities 2020 Aug;103:102749. [doi: 10.1016/j.cities.2020.102749]
50. Saha M, Chauhan D, Patil S, Kangas R, Heer J, Froehlich J. Urban accessibility as a socio-political problem. Proc ACM Hum-Comput Interact 2021 Jan 05;4(CSCW3):1-26 [FREE Full text] [doi: 10.1145/3432908]
51. Gharebaghi A, Mostafavi M, Chavoshi S, Edwards G, Fougeyrollas P. The role of social factors in the accessibility of urban areas for people with motor disabilities. IJGI 2018 Mar 24;7(4):131. [doi: 10.3390/ijgi7040131]

Abbreviations

CRPD: Convention on the Rights of Persons with Disabilities
UN: United Nations
UNESCO: United Nations Educational, Scientific and Cultural Organization

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Protocol

Combining Machine Learning, Patient-Reported Outcomes, and Value-Based Health Care: Protocol for Scoping Reviews

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Abstract

Background: Patient-reported outcome measures (PROMs) and patient-reported experience measures (PREMs) are self-reporting tools that can measure important information about patients, such as health priorities, experience, and perception of outcome. The use of traditional objective measures such as vital signs and lab values can be supplemented with these self-reported patient measures to provide a more complete picture of a patient's health status. Machine learning, the use of computer algorithms that improve automatically through experience, is a powerful tool in health care that often does not use subjective information shared by patients. However, machine learning has largely been based on objective measures and has been developed without patient or public input. Algorithms often do not have access to critical information from patients and may be missing priorities and measures that matter to patients. Combining objective measures with patient-reported measures can improve the ability of machine learning algorithms to assess patients' health status and improve the delivery of health care.

Objective: The objective of this scoping review is to identify gaps and benefits in the way machine learning is integrated with patient-reported outcomes for the development of improved public and patient partnerships in research and health care.

Methods: We reviewed the following 3 questions to learn from existing literature about the reported gaps and best methods for combining machine learning and patient-reported outcomes: (1) How are the public engaged as involved partners in the development of artificial intelligence in medicine? (2) What examples of good practice can we identify for the integration of PROMs into machine learning algorithms? (3) How has value-based health care influenced the development of artificial intelligence in health care? We searched Ovid MEDLINE(R), Embase, PsycINFO, Science Citation Index, Cochrane Library, and Database of Abstracts of Reviews of Effects in addition to PROSPERO and the ClinicalTrials website. The authors will use Covidence to screen titles and abstracts and to conduct the review. We will include systematic reviews and overviews published in any language and may explore additional study types. Quantitative, qualitative, and mixed methods studies are included in the reviews.

Results: The search is completed, and Covidence software will be used to work collaboratively. We will report the review using the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines and Critical Appraisal Skills Programme for systematic reviews.

Conclusions: Findings from our review will help us identify examples of good practice for how to involve the public in the development of machine learning systems as well as interventions and outcomes that have used PROMs and PREMs.

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KEYWORDS

machine learning; artificial intelligence; algorithm; eHealth; patient-reported outcome measures; patient-reported experience measures; patient experience; value-based care; scoping review

Introduction

Objective measures such as vital signs and lab values only provide a partial view of a patient's condition. Patient-reported outcome measures (PROMs) [1] and patient-reported experience measures (PREMs) [1] are subjective reports shared by patients that can help complete this view by filling in gaps that other methods are incapable of assessing, such as pain levels, patient experience, motivation, human factors, patient-related outcomes, and health priorities. PROMs are questionnaires measuring the patients' views of their health status. PREMs refer to data collected from patients about their experience within the health care system. These questionnaires can help us understand the patient perspective to identify goals for care and evaluate the impact of care.

Furthermore, earlier implementations of machine learning in medicine were developed without patient or public input and may be missing priorities and measures that matter to patients. Public and patient involvement can bring these measures together by defining end-user experience, meaning patient priorities implementation, and therefore provide enriched data for machine learning and more functional PROMs and PREMs.

Machine learning is an application of artificial intelligence (AI) that trains systems to automatically learn and improve from experience. In the past decade, machine learning has given us practical speech and speech-to-text recognition, algorithms for medical diagnosis, improvements in predictive epidemiology and public health, and prognostic treatment models. Although this is a powerful tool, these algorithms are only as reliable and free from bias as the data that are used to build and train them [2].

This review of reviews looks at ways to integrate machine learning with patient-reported outcomes for the development of improved public and patient partnerships in research and health care.

Methods

Review Questions

In this review, we will address the following 3 specific questions to learn about the best methods for combining machine learning and patient-reported outcomes:

- How are the public engaged as involved partners in the development of AI in medicine?
- What examples of good practice can we identify for the integration of PROMs into machine learning algorithms?
- How has value-based health care influenced the development of AI in health care?

Searches

This review covers a broad range of interrelated topics, and we will assess the overall data by conducting 3 separate scoping reviews. The first review will focus on the intersection of AI and PROMs. The second scoping review will focus on AI and public involvement. The third one will focus on AI and value-based health care. We have chosen to do 3 separate scoping reviews instead of 1 or multiple systematic reviews to more efficiently identify knowledge gaps and investigate the way the research was conducted [3,4]. Preliminary searches have indicated that large bodies of knowledge have been published concerning the integration of PROMs into statistical methods [5-7], but few have indicated frameworks for public and patient involvement in the development of AI. Search strategies for each review were developed by the team and reviewed by our information specialist (CS). Our search strategies use controlled terms and a range of techniques to optimize sensitivity. No language restrictions will be applied. Each review will include relevant date restrictions to further isolate informative and innovative research.

The MEDLINE database will be used to identify initial search results. Initial search results will be reviewed to confirm there are no significant exclusions. Once the final search strategy has been identified, we will expand our search to the following information sources: Ovid MEDLINE(R), Embase, PsycINFO, Science Citation Index, Cochrane Library, Database of Abstracts of Reviews of Effects, and PROSPERO (International Prospective Register of Systematic Reviews). Search strategies can be viewed in Multimedia Appendix 1.

Inclusion Criteria

We will include systematic reviews and overviews published in any language. Reviews will be included if they have searched a minimum of 2 databases, appraised the included studies, and provided a synthesis of the data and information retrieved. All findings will be reviewed and discussed by members of the author team until a consensus is reached. Once a preliminary set of eligible studies has been identified for each review based on outcome measures and broad inclusion criteria, we will progress to the next stage of evaluation. Each eligible study will be further evaluated based on narrower inclusion criteria to select the most relevant and informative research for each review. Narrower inclusion criteria will be specific to each research question. For the public engagement question, articles will be eligible if they discuss the involvement of the public in the development of AI or machine learning in medicine. For the question about examples of good practice, articles will be eligible if they discuss examples of integration of PROMs into machine learning algorithms. For the value-based care question, articles will be eligible if they discuss how value-based health care has or will impact the development of AI.

Exclusion Criteria

Upon initial screening of titles and abstracts, we will exclude articles meeting any of the following criteria:

- Papers not dealing with any form of or related forms of AI
- Papers in which no relevant outcomes are reported
- Papers describing protocols for future studies

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- Papers dealing with animal models
- Papers for which the full text is not accessible
- Papers that are not directly related to health care
- Papers that are theoretical models not tested on people
- Papers that are only about the methods of AI

Condition or Domain Being Studied

We are investigating 3 domains. In the first scoping review, we will study examples of how the general public has been involved in AI development, where the outcomes include aspects of the trial and the experiences and perspectives of the public, participants, or researchers. The second review will focus on machine learning algorithms that have used PROMs to improve their performance in a health care–related task. This will include any research that is investigating the use of PROMs to improve diagnostic or treatment approaches. We will include an analysis of the time and length of each study, and whether the research included a plan for protecting patient-generated data. The third review will investigate AI research that has focused on value-based care. Studies that have used AI to investigate, evaluate, or design value-based care systems will be included.

Data Extraction

The flow of information through different stages of our review will be guided by the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flowchart [8]. First, we will identify records through database searching and other sources, as described in Multimedia Appendix 1. Relevant results from each database and source of information will then be downloaded into Zotero (version 5.0.96.2; Corporation for Digital Scholarship), a management software for managing research materials. Results will then be uploaded into Covidence (Veritas Health Innovation), a web-based tool for screening references, for screening and analysis. After uploading them into Covidence, we will remove duplicate records. Titles and abstracts of potentially relevant articles will then be screened independently by at least 2 reviewers against the relevant inclusion criteria. Discrepancies will be resolved through discussion with the entire group, when necessary. Individuals recruited from the Cochrane Task Exchange, Stanford Medicine X, and Stanford Science Technology and Medicine Summer Internship will coproduce the study design and will be active in screening, data extraction, analysis, and prioritizing what to report, as well as editing and authoring tasks.

After excluding initial search results that do not meet our inclusion criteria, we will begin to review the full text of included records. Full-text review will be conducted by at least 2 authors, with an additional author reserved to mediate areas where agreement is uncertain. The authors will then come to an agreement through discussion. The full-paper review will result in the final set of included records. The authors will provide tables to show the characteristics of the included studies, similar to Table 1, and an additional table to show the author, year, and exclusion reason for excluded full studies, similar to Table 2.

Table 1. Table showing selected characteristics identified in included studies.

Study name	Characteristics					
	Intervention	Enablers	Barriers	Outcomes	Results	Time and length of study
Example study	Intervention used	Enabler to intervention, if any	Barrier to intervention, if any	Measures of outcome used	Result of intervention	Time and length of intervention

Table 2. Table of excluded studies.

Study name and year	Exclusion reason
Example study	Reason for exclusion

Public and Patient Involvement

Patients and members of the public will be involved in the review and will be trained to screen titles and abstracts, as well as conduct the risk of bias assessment. They will be mentioned as coauthors if they have met the standards for authorship. If they do not fulfill authorship criteria, they will be mentioned and thanked in the acknowledgments. Funding constraints and COVID-19 restrictions prevented us from involving them more actively in protocol building.

Dissemination

The research will be disseminated via social media and presented by the authors at conferences and convenings. The lessons learned and the findings will be used to teach our teenage and young adult learners at Stanford Anesthesia Summer Institute.

Main Outcomes

The following outcomes will be considered:

- Public involvement in AI research planning, conduct, or management
- Public involvement in research analysis
- Research recruitment, enrollment, and retention
- Factors that affect cooperation and participation
- PROMs
- PREMs
- Ethics related to the inclusion of patient-reported information in AI
- Factors relating to participant interaction with AI
- Barriers to acquiring PROMs and PREMs for use in AI research
- Cost-effectiveness outcomes relating to the inclusion of PROMs and PREMs in AI research

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Measures of Effect

Quantitative, qualitative, and mixed methods studies will be included in our reviews. If sufficient quantitative studies relating to the inclusion of PROMs in AI warrant a meta-analysis, we will perform it and calculate a weighted effect across the studies, using a random effects model. Depending on the type of patient-reported data collected, it may be useful to pool the data using an inverse variance method and analyze it using a random effects model. This may allow us to calculate statistical measures on PROMs, such as patients' symptoms, patient function, and physician communication [9]. After using a random effects model, it may still be desirable to identify sources of heterogeneity. If this is the case, we will use a subgroup analysis approach to investigate the reasons for heterogeneity. In the event of high heterogeneity, which is common in an emergent field, we will report data descriptively and include the insights found from the included mixed methods and qualitative narrative review papers.

Risk of Bias (Quality) Assessment

For quantitative studies, we will use the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) approach [10]. This approach provides a structured and transparent evaluation for summarizing the evidence for reviews. The GRADE approach classifies the quality of evidence of quantitative studies into one of 4 levels of high, moderate, low, and very low. The ratings of the quality of evidence describe how much confidence there is that the true effect lies close to that of the estimated effect.

Confidence in the Evidence from Reviews of Qualitative Research (CERQual) [11,12] will be used to summarize confidence in the findings of the qualitative reviews. This is based on the following 4 components: limitations of the methodology, relevance to the research question, coherence, and the adequacy of the data presented. CERQual enables ratings of "high," "medium," "low," and "very low". The starting point of "high confidence" reflects that each review finding is a reasonable representation of the question of interest, and it is downgraded if there are factors that would weaken this assumption. After assessing all 4 components independently, 2 authors will agree on the overall confidence for each review finding and the relevance to the review of reviews.

Strategy for Data Synthesis

For the study investigating public involvement, we will use a relational analysis to present our results. Broadly, a relational analysis is a type of content analysis in which concepts found in our review will be further analyzed by how they relate to each other. This may show us how data are managed or protected and who has access to the data. We are most interested in approaches to public involvement in AI research, as well as enablers and barriers to those approaches. With this technique, we will be able to use data from eligible sources to identify examples of strategies, enablers, barriers, and outcomes. Once we have identified these examples in our eligible sources of information, we will be able to visually present these data in a flowchart and discuss these observations within the discussion section. The template for how this chart will look can be seen in Figure 1.

For the review focusing on PROMs, we will chart the difference between the evidence used and the outcomes collected for different algorithms that use PROMs, as seen in Table 3. In this review, we are most interested in how PROMs are integrated into AI tools and what outcomes result from their use. Finally, for the study focusing on value-based care, we will use a table similar to Table 3.

Figure 1. Flow chart indicating how enablers and barriers contribute to interventions and outcomes.

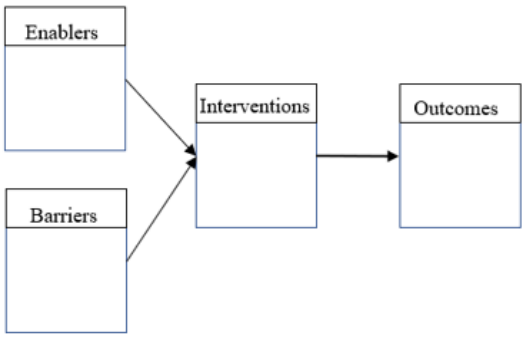

Table 3. Evidence and outcomes collected from included studies.

Reference	Evidence used			Outcomes collected		
	Evidence 1	Evidence 2	Evidence 3	Outcome 1	Outcome 2	Outcome 3
Example study 1	✓		✓	✓		✓
Example study 2		✓			✓	

Ethics Approval

Our unfunded scoping review was exempted from Stanford Institutional Review Board approval, as it does not access personal health information, and data are synthesized from already published materials.

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Results

By executing this proposed protocol, we are hoping to identify examples of good practice for how to include public involvement in the development of machine learning systems. We hope to identify enablers and barriers to public involvement, as well as interventions and outcomes that have used PROMs and PREMs. Lastly, we hope to identify examples of how value-based health care has influenced the development of AI systems in health care.

Discussion

Limitations

We have chosen to do 3 scoping reviews instead of full systematic reviews because research has indicated that scoping reviews will help us answer our research questions more efficiently [3]. In a scoping review, the goal is to determine what evidence is available rather than synthesizing evidence from multiple study designs and providing concrete guidance [13]. This is because scoping reviews are limited in their ability to provide concrete guidance. However, we are only aiming to examine the types of available evidence in this field and identify the key factors related to our topics. We are attempting to identify methods to include patient involvement in machine learning and explore how value-based care has impacted machine learning. We are not aiming to produce a specific answer to a specific clinical or policy-making question. Therefore, this limitation is acceptable.

Furthermore, scoping reviews generally provide an overview of existing evidence regardless of quality [13]. In our scoping reviews, we will be using the GRADE approach and CERQual to assess the quality of our sources. In this approach, we will discuss the qualities of reviews and determine whether the review should be included. Thus, we are directly addressing this limitation and still believe a scoping review is the right choice for each topic.

Conclusions

This protocol outlines our methods for 3 scoping reviews of published literature to discover effective strategies for the development of improved public and patient partnerships in AI and machine learning in research and health care.

Conflicts of Interest

None declared.

Multimedia Appendix 1
Search strategies.
[DOCX File , 18 KB - resprot_v11i7e36395_app1.docx]

References

1. Kingsley C, Patel S. Patient-reported outcome measures and patient-reported experience measures. BJA Education 2017 Apr;17(4):137-144. [doi: 10.1093/bjaed/mkw060]
2. Sun W, Nasraoui O, Shafto P. Evolution and impact of bias in human and machine learning algorithm interaction. PLoS One 2020 Aug 13;15(8):e0235502 [FREE Full text] [doi: 10.1371/journal.pone.0235502] [Medline: 32790666]
3. Munn Z, Peters MDJ, Stern C, Tufanaru C, McArthur A, Aromataris E. Systematic review or scoping review? Guidance for authors when choosing between a systematic or scoping review approach. BMC Med Res Methodol 2018 Nov 19;18(1):143 [FREE Full text] [doi: 10.1186/s12874-018-0611-x] [Medline: 30453902]
4. Brice A, Price A, Burls A, May Liew S. A protocol for a systematic review of methodological and qualitative factors that might influence the effectiveness of internet-based controlled clinical trialsvidence mapping and syntheses. PROSPERO. URL: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42014013308 [accessed 2022-06-10]
5. Wiering B, de Boer D, Delnoij D. Patient involvement in the development of patient-reported outcome measures: a scoping review. Health Expect 2017 Feb;20(1):11-23 [FREE Full text] [doi: 10.1111/hex.12442] [Medline: 26889874]
6. Kwan YH, Weng SD, Loh DHF, Phang JK, Oo LJY, Blalock DV, et al. Measurement properties of existing patient-reported outcome measures on medication adherence: systematic review. J Med Internet Res 2020 Oct 09;22(10):e19179 [FREE Full text] [doi: 10.2196/19179] [Medline: 33034566]
7. Kwon SB, Ku Y, Han H, Lee MC, Kim HC, Ro DH. A machine learning-based diagnostic model associated with knee osteoarthritis severity. Sci Rep 2020 Sep 25;10(1):15743 [FREE Full text] [doi: 10.1038/s41598-020-72941-4] [Medline: 32978506]
8. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JPA, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. BMJ 2009 Jul 21;339(jul21 1):b2700-b2700 [FREE Full text] [doi: 10.1136/bmj.b2700] [Medline: 19622552]
9. Peng HT, Rhind SG, Beckett A. Convalescent plasma for the prevention and treatment of COVID-19: a systematic review and quantitative analysis. JMIR Public Health Surveill 2021 Apr 7;7(4):e25500. [doi: 10.2196/25500]
10. Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. BMJ 2008 Apr 26;336(7650):924-926 [FREE Full text] [doi: 10.1136/bmj.39489.470347.AD] [Medline: 18436948]

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11. Colvin CJ, Garside R, Wainwright M, Munthe-Kaas H, Glenton C, Bohren MA, et al. Applying GRADE-CERQual to qualitative evidence synthesis findings-paper 4: how to assess coherence. Implement Sci 2018 Jan 25;13(Suppl 1):13 [FREE Full text] [doi: 10.1186/s13012-017-0691-8] [Medline: 29384081]
12. Lewin S, Glenton C, Munthe-Kaas H, Carlsen B, Colvin CJ, Gülmezoglu M, et al. Using qualitative evidence in decision making for health and social interventions: an approach to assess confidence in findings from qualitative evidence syntheses (GRADE-CERQual). PLoS Med 2015 Oct 27;12(10):e1001895. [doi: 10.1371/journal.pmed.1001895]
13. Peters MDJ, Godfrey CM, Khalil H, McInerney P, Parker D, Soares CB. Guidance for conducting systematic scoping reviews. Int J Evid Based Healthc 2015 Sep;13(3):141-146. [doi: 10.1097/XEB.0000000000000050] [Medline: 26134548]

Abbreviations

AI: artificial intelligence
CERQual: Confidence in the Evidence from Reviews of Qualitative Research
GRADE: Grading of Recommendations Assessment, Development, and Evaluation
PREM: patient-reported experience measure
PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PROM: patient-reported outcome measure
PROSPERO: International Prospective Register of Systematic Reviews

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Protocol

Quality Assessment of Digital Health Applications: Protocol for a Scoping Review

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Abstract

Background: All over the world, development and usage of mobile health (mHealth) apps is increasing. While apps offer numerous opportunities to improve health care, there are associated problems that differ significantly from those of traditional health care services. Further investigations on the quality of mHealth apps are needed to address these problems.

Objective: This study aims to identify and map research on quality assessment and quality assurance of mHealth apps and their transferability to continuous quality assurance of mHealth apps.

Methods: The scoping review will follow published methodological frameworks for scoping studies as well as Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews criteria. Electronic databases (Medline, EMBASE, and PsycINFO), reference lists of relevant articles, and websites of relevant institutions will be searched. Two reviewers will independently assess eligibility of articles. Therefore, a 2-stage (title and abstract, followed by full text) screening process was conducted. Quality management systems and quality assessment tools will be analyzed and included in our review. Particular focus is placed on quality dimensions.

Results: This scoping review provides an overview of the available evidence and identifies research gaps regarding continuous quality assessment of mHealth apps. Thereby, relevant quality dimensions and criteria can be identified and their eligibility and relevance for the development of a continuous quality assurance system of mHealth apps can be determined. Our results are planned to be submitted to an indexed, peer-reviewed journal in the second half of 2022.

Conclusions: This is the first review in the context of continuous quality assurance of mHealth apps. Our results will be used within the research "Continuous quality assurance of Digital Health Applications" ("QuaSiApps") project funded by the German Federal Joint Committee.

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KEYWORDS

digital health application; mHealth; mHealth app; quality assurance; quality assessment; mobile health; application; protocol; app; digital health; telehealth; eHealth

Introduction

Since the introduction of the Apple app Store (iOS) in 2008, mobile health (mHealth) apps have become increasingly popular. Today, inter alia promoted by the COVID-19 pandemic in 2020, the implementation of mHealth apps is even accelerated [1]. Overall, more than 350,000 health and fitness or medical apps are available from Apple App Store (iOS) and Google Play

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(Android) [1]. Many of them are not extensively tested for quality, mainly because they do not fall under medical device regulation [2].

In 1966, Donabedian [3] suggested a framework to evaluate the quality of medical care, consisting of an examination of structure, process, and outcome quality. While the assignment of quality criteria to these dimensions is in most cases straightforward, the identification of valuable quality criteria is often difficult. According to the International Organization for Standardization (ISO) 9000 standard, quality is defined as "the degree to which a set of inherent characteristics fulfills requirements" [4]. Given this definition, the assessment of quality brings a 3-fold challenge. First, the set of relevant characteristics has to be defined. Second, instruments are needed to measure the relevant characteristics. Third, the levels of requirements have to be defined. Mastering this challenge and implementing a quality management system is a strategic decision by a health care organization, which can help improve its overall performance and provide a good foundation for sustainable development initiatives [5].

Nowadays, international quality standards exist in health care. Those are, for example, quality management systems in health care (Deutsches Institut fur Normung [DIN] Europaische Norm [EN] 15224:2016 in connection with ISO 9001:2015), processes to analyze the risk to the quality, and safety of health care and continuity of care when telehealth services are used to support health care activities [6] and quality management systems specific to the medical device industry [7]. Owing to the importance of quality management in the context of health care, especially in the context of telehealth services and the medical device industry, further investigations on the quality of mHealth apps are needed.

This scoping review is one module of a larger research project. The overall project "Continuous quality assurance of Digital Health Applications" ("QuaSiApps") aims to develop a continuous quality assurance system for approved and refundable mHealth apps ("DiGA") in the German health care system [8]. The research project is funded by the German Federal Joint Committee (G-BA) [9].

The aim of this scoping review is to map the research conducted in the field of continuous quality assessment and quality assurance of mHealth apps. This includes quality management systems, quality dimensions, rating scales, quality measurement tools, quality criteria, as well as quality requirements to assess the quality of mHealth apps and their transferability to continuous quality assurance systems.

Methods

Overview

The review process will follow the 5 stages described by Arksey and O'Malley [10] and enhanced by Levac et al [11]: (1) identifying the research question (completed), (2) identifying relevant studies (completed), (3) selecting studies (ongoing), (4) charting the data and collating, and (5) summarizing and reporting the results. The manuscript will be prepared in accordance with the PRISMA-ScR (Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews) [12].

Data Sources and Search Strategy

The search strategy was developed in accordance with the JBI Manual for Evidence Synthesis concept describing 3 steps [13]. First, an initial limited search was conducted in EMBASE and Medline to search for relevant search terms contained in the title, abstract, or key words. Second, identified key words were combined and used as search queries in EMBASE, Medline, and additionally in PsycINFO. Finally, reference lists of articles included after full-text screening were screened for eligibility of inclusion.

On July 26, 2021, EMBASE, Medline, and PsycINFO were searched with the following systematic search string: ((((*"assessment*"* OR *"evaluation"* OR *"measurement"* OR *"score"* OR *"criteria"* OR *"scale"*) AND *"quality"*) OR (*"quality assurance"* OR *"quality indicators"* OR *"quality control"* OR *"quality assessment tool"* OR *"health care quality"* OR *"quality improvement"*) OR (*"norm"* OR "framework" OR *"guideline"*)) AND (*"web application"* OR *"mobile application"* OR *"mHealth"* OR *"virtual care"* OR *"healthcare app"* OR *"health care app"* OR *"mobile health"* OR *"health app"* OR *"smartphone application"*) AND (*"healthcare"* OR *"health care"*)).

The individual search terms were restricted to abstract, title, and key word search but expanded by indexing terms (MeSH and Emtree) as well as truncations. The appendix of this protocol includes the precise search strategy (Multimedia Appendices 1-3).

Articles were not included if the language was not English or German, and the search was limited to articles published between January 1, 2016, and July 8, 2021. A justification and explanation of the restrictions is given in the discussion of this protocol.

Besides the systematic search in databases, a structured study will be performed to discover gray literature, guidelines, and working papers from various governmental and nongovernmental institutions (Multimedia Appendix 4). Furthermore, relevant ISO and DIN standards will be included.

Inclusion and Exclusion Criteria

An explorative search, 2 publications [14,15], and internal discussion helped us develop inclusion and exclusion criteria (Textbox 1).

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Textbox 1. Inclusion and exclusion criteria.

Inclusion criteria

- Articles including the following:
  - development or
  - description or
  - application and description or
  - validation and description or
  - review (systematic) or
  - intended use, institutional linkage, or type of reporting of disease independent concepts of quality assessment or quality assurance in mobile health (mHealth) apps
- The investigated mHealth apps must fulfill the following criteria:
  - used by the patient and
  - used in outpatient treatment and
  - with more functions than the following: improvement of adherence, text-messaging, reminder or screening for primary prevention or (video) consultation or Disease education or Reading out and controlling of devices
- Language: English and German
- Articles published in 2016 or afterwards

Exclusion criteria

- The investigated mHealth app fulfills one of the following criteria:
  - health care practitioner use or
  - inpatient treatment or
  - with not more functions than the following: improvement of adherence, text-messaging, reminder or screening for primary prevention or (video) consultation or Disease education or Reading out and controlling of devices
- Research protocols, conference abstracts, letters to the editor, or expression of opinions

Study Screening and Selection

Identified citations were imported in Endnote X9 (Clarivate Analytics). After removing duplicates, our search strategy resulted in 2235 articles for title and abstract screening. Two reviewers (GG and NS) independently assessed the titles and abstracts of these articles to decide whether an article is eligible for full-text screening or not. Full-text screening and assessment against inclusion and exclusion criteria was conducted by the same reviewers. Reasons for noninclusion and exclusion were captured.

Articles assessed as eligible for the purpose of our review will be included and relevant information and (meta-)data will be extracted and summarized. Multimedia Appendix 5 provides a preliminary outlook on extracted information categories (Multimedia Appendix 5). Procedural purposes and usage of quality management systems are extracted separately.

In case of disagreement between the 2 reviewers, a third person (SN) will join the discussion and decide whether a text is eligible or not for inclusion. In case of missing data or uncertainty, the reviewers will contact authors of included papers.

Results

A structured search strategy was developed to find and summarize evidence for continuous quality measuring and quality assurance in the context of mHealth apps. Results of this search will be presented in the form of a scoping review. Flowcharts will be used to depict the process of article selection, and extracted data of included articles will be presented in tables as well as a narrative summary.

Discussion

This scoping review will identify concepts and studies of quality assessment and quality assurance of mHealth apps. Once a concept or study is identified and included, relevant quality dimensions and criteria will be extracted. The evidence thus gathered will be systematized by categorizing the extracted dimensions and criteria in overarching quality dimensions. Based on this, we will assess the relevance and transferability of extracted dimensions for continuous quality assurance.

Thereby, along with Arksey and O'Malley [10], we will summarize the evidence on continuous quality assurance of mHealth apps. This will also provide an overview on research gaps in the literature [10]. As part of our QuaSiApps project,

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the results will be used alongside those of another scoping reviews [16], focus groups, and stakeholder surveys to develop a continuous quality assurance system.

Regarding prior work, there are some aspects, such as usability or data privacy, that are well studied in the field of quality assurance of mHealth apps in general. However, which of these or other quality dimensions have relevance for continuous quality assurance remains unanswered. Furthermore, quality assessment in health care is based on the measurement of quality criteria [17]. However, methods of quality assessment of mHealth apps are heterogeneous. Azad-Khaneghah et al [15] reviewed mHealth usability and quality rating scales and compared them in terms of purpose, content, and intended target users. Nouri et al [14] additionally extracted and classified the criteria for assessing the quality of mHealth apps out of assessment tools or methods. Our review aims to incorporate the most recent evidence in this fast-moving environment and especially aims to shed light on concepts, guidelines, and working papers published by governmental and nongovernmental institutions. Further, our review is part of a larger research project focusing on continuous quality assurance in the German mHealth context. Thus, an emphasis will be placed on the determination of aspects involving continuous quality assurance.

However, besides usability and data privacy, quality assessment and continuous quality assurance in mHealth apps remains largely unexamined. Especially in the rapid evolving and changing field of mHealth apps, the development of a continuous quality assurance system is essential to guarantee high quality even beyond the app development or app approval to guarantee a safe and sustainable use.

Our scoping review has 2 major limitations owing to resource limitations. First, it includes only articles published after 2016. Second, articles were only considered if their language was English or German. The restriction of time is justified by the fact that Nouri et al [14] cover earlier relevant evidence about criteria for assessing the quality of mHealth apps in their systematic review. If our review does not cover all criteria reported by Nouri et al [14], we shall supplement our review with their findings. The language restriction was made because English and German were the only common languages of the reviewers. Regarding the search strategy of the proposed scoping review, it should be considered that there is still inconsistency regarding terminology [16].

Therefore, we pilot-tested different terms and compared the results to guarantee a valid search strategy. While we use the term “Application” in accordance with the German Federal Institute for Drugs and Medical Devices, a consensus paper recommends the use of “App” [18].

This scoping review gathers existing studies and concepts on quality assessment and quality assurance of mHealth apps. This will be a basis for the development of a continuous quality assurance system for mHealth apps. It helps to identify the relevant quality dimensions, which should be considered in such a concept.

Conclusions

This scoping review will provide deeper insight into the field of quality measurement and quality assurance in the context of mHealth apps. It will provide an overview of relevant quality dimensions and quality criteria especially with relevance for continuity. Our research findings can serve as a fundament for the development of continuous quality assurance systems.

Acknowledgments

This research is part part of a wider research project (Continuous quality assurance of Digital Health Applications (=“QuaSiApps”)) funded by the German Federal Joint Committee (funding code: 01VSF20007 – QuaSiApps). We acknowledge support by the Open Access Publication Fund of the University of Duisburg-Essen.

Conflicts of Interest

None declared.

Multimedia Appendix 1
Search strategy; Embase.
[DOCX File , 15 KB - resprot_v11i7e36974_app1.docx]

Multimedia Appendix 2
Search strategy Medline via Ovid.
[DOCX File , 15 KB - resprot_v11i7e36974_app2.docx]

Multimedia Appendix 3
Search strategy PsycINFO via Ovid.
[DOCX File , 15 KB - resprot_v11i7e36974_app3.docx]

Multimedia Appendix 4
Sources of gray literature.

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[DOCX File , 14 KB - resprot_v11i7e36974_app4.docx]

Multimedia Appendix 5
Data extraction.
[DOCX File , 13 KB - resprot_v11i7e36974_app5.docx]

References

1. Digital Health Trends 2021: Innovation, evidence, regulation, and adoption. IQVIA. 2021. URL: https://www.iqvia.com/insights/the-iqvia-institute/reports/digital-health-trends-2021 [accessed 2022-04-05]
2. Examples of Mobile Apps That Are NOT Medical Devices. US Food and Drug Administration. 2018. URL: https://tinyurl.com/jxwctrve [accessed 2022-04-05]
3. Donabedian A. Evaluating the quality of medical care. 1966. Milbank Q 2005;83(4):691-729 [FREE Full text] [doi: 10.1111/j.1468-0009.2005.00397.x] [Medline: 16279964]
4. ISO 9000:2015 Quality management systems — Fundamentals and vocabulary. International Organization for Standardization. 2015. URL: https://www.iso.org/standard/45481.html [accessed 2022-04-05]
5. ISO 9001:2015 Quality management systems — Requirements. International Organization for Standardization. 2015. URL: https://www.iso.org/standard/62085.html [accessed 2022-04-05]
6. ISO 13131:2021 Health informatics — Telehealth services — Quality planning guidelines. International Organization for Standardization. 2021. URL: https://www.iso.org/standard/75962.html [accessed 2022-04-05]
7. ISO 13485:2016 Medical devices – Quality management systems – Requirements for regulatory purposes. International Organization for Standardization. 2016. URL: https://www.iso.org/standard/59752.html [accessed 2022-05-04]
8. The Fast-Track Process for Digital Health Applications (DiGA) according to Section 139e SGB V: A Guide for Manufacturers, Service Providers and Users. Federal Institute for Drugs and Medical Devices. URL: https://www.bfarm.de/SharedDocs/Downloads/EN/MedicalDevices/DiGA_Guide.pdf?__blob=publicationFile [accessed 2022-04-05]
9. QuaSiApps - Ongoing quality assurance of health apps used in statutory health insurance. Gemeinsamer Bundesausschuss Innovationsausschuss. URL: https://tinyurl.com/2s44w75h [accessed 2022-10-01]
10. Arksey H, O'Malley L. Scoping studies: towards a methodological framework. Int J Soc Res Methodol 2005 Feb;8(1):19-32 [FREE Full text] [doi: 10.1080/1364557032000119616]
11. Levac D, Colquhoun H, O'Brien KK. Scoping studies: advancing the methodology. Implement Sci 2010 Sep 20;5:69 [FREE Full text] [doi: 10.1186/1748-5908-5-69] [Medline: 20854677]
12. Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, et al. PRISMA Extension for Scoping Reviews (PRISMA-ScR): checklist and explanation. Ann Intern Med 2018 Oct 02;169(7):467-473 [FREE Full text] [doi: 10.7326/M18-0850] [Medline: 30178033]
13. Aromataris E. JBI Manual for Evidence Synthesis. JBI 2020 [FREE Full text] [doi: 10.46658/JBIMES-20-01]
14. Nouri R, Kalhori SRN, Ghazisaeedi M, Marchand G, Yasini M. Criteria for assessing the quality of mHealth apps: a systematic review. J Am Med Inform Assoc 2018 Aug 01;25(8):1089-1098 [FREE Full text] [doi: 10.1093/jamia/ocy050] [Medline: 29788283]
15. Azad-Khaneghah P, Neubauer N, Miguel Cruz A, Liu L. Mobile health app usability and quality rating scales: a systematic review. Disabil Rehabil Assist Technol 2021 Oct;16(7):712-721. [doi: 10.1080/17483107.2019.1701103] [Medline: 31910687]
16. Giebel GD, Speckemeier C, Abels C, Börchers K, Wasem J, Blase N, et al. Problems and barriers related to the use of digital health applications: protocol for a scoping review. JMIR Res Protoc 2022 Apr 21;11(4):e32702 [FREE Full text] [doi: 10.2196/32702] [Medline: 35451979]
17. Arah OA, Westert GP, Hurst J, Klazinga NS. A conceptual framework for the OECD Health Care Quality Indicators Project. Int J Qual Health Care 2006 Sep;18 Suppl 1:5-13. [doi: 10.1093/intqhc/mzl024] [Medline: 16954510]
18. Lewis TL, Boissaud-Cooke MA, Aungst TD, Eysenbach G. Consensus on use of the term "App" versus "Application" for reporting of mHealth research. J Med Internet Res 2014 Jul 17;16(7):e174; discussion e174 [FREE Full text] [doi: 10.2196/jmir.3460] [Medline: 25033233]

Abbreviations

DIN: Deutsches Institut fur Normung
EN: Europaische Norm
G-BA: German Federal Joint Committee
mHealth: mobile health
PRISMA-ScR: Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews
QuaSiApps: Continuous quality assurance of Digital Health Applications

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Protocol

Digital Technologies for Health Promotion and Disease Prevention in Older People: Protocol for a Scoping Review

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Abstract

Background: Digital technologies could contribute to health promotion and disease prevention. It is unclear if and how such digital technologies address the health needs of older people in nonclinical settings (ie, daily life).

Objective: This study aims to identify digital technologies for health promotion and disease prevention that target the needs of older people in nonclinical settings by performing a scoping review of the published literature. The scoping review is guided by the framework of Arksey and O'Malley.

Methods: Our scoping review follows the PRISMA-ScR (Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews) guidelines. The information sources are bibliographic databases (MEDLINE, PsycINFO, CINAHL, and SCOPUS) and bibliographies of any included systematic reviews. Manual searches for additional studies will be performed in Google Scholar and most relevant journals. The electronic search strategy was developed in collaboration with a librarian who performed the search for studies on digital technologies for health promotion and disease prevention targeting the needs of older people. Study selection and data coding will be performed independently by 2 authors. Consensus will be reached by discussion. Eligibility is based on the PCC (Population, Concept, and Context) criteria as follows: (1) older people (population); (2) any digital (health) technology, such as websites, smartphone apps, or wearables (concept); and (3) health promotion and disease prevention in nonclinical (daily life, home, or community) settings (context). Primary studies with any design or reviews with a systematic methodology published in peer-reviewed academic journals will be included. Data items will address study designs, PCC criteria, benefits or barriers related to digital technology use by older people, and evidence gaps. Data will be synthesized using descriptive statistics or narratively described by identifying common themes. Quality appraisal will be performed for any included systematic reviews, using a validated instrument for this study type (A Measurement Tool to Assess Systematic Reviews, version 2 [AMSTAR2]).

Results: Following preliminary literature searches to test and calibrate the search syntax, the electronic literature search was performed in March 2022 and manual searches were completed in June 2022. Study selection based on titles and abstracts was completed in July 2022, and the full-text screen was initiated in July 2022.

Conclusions: Our scoping review will identify the types of digital technologies, health targets in the context of health promotion and disease prevention, and health benefits or barriers associated with the use of such technologies for older people in nonclinical settings. This knowledge could guide further research on how digital technologies can support healthy aging.

International Registered Report Identifier (IRRID): PRR1-10.2196/37729

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(JMIR Res Protoc 2022;11(7):e37729) doi:10.2196/37729

KEYWORDS

digital technology; health technology; digital public health; health promotion; disease prevention; healthy aging; elderly population; older adult; older population; scoping review

Introduction

Digital technologies, such as wearable devices, smartphone apps, and health websites, could contribute to health promotion and disease prevention in the general population [1]. In particular, younger, more educated, and wealthier members of the general population use digital technologies for healthy lifestyle promotion and report higher perceived digital health literacy [2]. Due to aging of the world population, digital technologies for healthy lifestyle promotion should also target the specific needs of older people. However, it is unclear if and what digital technologies exist for this population.

In the digitized world, surprisingly, little is known about the needs of older people regarding their use of digital technologies for healthy lifestyle promotion [3]. Although older people are considered "nondigital natives" and their use of digital technologies is associated with various barriers, such technologies could also facilitate healthy aging via access to health information and the provision of health care [4,5]. A research focus on this population is important to better understand how older people use and engage with digital technologies for healthy aging [6]. For example, access to digital health offers is possible only if older people possess appropriate technological devices, such as tablets or smartphones [7,8]. The initial adoption of such technologies depends on their acceptance by the target population. Digital technologies for older people should be easy to learn and explicitly communicate their usefulness to users [9]. Finally, sustained engagement with the technologies is necessary for their successful use. For example, adequate digital health literacy [10] and human support [11,12] are required to operate and potentially benefit from digital technologies. In general, co-creation and feedback from older users are required to develop appropriate digital technologies for healthy aging in this target population [13-15]. Furthermore, evaluation of cost-effectiveness [16] and user outcomes in the context of health promotion and disease prevention [17] is required to better understand if and how digital technologies work.

Recent scoping reviews suggest that digital health technologies for older people are used predominantly in the clinical context of disease management. For example, digital technologies may elicit behavioral changes across a range of health conditions that are required to improve disease and medication management among people aged 60 years or above [18]. Furthermore, interventions for health promotion and disease prevention targeting the needs of older people are often nondigital (only 12 out of 486 reviews addressed eHealth interventions for this population) [19]. Finally, the most common health target of digital interventions for health promotion and disease prevention is physical activity, according to a scoping review [20] and recent systematic reviews that assessed the efficacy of such interventions in older people (Table 1). As illustrated in Table 1 and discussed in other scoping reviews [17,21], the terminology in the field of digital health promotion and disease prevention is highly diverse, and a uniform definition of the age of older people does not exist. Therefore, a new scoping review is required to more broadly identify any available digital technologies that target any aspects of healthy aging in nonclinical settings (ie, daily life).

Table 1. Selected systematic reviews on digital technologies for older people.

Review citation	Population age (older people; years)	Digital technologies	Health outcomes
Muellmann et al, 2018 [22]	55+	eHealth	Physical activity
Buyl et al, 2020 [23]	50+	eHealth	Physical activity, diet, quality of life, and well-being
Kwan et al, 2020 [24]	50+	eHealth	Physical activity
McGarrigle et al, 2020 [25]	50+	mHealth[a] and eHealth	Physical activity
Stara et al, 2020 [26]	50+	Digital coaching	Physical activity, healthy eating, stress management, and tobacco cessation
Janhunen et al, 2021 [27]	60+	Exergaming	Walking
Nunez de Arenas-Arroyo et al, 2021 [28]	55+	eHealth	Physical activity

[a]mHealth: mobile health.

This study aims to identify digital technologies for health promotion and disease prevention that address the needs of older people using a scoping review of published literature. The scoping review is guided by a framework for scoping studies proposed by Arksey and O'Malley [29].

Our broad objectives are to identify and examine the research activity in the field of digital technologies for health promotion

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and disease prevention that target the needs of older people in nonclinical settings and to identify evidence gaps that could guide future research. The scoping review will address the following specific objectives: (1) to identify the existing digital technology types (eg, smartphone apps, websites, and wearables) for health promotion and disease prevention that target the needs of older people, (2) to describe the health context of such digital technologies, including health targets (eg, physical activity, nutrition, and cognition) and health purposes (eg, mobility promotion and lifestyle monitoring), (3) to describe the target populations of such technologies in terms of sociodemographic characteristics (especially age), health status (ie, healthy, at risk for any disease, or with any disease), and settings with nonclinical focus (eg, daily life, home, or community), (4) to assess the use pattern in terms of any health benefits or barriers associated with the use of such technologies for older people in nonclinical settings, and (5) to identify any evidence gaps.

Methods

Study Design

Our scoping review follows the PRISMA-ScR (Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews) guidelines [30]. The PRISMA-ScR checklist will be reported in an appendix.

Protocol and Registration

This protocol was written before the study commenced (ie, before the electronic literature search was performed). The study was registered at the Open Science Framework [31].

Eligibility Criteria

The eligibility for our scoping review is based on the PCC (Population, Concept, and Context) criteria (Textbox 1).

Detailed definitions of the PCC criteria are provided in Textbox 2.

Textbox 1. Eligibility criteria for the scoping review.

Inclusion criteria

1. Population: older people
2. Concept: digital health technologies
3. Context: health promotion and disease prevention
4. Setting: nonclinical (eg, daily life, home, and community)
5. Study type: primary studies with any design or data type (quantitative and qualitative) and reviews with systematic methodology
6. Publication status: published in a peer-reviewed journal
7. Publication language: English, German, or French
8. Full-text accessible

Exclusion criteria

1. Older people not included
2. Digital health technologies not included
3. Other context than health promotion and disease prevention
4. Clinical setting (eg, aged care and clinical facility)
5. Other study types: protocols or narrative reviews
6. Other publication status: published without peer review, dissertations, books, conference papers, comments, corrections, letters, and editorials
7. Publication language other than English, German, or French
8. Full-text not accessible

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Textbox 2. Definitions of the inclusion criteria in the scoping review.

Population: older people

- Older people include populations with the age range defined by study authors.
- Studies with older people of any gender or health status (ie, healthy, at risk for any disease, or with any disease) will be included.
- Studies will be excluded if older people are not the focus of the study (eg, focus on carers of older people) or if they are included among people of any age or with middle-aged adults.

Concept: digital health technologies

- Digital technologies are defined as any digitally supported health technologies. These technologies may include the components of (1) eHealth, that is, the use of information and communications technology to support health and (2) mobile health (mHealth), that is, the use of digital devices or tools with mobile and wireless technologies to support health objectives according to a World Health Organization guideline on digital interventions [32].
- Studies will be included if they use any "traditional" technologies, such as websites accessed via computer or mobile telephones, or any "modern" technologies, such as smartphone apps, wearables, or exergaming.
- Studies will be included if digital health technologies are used alone or as part of a health intervention.
- Studies will be excluded if landline telephones are used as the main technology in the health context.

Context: health promotion and disease prevention

- Health promotion and disease prevention (primary, secondary, or tertiary) will be defined as any measures used to improve or maintain healthy lifestyle, prevent the onset of new diseases, or prevent worsening of existing diseases.
- Studies will be included if they focus on different aspects of healthy aging, such as physical activity, nutrition, mental and cognitive functioning, or sleep.
- Studies will be excluded if they focus on dental health, disease management, or digital technology development.

Since our scoping review focuses on 3 broad topics (digital technologies, health promotion and disease prevention, and older people), we aim to identify primary studies with any design (randomized or nonrandomized with quantitative or qualitative data) and reviews with a systematic methodology (rapid, scoping, systematic, or overview of reviews). This approach will assure that the relevant literature will be identified either in our literature search or in other reviews. Furthermore, identification of other reviews in this rapidly developing field can potentially reduce research waste that occurs when new reviews are produced, although reviews on similar topics already exist [17,33].

Information Sources

The information sources for our scoping review are (1) 4 international bibliographic databases (MEDLINE through OVID, PsycINFO through OVID, CINAHL through EBSCO, and SCOPUS), (2) bibliographies of any included systematic reviews, (3) Google Scholar, and (4) most relevant journals in the field. These databases were chosen because they identified the most relevant literature in our searches for digital technologies in other public health contexts. Due to potential financial interests in the field of digital health technologies, grey (nonpeer reviewed) literature will not be searched for. Instead, we aim to locate only published and peer-reviewed literature that may critically and objectively evaluate the health applications of such technologies in older people.

Search Strategy

The electronic search strategy was developed in collaboration with an experienced librarian on our team who also performed the search and deduplicated the results. The development and reporting of the search strategy adheres to PRESS (Peer Review of Electronic Search Strategies) [34] and PRISMA-S (PRISMA Statement for Reporting Literature Searches in Systematic Reviews) [35] guidelines. The preliminary search syntax was developed based on our own syntax from a scoping review on the evaluation of digital interventions for physical activity promotion [17,36] and the search strategies reported in other relevant reviews (Table 1). According to the PRESS guideline [34], we first adapted the preliminary syntax to match our PCC criteria (Textbox 1) as follows: (1) digital technologies, (2) older people, and (3) health promotion and disease prevention. Preliminary literature searches were performed in MEDLINE throughout January to February 2022 to derive the most optimal combination of search terms and calibrate the search syntax. The searches were performed by the librarian, and the results were imported into EndNote X9 (Clarivate) and sorted by publication date. The oldest and newest sources were screened for relevance by 1 author, and feedback was given to the librarian. Once a fortnight, the search syntax and the relevance of results were discussed in the team. Following our discussion, the search syntax was adjusted and tested by the librarian in MEDLINE. The impact of syntax changes on the results was assessed by 1 author and subsequently discussed in the team.

The following aspects of the search syntax were implemented according to the PRESS guideline [34] and verified during our team discussions: (1) quality of translation of the research question into search terms done by inspecting the number of hits per syntax line, (2) appropriate use of adjacency proximity operators done by comparing the number of hits following different adjacency limits, (3) choice of subject headings done by inspecting the number of hits per syntax line, (4) text word

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searching done by inspecting the truncation and inclusion of British and American spellings, and (5) spelling and any syntax errors done by reading the syntax strategy line by line and inspecting the use of Boolean operators and brackets. There were no filters or limits used in the syntax.

Once consensus on the most effective search strategy was reached and approved by the team, the search strategy from MEDLINE was adapted to each other database individually by the librarian. A summary of the search strategy is reported in Table 2, and the full search strategy will be reported in an appendix.

Table 2. Summary of the search strategy in our scoping review.

Variable	Search topic 1: Digital technologies	Search topic 2: Older people	Search topic 3: Health promotion and disease prevention
Example search terms	Telemedicine, mobile applications, internet-based or digital intervention, fitness trackers, wearables, video games, or social media	Older, elderly or senior separated by up to three terms from people, adults, or population	Health (promotion or prevention)
Search fields	Titles or abstracts	Titles or abstracts	Titles, abstracts, or keywords
Comments	Relevant MeSH (Medical Subject Headings) terms were selected in MEDLINE and corresponding subject headings were selected in PsycINFO and CINAHL.	Adjacency with up to three terms was used to identify sources in which the words “older people” were separated by additional terms, such as older “healthy” people.	We relied on author keywords or database classification systems to identify sources investigating health promotion and disease prevention, even if these terms were not used in titles or abstracts.

The electronic literature search was performed in each database separately from database inception through March 3, 2022. The search results were exported into individual libraries in EndNote and subsequently merged into a single library. This single library was exported into deduplication software Deduplicator [37], automatically deduplicated, and manually checked, and following duplicate removal, the results were imported back into a new library in EndNote.

Selection of Sources of Evidence

Study selection will be performed in EndNote by 2 authors independently, and final consensus will be reached by discussion. The study selection procedure will involve automatic and manual elements as follows. First, all sources from the electronic search will be automatically divided into 2 libraries using the smart groups function in EndNote by 1 author as follows: (1) library I1 with sources fulfilling the inclusion criterion 1 (with the words “older people” in titles; Textbox 1) and (2) library E1 with sources fulfilling the exclusion criterion 1 (without the words “older people” in titles; Textbox 1). All titles in library E1 will be manually screened for inclusion by 2 authors independently. Sources will be excluded if other populations, such as adolescents, are mentioned in titles. Abstracts will be read if the titles do not mention the study population. Any sources that focus on older people in library E1 will be moved to library I1 for further inspection. Library I1 will be subdivided into further libraries using the smart groups function in EndNote by 1 author. For example, a smart group of sources with the term “protocol” in titles or abstracts will be created within library I1 and exported into a new library E5. Titles of sources in library E5 will be manually screened by 2 authors independently to confirm that sources identified by EndNote as study protocols were indeed study protocols. Any incorrectly classified sources will be moved back to library I1 for further inspection. This procedure will continue until all sources in library I1 will be either selected for full-text inspection (located in library I1) or excluded based on title or abstract screening and moved to libraries E1 to E7.

Following the title and abstract screening, full-text inspection of all sources in library I1 will be done manually by 2 authors independently. Consensus will be reached by discussion.

Once study selection from the database searches is complete, supplementary searches for additional studies will be performed by 1 author, and another author will check and approve the selection. Manual searches will be performed using bibliographies of any included systematic reviews. Additional searches will also be performed using Google Scholar and the websites of the most relevant journals in the field of digital public health identified in another scoping review [38] or suggested by the peer reviewers of this article. The following journals will be searched: JMIR mHealth and uHealth, Journal of Medical Internet Research, BMC Public Health, JMIR Aging, The Lancet Digital Health, PLOS Digital Health, and Frontiers in Digital Health.

A summary of study selection will be reported on the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flowchart. A list of included and excluded studies and reasons for exclusion after the full-text assessment will be reported in an appendix. Study selection from the electronic search was initiated in March 2022.

Data Charting

Data coding will be performed using a single spreadsheet (Excel, version 10; Microsoft Corp) that will be developed and calibrated within the team. If necessary, a coding manual will be developed to assure high interrater reliability of coding. Data coding will be performed by 2 authors independently, and consensus will be reached by discussion.

Data Items

A list of data items (Textbox 3) will be developed by 2 authors to address the objectives of our scoping review. If applicable, data will be coded quantitatively into predefined categories or qualitatively using author statements. Data items addressing the overlap in primary studies will be used to assess the uniqueness of evidence among the included reviews and between our

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electronic search and the included reviews. Specifically, the primary studies included in each review will be inserted into an additional spreadsheet (Excel, version 10) and manually compared among the reviews (sorted from the oldest to the newest) and against our list of included studies. Any primary studies included in only 1 review will be classified as unique. We will also assess the overlap in primary studies between our electronic search and the included reviews. Any primary studies identified in our search but not included in any review will be classified as unique. All coded data will be reported in an appendix.

Textbox 3. Data items in the scoping review.

Bibliographic information

- First author, publication year, publication date, corresponding author region, title, and funding sources

Study design

- Study type: primary study or review
- Primary study design: randomized or nonrandomized
- Primary study data type: quantitative, qualitative, or mixed
- Review type: rapid, scoping, systematic, or overview of reviews
- Primary studies in reviews: number per review, overlap in primary studies among all reviews, and overlap in primary studies among reviews and our electronic search

Study aim and focus

- Study aim according to authors
- Study focus: evaluation, feasibility, efficacy, or other

Population (older people)

- Sample size
- Sociodemographic characteristics: age, gender, and others (eg, working or retired, socioeconomic status, country of data collection, and digital health competence)
- Health status: healthy (without or at risk for any disease) or clinical (with any disease)
- Setting: daily life, home, community, or others with examples

Concept (digital technology)

- Type: any digital technology (telemedicine, eHealth, or mHealth), wearable device, smartphone or other mobile tool, app, internet, website, exergaming, virtual reality, or others with examples

Context (health promotion and disease prevention)

- Health target: physical activity, nutrition, mental and cognitive functioning, sleep, or others with examples
- Health purpose: healthy lifestyle promotion, disease prevention (primary, secondary, or tertiary), lifestyle monitoring, reminders, performance feedback, social or virtual network development, or other

Use pattern (benefits vs barriers)

- Duration
- Benefits (eg, acceptability, engagement, and outcome evaluation)
- Barriers (eg, reasons for attrition and difficulties with use)

Evidence gaps

- Study conclusions or author statements focusing on ideas for future research

Critical Appraisal of Individual Sources of Evidence

Except for systematic reviews, the critical appraisal of included studies will not be performed because our scoping review aims to broadly identify digital technologies for older people rather than to evaluate their efficacy in the context of healthy aging. The quality of existing evidence will be discussed based on study designs identified in the scoping review.

The critical appraisal of systematic reviews will be performed according to guidelines for overviews of systematic reviews [39] with a validated tool for systematic reviews (A Measurement Tool to Assess Systematic Reviews, version 2

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[AMSTAR2] [40]). AMSTAR2 consists of 16 items (7 critical and 9 noncritical). The appraisal outcome is the overall confidence rating in the results of a systematic review (critically low, low, moderate, or high) based on a combination of scores on critical and noncritical items [40]. Critically low ratings are assigned if at least two critical items are not fulfilled (rated as no) on AMSTAR2.

The appraisals will be performed according to a 2-step procedure described in our protocol for another scoping review [36]. In the first step, 2 items on AMSTAR2 (item 2: presence of a review protocol and item 7: presence of a list of excluded studies) will be rated to identify any systematic reviews with critically low confidence ratings. These 2 items were chosen because they are typically not fulfilled in systematic reviews of nondigital or digital health interventions [17,33,41]. In the second step, any systematic reviews that fulfill item 2, item 7, or both will be rated with all 16 AMSTAR2 items according to AMSTAR2 guidance [40].

A spreadsheet (Excel, version 10) will be developed and used for appraising systematic reviews with AMSTAR2. All systematic reviews will be independently appraised by 2 authors, and consensus will be reached by discussion. The overall confidence ratings for each systematic review will be reported in an appendix.

Synthesis of Results

Data will be synthesized according to the objectives of our scoping review. The quantitative data items and AMSTAR2 appraisal outcomes for all systematic reviews will be synthesized using descriptive statistics (frequencies, means, and SDs, if applicable). The qualitative data items will be narratively described by identifying common themes.

Results

Following preliminary literature searches to test and calibrate the search syntax, the electronic literature search was performed in March 2022 and manual searches were completed in June 2022. Study selection based on titles and abstracts was completed in July 2022, and the full-text screen was initiated in July 2022.

Discussion

Principal Findings

Our electronic search identified just over 2000 sources. Study selection is expected to be completed in July 2022. The smart groups function in EndNote helped us to initially manage and automatically sort the literature. EndNote was very precise at identifying certain publication types, such as reviews, study protocols, dissertations, books, and conference papers. EndNote also helped us to identify sources with other populations, such as young people, and other settings, such as aged care. Most human judgement was required to decide if technologies used in studies were digital, and if so, if they were used in the context of health promotion and disease prevention. Furthermore, the study population was not mentioned in the titles of about 25% of search results, and the abstracts of these studies had to be manually assessed. So far, there have been only few minor disagreements between the 2 authors involved in the title and abstract screening. These disagreements were resolved by discussion between both authors based on additional information for or against inclusion.

Fully automated and preliminary sorting of studies into smart groups in EndNote showed that various digital technologies are used for health promotion and disease prevention by older people, including any technologies (digital, virtual, video, eHealth, or telehealth), websites accessed via a computer, SMS (text messages) or mobile phones, exergaming, smartphones, or wearables. The studies addressed different health targets, including physical activity, mental health and wellness, nutrition, and cognitive functioning. The study focus is on effectiveness, feasibility, or evaluation of digital technologies.

Comparison With Prior Work

Two interesting aspects of our scoping review are to identify the digital technologies preferred by older people and to assess the reasons for using such technologies in the health context. Our preliminary inspection of studies suggests that while older people may use more modern technologies, such as smartphone apps or wearables, they also use (and possibly prefer) other technological solutions and devices, such as websites accessed via computers. Furthermore, while physical activity was the primary focus of previous reviews in this field (eg, the review by Taylor et al [20] and reviews listed in Table 1), healthy aging is associated with various health outcomes. According to our preliminary inspection of studies, these may also include nutrition, and mental and cognitive functioning. It is likely that we will identify other aspects of health promotion and disease prevention in the final sample of studies, including weight management, substance use prevention, sleep monitoring, and promotion of social functioning.

Strengths and Limitations

The main strength of our scoping review is the electronic search syntax that was iteratively tested and revised by an experienced librarian on our team. Regardless of frequent piloting, there are several potential limitations in our search strategy, meaning that we might have missed some relevant studies in this new field. First, the research field of digital health promotion and disease prevention [21] and the terminology in this field [17] are highly diverse and nonstandardized. For example, 40 reviews of similar (digital) interventions in the same field (physical activity promotion) located different published primary studies in their searches, meaning that about 80% of studies were included in only 1 of the 40 reviews [17]. Second, the age range of older people typically varies among studies. To circumvent this problem, there is no age limitation for older people in our scoping review. Instead, the age range of participants will be coded to investigate any patterns in the results. Third, the terms “health promotion” and “disease prevention” can address very different health targets and are typically not mentioned in study titles or abstracts. Our preliminary searches showed that the most relevant studies were obtained when these terms were included in keyword searches but not when they were omitted from the search syntax. Manual searches for additional studies in other reviews or in the most relevant journals may be essential

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in this new field. Finally, we focus only on (objective) peer-reviewed literature published in academic journals. This choice is guided by the general difficulty in assessing any financial interests associated with digital technologies that may be present in nonacademic literature.

Dissemination Plan

We plan to publish the results of our scoping review in a peer-reviewed academic journal and also to disseminate our findings using plain-language summaries in English and German. Such summaries may facilitate the knowledge translation from our scoping review to a broader audience, including stakeholders working in the field of health promotion or the target population of older people. In general, knowledge translation is required to successfully process scientific findings before they can be applied in practice. Public health stakeholders involved in promoting physical activity among the elderly in Germany identified such short summaries as a strategy that could aid their work [42].

Conclusions

Our scoping review will identify the types of digital technologies, health targets in the context of health promotion and disease prevention, and use benefits or barriers for older people in nonclinical settings. This knowledge could guide further research on how digital technologies can support healthy aging.

Acknowledgments

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Authors' Contributions

KKDS conceptualized the study, developed the methodology, wrote the first draft of the manuscript, and reviewed and edited the manuscript. LM developed the methodology, wrote the first draft of the manuscript, and reviewed and edited the manuscript. LC developed the methodology, and reviewed and edited the manuscript. HZ conceptualized the study, developed the methodology, and reviewed and edited the manuscript.

Conflicts of Interest

None declared.

References

1. Zeeb H, Pigeot I, Schüz B, Leibniz-WissenschaftsCampus Digital Public Health Bremen. [Digital public health-an overview]. Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz 2020 Feb 09;63(2):137-144. [doi: 10.1007/s00103-019-03078-7] [Medline: 31919531]
2. De Santis KK, Jahnel T, Sina E, Wienert J, Zeeb H. Digitization and health in Germany: Cross-sectional nationwide survey. JMIR Public Health Surveill 2021 Nov 22;7(11):e32951 [FREE Full text] [doi: 10.2196/32951] [Medline: 34813493]
3. Ienca M, Schneble C, Kressig RW, Wangmo T. Digital health interventions for healthy ageing: a qualitative user evaluation and ethical assessment. BMC Geriatr 2021 Jul 02;21(1):412 [FREE Full text] [doi: 10.1186/s12877-021-02338-z] [Medline: 34215209]
4. Pywell J, Vijaykumar S, Dodd A, Coventry L. Barriers to older adults' uptake of mobile-based mental health interventions. Digit Health 2020;6:2055207620905422 [FREE Full text] [doi: 10.1177/2055207620905422] [Medline: 32110429]
5. Wilson J, Heinsch M, Betts D, Booth D, Kay-Lambkin F. Barriers and facilitators to the use of e-health by older adults: a scoping review. BMC Public Health 2021 Aug 17;21(1):1556 [FREE Full text] [doi: 10.1186/s12889-021-11623-w] [Medline: 34399716]
6. Kebede AS, Ozolins L, Holst H, Galvin K. The digital engagement of older people: Systematic scoping review protocol. JMIR Res Protoc 2021 Jul 5;10(7):e25616. [doi: 10.2196/25616]
7. Bommakanti KK, Smith LL, Liu L, Do D, Cuevas-Mota J, Collins K, et al. Requiring smartphone ownership for mHealth interventions: who could be left out? BMC Public Health 2020 Jan 20;20(1):81 [FREE Full text] [doi: 10.1186/s12889-019-7892-9] [Medline: 31959145]
8. Langford A, Orellana K, Kalinowski J, Aird C, Buderer N. Use of tablets and smartphones to support medical decision making in US adults: Cross-sectional study. JMIR Mhealth Uhealth 2020 Aug 12;8(8):e19531 [FREE Full text] [doi: 10.2196/19531] [Medline: 32784181]
9. Raja M, Bjerkan J, Kymre IG, Galvin KT, Uhrenfeldt L. Telehealth and digital developments in society that persons 75 years and older in European countries have been part of: a scoping review. BMC Health Serv Res 2021 Oct 26;21(1):1157 [FREE Full text] [doi: 10.1186/s12913-021-07154-0] [Medline: 34696789]
10. Pourrazavi S, Kouzekanani K, Bazargan-Hejazi S, Shaghaghi A, Hashemiparast M, Fathifar Z, et al. Theory-based E-health literacy interventions in older adults: a systematic review. Arch Public Health 2020 Aug 10;78(1):72 [FREE Full text] [doi: 10.1186/s13690-020-00455-6] [Medline: 32793345]

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11. Preusse KC, Mitzner TL, Fausset CB, Rogers WA. Older adults' acceptance of activity trackers. J Appl Gerontol 2017 Feb;36(2):127-155 [FREE Full text] [doi: 10.1177/0733464815624151] [Medline: 26753803]
12. Puri A, Kim B, Nguyen O, Stolee P, Tung J, Lee J. User acceptance of wrist-worn activity trackers among community-dwelling older adults: Mixed method study. JMIR Mhealth Uhealth 2017 Nov 15;5(11):e173 [FREE Full text] [doi: 10.2196/mhealth.8211] [Medline: 29141837]
13. Pollet S, Denison-Day J, Bradbury K, Essery R, Grey E, Western M, et al. A qualitative exploration of perceptions of a digital intervention to promote physical activity in older adults. J Aging Phys Act 2021 Jun 01;29(3):442-454. [doi: 10.1123/japa.2019-0484] [Medline: 33348316]
14. Schmied M, Igerc I, Schneider C. A digital health coach for younger seniors - User centred requirements collection. Stud Health Technol Inform 2020 Jun 23;271:137-144. [doi: 10.3233/SHTI200089] [Medline: 32578556]
15. Seifert A, Reinwand DA, Schlomann A. Designing and using digital mental health interventions for older adults: Being aware of digital inequality. Front Psychiatry 2019 Aug 9;10:568 [FREE Full text] [doi: 10.3389/fpsyt.2019.00568] [Medline: 31447716]
16. Ghani Z, Jarl J, Sanmartin Berglund J, Andersson M, Anderberg P. The cost-effectiveness of mobile health (mHealth) interventions for older adults: Systematic review. Int J Environ Res Public Health 2020 Jul 22;17(15):5290 [FREE Full text] [doi: 10.3390/ijerph17155290] [Medline: 32708016]
17. De Santis KK, Jahnel T, Matthias K, Mergenthal L, Al Khayyal H, Zeeb H. Evaluation of digital interventions for physical activity promotion: Scoping review. JMIR Public Health Surveill 2022 May 23;8(5):e37820 [FREE Full text] [doi: 10.2196/37820] [Medline: 35604757]
18. Zaslavsky O, Roopsawang I, Chen AT. Promoting behavioral change in mobile health interventions for older adults: A scoping review. Res Gerontol Nurs 2020 Mar 01;13(2):102-116 [FREE Full text] [doi: 10.3928/19404921-20191031-01] [Medline: 31697395]
19. Chiu C, Hu J, Lo Y, Chang E. Health promotion and disease prevention interventions for the elderly: A scoping review from 2015-2019. Int J Environ Res Public Health 2020 Jul 24;17(15):5335 [FREE Full text] [doi: 10.3390/ijerph17155335] [Medline: 32722162]
20. Taylor J, Walsh S, Kwok W, Pinheiro MB, de Oliveira JS, Hassett L, et al. A scoping review of physical activity interventions for older adults. Int J Behav Nutr Phys Act 2021 Jun 30;18(1):82 [FREE Full text] [doi: 10.1186/s12966-021-01140-9] [Medline: 34193157]
21. Stark AL, Geukes C, Dockweiler C. Digital health promotion and prevention in settings: Scoping review. J Med Internet Res 2022 Jan 28;24(1):e21063 [FREE Full text] [doi: 10.2196/21063] [Medline: 35089140]
22. Muellmann S, Forberger S, Möllers T, Bröring E, Zeeb H, Pischke CR. Effectiveness of eHealth interventions for the promotion of physical activity in older adults: A systematic review. Prev Med 2018 Mar;108:93-110. [doi: 10.1016/j.ypmed.2017.12.026] [Medline: 29289643]
23. Buyl R, Beogo I, Fobelets M, Deletroz C, Van Landuyt P, Dequanter S, et al. e-Health interventions for healthy aging: a systematic review. Syst Rev 2020 Jun 03;9(1):128 [FREE Full text] [doi: 10.1186/s13643-020-01385-8] [Medline: 32493515]
24. Kwan RYC, Salihu D, Lee PH, Tse M, Cheung DSK, Roopsawang I, et al. The effect of e-health interventions promoting physical activity in older people: a systematic review and meta-analysis. Eur Rev Aging Phys Act 2020 Apr 21;17(1):7 [FREE Full text] [doi: 10.1186/s11556-020-00239-5] [Medline: 32336996]
25. McGarrigle L, Todd C. Promotion of physical activity in older people using mHealth and eHealth technologies: Rapid review of reviews. J Med Internet Res 2020 Dec 29;22(12):e22201 [FREE Full text] [doi: 10.2196/22201] [Medline: 33372894]
26. Stara V, Santini S, Kropf J, D'Amen B. Digital health coaching programs among older employees in transition to retirement: Systematic literature review. J Med Internet Res 2020 Sep 24;22(9):e17809. [doi: 10.2196/17809]
27. Janhunen M, Karner V, Katajapuu N, Niiranen O, Immonen J, Karvanen J, et al. Effectiveness of exergame intervention on walking in older adults: A systematic review and meta-analysis of randomized controlled trials. Phys Ther 2021 Sep 01;101(9):A [FREE Full text] [doi: 10.1093/ptj/pzab152] [Medline: 34160022]
28. Núñez de Arenas-Arroyo S, Cavero-Redondo I, Alvarez-Bueno C, Sequí-Domínguez I, Reina-Gutiérrez S, Martínez-Vizcaíno V. Effect of eHealth to increase physical activity in healthy adults over 55 years: A systematic review and meta-analysis. Scand J Med Sci Sports 2021 Apr 16;31(4):776-789. [doi: 10.1111/sms.13903] [Medline: 33280182]
29. Arksey H, O'Malley L. Scoping studies: towards a methodological framework. International Journal of Social Research Methodology 2005 Feb;8(1):19-32. [doi: 10.1080/1364557032000119616]
30. Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, et al. PRISMA extension for scoping reviews (PRISMA-ScR): Checklist and explanation. Ann Intern Med 2018 Sep 04;169(7):467. [doi: 10.7326/M18-0850]
31. De Santis KK, Mergenthal L, Christianson L, Zeeb H. Open Science Framework. Digital technologies for health promotion and disease prevention for older people: Scoping review protocol summary. URL: https://osf.io/7wfub/ [accessed 2022-05-09]
32. WHO Guideline: Recommendations on digital interventions for health system strengthening. World Health Organization. 2019. URL: https://www.who.int/publications/i/item/9789241550505 [accessed 2022-07-12]

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33. De Santis KK, Lorenz RC, Lakeberg M, Matthias K. The application of AMSTAR2 in 32 overviews of systematic reviews of interventions for mental and behavioural disorders: A cross-sectional study. Res Synth Methods 2022 Jul 28;13(4):424-433. [doi: 10.1002/jrsm.1532] [Medline: 34664766]
34. McGowan J, Sampson M, Salzwedel DM, Cogo E, Foerster V, Lefebvre C. PRESS peer review of electronic search strategies: 2015 guideline statement. J Clin Epidemiol 2016 Jul;75:40-46 [FREE Full text] [doi: 10.1016/j.jclinepi.2016.01.021] [Medline: 27005575]
35. Rethlefsen ML, Kirtley S, Waffenschmidt S, Ayala AP, Moher D, Page MJ, PRISMA-S Group. PRISMA-S: an extension to the PRISMA Statement for Reporting Literature Searches in Systematic Reviews. Syst Rev 2021 Jan 26;10(1):39 [FREE Full text] [doi: 10.1186/s13643-020-01542-z] [Medline: 33499930]
36. De Santis KK, Jahnel T, Mergenthal L, Zeeb H, Matthias K. Evaluation of digital interventions for physical activity promotion: Protocol for a scoping review. JMIR Res Protoc 2022 Mar 3;11(3):e35332. [doi: 10.2196/35332]
37. Deduplicator. Systematic Review Accelerator. URL: https://sr-accelerator.com/#/deduplicator [accessed 2022-05-05]
38. Taj F, Klein MCA, van Halteren A. Digital health behavior change technology: Bibliometric and scoping review of two decades of research. JMIR Mhealth Uhealth 2019 Dec 13;7(12):e13311 [FREE Full text] [doi: 10.2196/13311] [Medline: 31833836]
39. Pollock M, Fernandes R, Becker L, Pieper D, Hartling L. Chapter V: Overviews of Reviews. The Cochrane Collaboration. URL: https://training.cochrane.org/handbook/current/chapter-v [accessed 2022-07-12]
40. Shea BJ, Reeves BC, Wells G, Thuku M, Hamel C, Moran J, et al. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. BMJ 2017 Sep 21;358:j4008 [FREE Full text] [doi: 10.1136/bmj.j4008] [Medline: 28935701]
41. Matthias K, Rissling O, Pieper D, Morche J, Nocon M, Jacobs A, et al. The methodological quality of systematic reviews on the treatment of adult major depression needs improvement according to AMSTAR 2: A cross-sectional study. Heliyon 2020 Sep;6(9):e04776 [FREE Full text] [doi: 10.1016/j.heliyon.2020.e04776] [Medline: 32939412]
42. Bußkamp A, Vonstein C, Tillmann J, Roßmann C, De Bock F. [Promotion of physical activity among the elderly as an example of knowledge translation: How do scientific findings enter community practice?]. Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz 2021 May 09;64(5):560-567 [FREE Full text] [doi: 10.1007/s00103-021-03311-2] [Medline: 33837439]

Abbreviations

AMSTAR2: A Measurement Tool to Assess Systematic Reviews, version 2
PCC: Population, Concept, and Context
PRESS: Peer Review of Electronic Search Strategies
PRISMA-ScR: Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews

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Protocol

Playground Inclusivity for Children With a Disability: Protocol for a Scoping Review

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Abstract

Background: Although playgrounds are designed to promote outdoor play, children with disabilities may be unable to engage in these spaces due to intrinsic and extrinsic factors. Previous research has examined inclusive/accessible playground design when developing new playgrounds; however, it is unclear if there is a best-practice tool for evaluating the inclusivity of existing playground structures.

Objective: A scoping review of both peer-reviewed and grey literature will be employed to explore evaluation tools for playground inclusivity, to enable the participation of children with disabilities.

Methods: The conduct of this study will adhere to the PRISMA-ScR (Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews) guidelines. A search for peer-reviewed research studies will be conducted in the following electronic databases: MEDLINE, Scopus, CINAHL, and Embase. Grey literature will be examined via a three-step process: (1) a search in the Canadian Health Research Collection Database; (2) a targeted Google search; and (3) reference list searching. Titles, abstracts, keywords, and full texts of identified studies will be independently screened for inclusion by two reviewers. A synthesis of included articles will describe the publication and auditing tool details. A summary of the findings will highlight the types of playgrounds measured, types of disability considered, measures of inclusion used, and psychometric properties.

Results: Database searches for peer-reviewed articles were completed in December 2021. A total of 1471 unique records were returned after the removal of 559 duplicate records. Full texts of 167 studies meeting eligibility criteria will be reviewed. The peer-reviewed research search will guide the grey literature search. The scoping review is planned for completion in 2022.

Conclusions: A rigorous search of the literature will determine the availability of tools for evaluating existing playground structures for the inclusivity of children with disabilities. The results will inform recommendations on tool applications, and applicable knowledge translation activities.

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(JMIR Res Protoc 2022;11(7):e37312) doi:10.2196/37312

KEYWORDS

playground; inclusion; children; disability; scoping review; protocol; youth; inclusivity; participation; young; accessibility; design; structure; application

Introduction

Background

Play is an internationally recognized, fundamental experience of childhood. The United Nations (1989) [1] emphasized play as a priority in the *Convention on the Rights of a Child*, indicating that every child has the right to participate in age-appropriate play and recreation. Providing children with environments that support unstructured play opportunities is crucial to their physical, social, cognitive, and emotional development, and their long-term health and well-being [2,3]. Unstructured play is any self-chosen, immersive activity defined by the child, with no extrinsic goals, and undertaken for enjoyment [4]. Outdoor unstructured play offers opportunities for enhanced surroundings that facilitate sensory experiences, increase physical and social competencies, and promote fine and gross motor skill development [5]. When children play outside, they engage in rich, diverse, and active play [6]. Research in populations of typically developing children has shown outdoor unstructured play improves physical activity levels and cardiorespiratory fitness, and decreases sedentary behaviour, positively impacting children's health [7-9].

Playgrounds are defined by the Canadian Standards Agency (2020) [10] as any fixed equipment used for play, typically found in parks, schoolyards, and childcare and recreation facilities. These environmental fixtures are designed to promote children's outdoor, active, and imaginative play without financial barriers. Furthermore, playgrounds are an environmental context where children can develop social, physical, and motor skills through play and interaction with others [11,12]. Although access to playground infrastructure has been positively correlated with outdoor play for typically developing children [2], research suggests that children with disabilities do not share equal opportunities for accessing and engaging with playgrounds as their peers without disabilities [13], and face exclusion from community play spaces [14].

"Disability" is defined by the *United Nations Convention on the Rights of Persons with Disabilities* (2006) [15] as "physical, mental, intellectual or sensory impairments which, in interaction with various barriers, may hinder full and effective participation in society on an equal basis with others." Recent research indicates an estimated 240 million children (under the age of 18 years) worldwide have one or more disabilities [16]. Children with disabilities may have unequal access to play opportunities due to such barriers (eg, restricted mobility, difficulty understanding play contexts or initiating/sustaining play with others [17]) that impede their full participation. In playgrounds, children's play behaviours are determined by interactions with others and physical competence within the setting [18]. This means children who experience disabilities can experience exclusion from participation in play, due to factors such as inadequate access, inadequate play options and play value, and limited opportunities for social interaction [11].

Although outdoor play provides opportunities supportive of the health, development and well-being of all children, exclusionary environments limit the opportunities of children with disabilities to engage in these spaces [19]. Article 23 of the *Convention on the Rights of a Child* (1989) [1] indicates that children with disabilities "should enjoy a full and decent life, in conditions which ensure dignity, promote self-reliance and facilitate the child's active participation in the community." Furthermore, "to achieve full inclusion, an accessible, barrier-free physical and social environment is necessary" [20]. A greater understanding of how to support and facilitate children's interaction within playground environments is crucial to providing an inclusive experience and extending the benefits of participating in outdoor play.

Making an environment more "accessible" focuses on changing the design of the physical space to remove barriers that prevent full participation by people with disabilities. This is typically guided by local policy standards [21]. Making an environment accessible, however, does not make it *inclusive* [22]. Although "inclusion" encompasses accessibility, it is defined as the process of enabling the full participation of individuals with disabilities in activities, emphasizing the range of human diversity, to provide a space where all people belong [23]. Spencer-Cavaliere and Watkinson (2010) [24] indicate that there are three important aspects of inclusion for children with disabilities in the experience of play: (1) gaining entry to play, (2) feeling like a legitimate participant, and (3) having friends. Inclusion on the playground means creating environments where all children have equal access to opportunities for engaging in the physical and social aspects of play [25]. Therefore, targeting inclusion as an area for intervention, rather than accessibility alone, offers a more comprehensive approach that considers the subjective experience of children with disabilities and their families during playground visits [21,24].

Although installing new playgrounds that are inclusive for all users would be ideal, it is not realistic. Therefore, it is important to have access to tools to evaluate existing playground structures and set priorities for making changes/updates to improve inclusion. Playground audits are an example of a tool that can be used to measure and evaluate the detailed attributes of the play space environment [26,27]. Employing auditing tools to evaluate playground inclusion allows for investigation into the equity of the environment for children of all abilities, and the prioritization of necessary steps for action. Audits have been deemed important measures for evaluating the inclusion of children with disabilities in playground settings [28] and can be used in both research and practice [27]. However, it is unclear if a best-practice tool exists for evaluating the inclusivity of existing playgrounds. This warrants investigation, to bridge research with practice to offer tools and strategies that are usable

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for stakeholders at all levels to investigate the inclusivity of existing playgrounds.

Rationale and Objectives

This research builds upon 4 previous systematic/scoping reviews that have examined inclusive/accessible playground design, focusing on the development of new playgrounds [21,22,25,29]. What these 4 studies do not offer is a tool to evaluate the inclusivity of *existing* playground structures. This is crucial knowledge for informing approaches to retrofitting playgrounds, intended to create supportive environments for children with disabilities to engage in unstructured outdoor play.

The purpose of this study is to explore *which tools exist to evaluate playground inclusivity to enable the participation of children with disabilities.* Playground inclusion will be operationalized as creating an environment where children have equal access to social and physical aspects of play, regardless of ability [25,30]. Unlike previous research, this study will narrow the breadth of evidence to examine literature that provides auditing tools to evaluate the design of existing playground structures. The identification, collation, and synthesis of tools to audit playground inclusivity have important implications for improving the participation and inclusion of *all* children in play opportunities. This review aims to inform evidence-based decision-making and the application of tools for practitioners (eg, government officials, child development and recreation practitioners, playground developers, and community disability champions) who are interested in evaluating local community playgrounds for inclusion.

Methods

Study Design

To explore available playground auditing tools, a scoping review will be conducted. Scoping reviews are a useful knowledge mobilization strategy to synthesize the heterogenous evidence available (ie, peer-reviewed research and grey literature), to determine gaps in knowledge, and to inform policy and practice [31,32]. The conduct of this study will adhere to the PRISMA-ScR (Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews) guidelines [33] and the study has been prospectively registered with the Open Science Framework (registration number: rycmj). Significant amendments to this scoping review protocol will be recorded in Open Science Framework.

Search Strategy

The search strategy was developed in consultation with a Health Sciences Teaching and Learning Librarian at Western University and with all authors (consisting of experts in the fields of children's health, physical activity, occupational therapy, disability/inclusion, geography, and planning). The primary author conducted an initial scan of the inclusive playground literature. It was determined that a variety of approaches have been used to audit playgrounds in both research and practice. Therefore, both peer-reviewed publications in scientific journals and grey literature (ie, government reports, research-informed articles, organizational publications) will be included in this review.

The primary search strategy will use electronic database searching, focusing on empirical research studies that employed quantitative and qualitative methods. The search strategy will include three key components: (1) the playground environment; (2) children with disabilities; and (3) audit tools for evaluating the inclusivity of the playground. The first two themes, environment and disability, will be searched with relevant keywords and Medical Subject Headings terms, combined using Boolean operators and adjusted for each database (see Multimedia Appendix 1 for the MEDLINE search strategy). The following databases will be searched: MEDLINE, Scopus, CINAHL, and Embase. Due to the plethora of terminology available to refer to audit tools (eg, toolkit, evaluation, audit, checklist, assessment), the third theme will be evaluated by hand during the screening process as a component of the inclusion/exclusion criteria. An audit tool will be considered broadly as any tool that can be employed to conduct an evaluation of the playground for inclusion of children with disabilities, using questions that can be completed by a playground auditor.

Inclusion and Exclusion Criteria

Reference lists of all included studies will be hand-searched for additional articles and grey literature meeting inclusion criteria. Four previous systematic/scoping reviews examined inclusive/accessible playground design. Although these articles will not be included in the data analysis, the authors will screen the reference lists and articles/reports that have cited these reviews since publication, to identify additional eligible literature.

Peer-reviewed research identified through the search strategy, citation tracking, and hand searching will be screened according to the outlined inclusion criteria (Textbox 1) and exclusion criteria (Textbox 2).

Textbox 1. Inclusion criteria of peer-reviewed literature.

1. The literature must be written in English or French.
2. The primary focus of the resource must evaluate the accessibility and inclusivity of existing playground structures.
3. The resource must include a tool to conduct an evaluation of the playground for inclusion of children with disabilities, using questions that can be completed by a playground auditor.
4. The resource focuses on any type of disability. Disability will be defined according to the *United Nations Convention on the Rights of Persons with Disabilities* [15]
5. The resource was published after 2000.

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Textbox 2. Exclusion criteria of peer-reviewed literature.

1. The full-text article cannot be obtained.
2. The "playground" is defined in an alternate context (eg, an environmental playground of bacteria [21]).
3. The focus of the paper is strictly on the epidemiology of injury or design playground safety [21].

Grey literature will be captured in this review to reflect the implementation of auditing tools in a practical context, across a variety of sectors/disciplines, internationally. To ensure a rigorous search method is employed, a three-step process for recording the relevant literature will be employed [34]. Step 1 will involve a search of a relevant grey-literature database, the Canadian Health Research Collection Database. Then, a targeted web-based Google search will be conducted. Finally, the reference lists of all peer-reviewed and grey literature included in the full-text screening stages will be examined for additional grey resources.

Grey literature must meet all inclusion and exclusion criteria specified for the peer-reviewed research (Textboxes 1 and 2). Acknowledging the potential volume of grey literature and tools available/used by individual organizations, an additional inclusion criterion will be placed on grey literature. To ensure that the results of this scoping review reflect best practices for end users, the grey literature resource must transparently report how a tool was developed. Two additional exclusion criteria will also be included: (1) grey literature that conducts secondary applications of tools with unjustified modifications to an original tool reported by another organization will not be included; and (2) examples of organizations applying existing tools in practice will not be included. In these situations, the primary source of the tools will be assessed for inclusion in this review.

It was determined that searches will be limited to work published from 2000 to present, to align with the search strategies of the 4 previous systematic/scoping reviews [21,22,25,29]. We expect that most peer-reviewed articles captured in this review will likely have been assessed in the 4 previous reviews examining playground design for inclusion/accessibility. Therefore, the search strategies were examined for consistency. Three of the reviews used search strategies that employed an inclusion timeline prior to 2000 [21,22,25], with a total of 8 articles included across the studies [35-41] (with one duplicated). To determine if the included articles were relevant to this study, they were screened by the primary author for their coherence with the eligibility criteria (Textboxes 1 and 2). No articles met the present inclusion parameters; therefore, the inclusion timeline of 2000 to present in this review is considered comprehensive.

Screening Process

Title and abstract screening of literature will be conducted by two independent researchers using the outlined eligibility criteria in Covidence [42]. Full-text records of the included peer-reviewed articles will be imported into Covidence for full-text screening by the same two reviewers. Any discrepancies will be discussed with a third reviewer until consensus is achieved. Full texts of the grey literature extracted from the 3-step process will be assessed by both screeners for inclusion, using Microsoft Excel. Literature carried forward from the full-text phase will be reviewed by all authors for consensus on inclusion/exclusion in this review. The results and study inclusion process will adhere to the "PRISMA 2020 flow diagram for new systematic reviews which included searches of databases, registers and other sources" [43].

Data Extraction

Searches in all electronic databases will be run within the same week, to ensure data retrieval within the same time frame. Search results will be extracted to Covidence software [42], where they will be organized for the review phases (title/abstract screening, full-text screening, and data extraction). A search log to record the initial strategy and subsequent modifications (including reference list searching), and details on the identified studies, will be maintained by the primary author, in accordance with the PRISMA guidelines [33].

To adequately represent the findings from the peer-reviewed research and grey literature, two data extraction tables will be maintained. For each included article, data will be extracted using a targeted rule set presented in a standardized form. For the peer-reviewed research, the extracted data will include the following: (1) study details (ie, title, authors, year, country, design, purpose, participant details); (2) auditing tool details (ie, disability and environment factors assessed, tool used to conduct evaluation, measure of inclusion, questions used, components assessed, and psychometric properties); and (3) results of the study. This information will aim to contextualize the methodology for researchers considering conducting similar studies. For the grey literature, the extracted data will include the following: (1) resource details (ie, title, authors, year, country, resource type, purpose); (2) auditing tool details (ie, disability and environment factors assessed, measure of inclusion, tool used to conduct evaluation, questions used, rationale/evidence grounding tool, target audience/user group, components assessed, and psychometric properties); and (3) results of the playground audit (if applicable).

Data Synthesis

The results will first summarize the main findings of this review including: (1) the screening process (from initial search to final selection of papers); (2) a descriptive numerical summary of the included studies; and (3) an outline of the audit tools used in research and practice. A synthesis of questions employed by the tools will be grouped thematically. The auditing tools will be summarized into 13 recommendations and one "promising practice" by Brown and colleagues [21], an evidence-based resource intended to provide guidance when designing new playgrounds with consideration to both the physical design and the surrounding built and social environments. Recommendations for future research and practice will be provided. All authors will be involved in this process.

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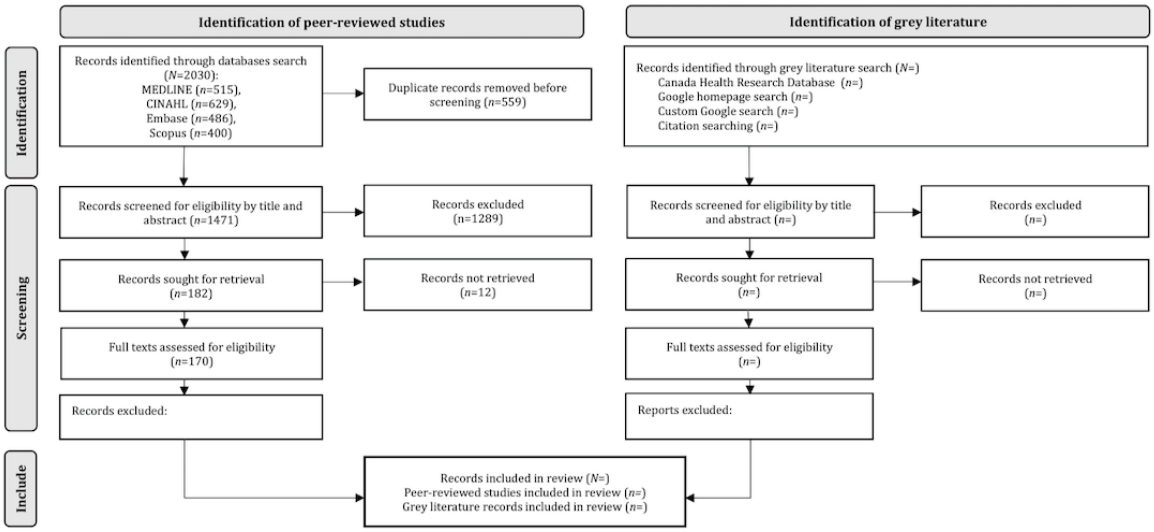
Results

The electronic database searching for peer-reviewed literature was completed in December 2021. The search yielded 2030 results. All titles and abstract results were uploaded into Covidence [42]. There were 559 duplicate records removed in Covidence. Two independent reviewers screened the resulting 1471 records in Covidence, and 1289 were deemed irrelevant based on the eligibility criteria. As a result, the search produced 170 studies meeting the eligibility criteria. Figure 1 displays the PRISMA flow diagram representing findings available to date. Full-text findings in the peer-reviewed research will guide the grey literature review. The scoping review is planned for completion in 2022.

Figure 1. PRISMA flow diagram of findings to date. Inclusion criteria of white literature.



Discussion

Overview

This scoping review of both peer-reviewed studies and grey literature will be conducted to explore the tools that exist in research and practice to audit playgrounds for inclusivity, to enable the participation of children with disabilities. A synthesis of included articles will describe the auditing tools available and provide recommendations for researchers and stakeholders. Based on the preliminary results of this review, we hypothesize that our findings will demonstrate heterogeneity in the types and diversity of tools available. We will determine whether current resources are validated and evidence-informed, or if the generation of new resources should be considered.

Evaluating for Inclusive Play on Existing Playgrounds

Play is considered a fundamental occupation of childhood and has important implications for children's health and well-being [44-47]. Although playground structures are created with the intention to support play opportunities, children with a disability may experience barriers to engaging with these environmental structures [11]. This is an issue worth addressing as nearly 1 in 10 children worldwide have one or more disabilities [16]. Access to inclusive community playgrounds is crucial to provide health-supportive play opportunities for children of all abilities. To ensure all children can engage as equal participants despite disabilities, it is essential that researchers and practitioners engage in opportunities to evaluate community playgrounds [28].

Previous literature has examined methods for planning and developing new playgrounds for inclusion [21,22,25,29]. However, research has demonstrated that a clear, valid, and reliable strategy is needed to support opportunities for upgrading current community playgrounds to facilitate the inclusion of all children [48]. This review will expand on previous work by identifying, collating, and synthesizing tools available to audit existing playgrounds for inclusivity. Providing community stakeholders with the ability to evaluate existing playgrounds for inclusion is a crucial step in creating environments supportive of all children's ability to participate in play, regardless of a disability. By synthesizing the results of this study to align with previous recommendations for building inclusive playgrounds [21], this review will identify tools that evaluate key opportunities for supporting and facilitating inclusion to guide evidence-informed decision-making, with the goal of future implementation of these tools in research and practice.

Strengths and Limitations

The study offers an examination of tools to evaluate existing playground structures for inclusion and retrofitting, using a robust scoping review methodology to examine the extent of heterogeneous evidence available (ie, peer-reviewed and grey literature) to inform policy and practice, which are strengths of this work. However, there are limitations that must be acknowledged. Grey literature can be difficult to examine through typical systematic methods; therefore, we will attempt to minimize this potential limitation by using a research-informed strategy in consultation with a research librarian to limit discrepancies in locating and reporting these articles [34]. Furthermore, while psychometric testing of tools provided in the grey literature may be unclear or unavailable, we will attempt to mitigate this limitation by ensuring resources transparently report how a tool was developed and by drawing on their primary applications only. A final limitation to note is

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that language/culture bias may be present, as the articles will be limited to publications in English and French.

Dissemination Plan

Engaging in intentionally planned and tailored knowledge translation activities is essential to sharing the findings of this review with key stakeholders, to inform evidence-based decision-making in research and practice. This will include community engagement sessions, conference presentations, executive summaries, and interactive recommendations for practice. This study makes an important contribution to the literature by systematically summarizing the available resources, bridging research with practice to offer tools and strategies to evaluate existing playground structures. This will aid in informing resource allocation for improving inclusivity for children with disabilities in their everyday environments.

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Conflicts of Interest

None declared.

Multimedia Appendix 1
MEDLINE search strategy.
[DOCX File , 15 KB - resprot_v11i7e37312_app1.docx]

References

1. United Nations. Vol. 1, Chapter IV. Human Rights. 11. Convention on the Rights of the Child. 1989. URL: https://treaties.un.org/doc/Treaties/1990/09/19900902%2003-14%20AM/Ch_IV_11p.pdf [accessed 2022-07-05]
2. Lee R, Lane S, Brown G, Leung C, Kwok S, Chan S. Systematic review of the impact of unstructured play interventions to improve young children's physical, social, and emotional wellbeing. Nurs Health Sci 2020 Jun;22(2):184-196 [FREE Full text] [doi: 10.1111/nhs.12732] [Medline: 32358875]
3. Milteer R, Ginsburg K, Council On Communications And Media, Committee On Psychosocial Aspects Of Child And Family Health. The importance of play in promoting healthy child development and maintaining strong parent-child bond: focus on children in poverty. Pediatrics 2012 Jan;129(1):e204-e213 [FREE Full text] [doi: 10.1542/peds.2011-2953] [Medline: 22201149]
4. Else P. Declaration on the Importance of Play. International Play Association. 2014. URL: http://ipaworld.org/wp-content/uploads/2015/05/IPA_Declaration-FINAL.pdf [accessed 2022-06-01]
5. Dinkel D, Snyder K, Patterson T, Warehime S, Kuhn M, Wisneski D. An exploration of infant and toddler unstructured outdoor play. European Early Childhood Education Research Journal 2019 Feb 14;27(2):257-271 [FREE Full text] [doi: 10.1080/1350293x.2019.1579550]
6. Loebach J, Cox A. Tool for Observing Play Outdoors (TOPO): A new typology for capturing children's play behaviors in outdoor environments. Int J Environ Res Public Health 2020 Aug 04;17(15):5611 [FREE Full text] [doi: 10.3390/ijerph17155611] [Medline: 32759703]
7. Gray C, Gibbons R, Larouche R, Sandseter E, Bienenstock A, Brussoni M, et al. What is the relationship between outdoor time and physical activity, sedentary behaviour, and physical fitness in children? A systematic review. Int J Environ Res Public Health 2015 Jun 08;12(6):6455-6474 [FREE Full text] [doi: 10.3390/ijerph120606455] [Medline: 26062039]
8. Brussoni M, Gibbons R, Gray C, Ishikawa T, Sandseter E, Bienenstock A, et al. What is the relationship between risky outdoor play and health in children? A systematic review. Int J Environ Res Public Health 2015 Jun 08;12(6):6423-6454 [FREE Full text] [doi: 10.3390/ijerph120606423] [Medline: 26062038]
9. Stone M, Faulkner G. Outdoor play in children: associations with objectively-measured physical activity, sedentary behavior and weight status. Prev Med 2014 Aug;65:122-127 [FREE Full text] [doi: 10.1016/j.ypmed.2014.05.008] [Medline: 24836417]
10. Canadian Standards Association. Children's Playground Equipment and Surfacing. In: CSA Z614:20 National Standard of Canada. Toronto: CSA Group; Mar 2020.
11. Moore A, Lynch H, Boyle B. Can universal design support outdoor play, social participation, and inclusion in public playgrounds? A scoping review. Disabil Rehabil 2020 Dec 10:1-22. [doi: 10.1080/09638288.2020.1858353] [Medline: 33300821]
12. Reimers A, Schoeppe S, Demetriou Y, Knapp G. Physical activity and outdoor play of children in public playgrounds - Do gender and social environment matter? Int J Environ Res Public Health 2018 Jun 28;15(7):1356 [FREE Full text] [doi: 10.3390/ijerph15071356] [Medline: 29958386]

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13. Prellwitz M, Skär L. Usability of playgrounds for children with different abilities. Occup Ther Int 2007;14(3):144-155 [FREE Full text] [doi: 10.1002/oti.230] [Medline: 17624873]
14. Lynch H, Moore A, Edwards C, Horgan L. Advancing play participation for all: The challenge of addressing play diversity and inclusion in community parks and playgrounds. British Journal of Occupational Therapy 2019 Dec 05;83(2):107-117. [doi: 10.1177/0308022619881936]
15. United Nations. Convention on the Rights of Persons with Disabilities. New York: United Nations General Assembly; Dec 06, 2006.
16. UNICEF Division of Data, Analytics, Planning and Monitoring. Seen, Counted, Included: Using Data to Shed Light on the Well-Being of Children With Disabilities. New York: United Nations Children's Fund; 2021.
17. Woolley H. Now being social: The barrier of designing outdoor play spaces for disabled children. Child Soc 2012 Jul 31;27(6):448-458. [doi: 10.1111/j.1099-0860.2012.00464.x]
18. Barbour AC. The impact of playground design on the play behaviors of children with differing levels of physical competence. Early Childhood Research Quarterly 1999 Jan;14(1):75-98. [doi: 10.1016/s0885-2006(99)80007-6]
19. Van Melik R, Althuizen N. Inclusive play policies: Disabled children and their access to Dutch playgrounds. Tijd voor Econ & Soc Geog 2020 Jul 13;113(2):117-130. [doi: 10.1111/tesg.12457]
20. United Nations. Guidance for Human Rights Monitors Professional Training Series. Monitoring the Convention on the Rights of Persons with Disabilities. New York: Office of the United Nations High Commissioner for Human Rights; 2010. URL: https://www.ohchr.org/Documents/Publications/Disabilities_training_17EN.pdf [accessed 2022-07-05]
21. Brown DMY, Ross T, Leo J, Buliung RN, Shirazipour CH, Latimer-Cheung AE, et al. A scoping review of evidence-informed recommendations for designing inclusive playgrounds. Front Rehabilit Sci 2021 May 24;2:664595. [doi: 10.3389/fresc.2021.664595]
22. Fernelius CL, Christensen KM. Systematic review of evidence-based practices for inclusive playground design. Children, Youth and Environments 2017;27(3):78. [doi: 10.7721/chilyoutenvi.27.3.0078]
23. Okoro CA, Hollis ND, Cyrus AC, Griffin-Blake S. Prevalence of disabilities and health care access by disability status and type among adults - United States, 2016. MMWR Morb Mortal Wkly Rep 2018 Aug 17;67(32):882-887 [FREE Full text] [doi: 10.15585/mmwr.mm6732a3] [Medline: 30114005]
24. Spencer-Cavaliere N, Watkinson E. Inclusion understood from the perspectives of children with disability. Adapt Phys Activ Q 2010 Oct;27(4):275-293. [doi: 10.1123/apaq.27.4.275] [Medline: 20956835]
25. Mejeur M, Schmitt G, Wolcott H. A systematic review of the best practices for playground inclusion. Pediatrics 2013;1:1-48 [FREE Full text]
26. Brownson RC, Hoehner CM, Day K, Forsyth A, Sallis JF. Measuring the built environment for physical activity: state of the science. Am J Prev Med 2009 Apr;36(4 Suppl):S99-123.e12 [FREE Full text] [doi: 10.1016/j.amepre.2009.01.005] [Medline: 19285216]
27. Kaczynski AT, Stanis SAW, Besenyi GM. Development and testing of a community stakeholder park audit tool. Am J Prev Med 2012 Mar;42(3):242-249. [doi: 10.1016/j.amepre.2011.10.018] [Medline: 22341161]
28. Woolley With H, Armitage M, Bishop J, Curtis M, Ginsborg J. Going outside together: good practice with respect to the inclusion of disabled children in primary school playgrounds. Children's Geographies 2006 Dec;4(3):303-318 [FREE Full text] [doi: 10.1080/14733280601005666]
29. Moore A, Lynch H. Accessibility and usability of playground environments for children under 12: A scoping review. Scand J Occup Ther 2015;22(5):331-344. [doi: 10.3109/11038128.2015.1049549] [Medline: 26065905]
30. Moore A, Boyle B, Lynch H. Designing for inclusion in public playgrounds: a scoping review of definitions, and utilization of universal design. Disabil Rehabil Assist Technol 2022 Mar 09:1-13. [doi: 10.1080/17483107.2021.2022788] [Medline: 35138989]
31. Munn Z, Peters MDJ, Stern C, Tufanaru C, McArthur A, Aromataris E. Systematic review or scoping review? Guidance for authors when choosing between a systematic or scoping review approach. BMC Med Res Methodol 2018 Nov 19;18(1):143 [FREE Full text] [doi: 10.1186/s12874-018-0611-x] [Medline: 30453902]
32. Peters MDJ, Godfrey CM, Khalil H, McInerney P, Parker D, Soares CB. Guidance for conducting systematic scoping reviews. Int J Evid Based Healthc 2015 Sep;13(3):141-146. [doi: 10.1097/XEB.0000000000000050] [Medline: 26134548]
33. Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, et al. PRISMA extension for scoping reviews (PRISMA-ScR): checklist and explanation. Ann Intern Med 2018 Oct 02;169(7):467-473 [FREE Full text] [doi: 10.7326/M18-0850] [Medline: 30178033]
34. Godin K, Stapleton J, Kirkpatrick SI, Hanning RM, Leatherdale ST. Applying systematic review search methods to the grey literature: a case study examining guidelines for school-based breakfast programs in Canada. Syst Rev 2015 Oct 22;4:138 [FREE Full text] [doi: 10.1186/s13643-015-0125-0] [Medline: 26494010]
35. Chesney DA, Axelson PW. Preliminary test method for the determination of surface firmness. IEEE Trans Rehabil Eng 1996 Sep;4(3):182-187. [doi: 10.1109/86.536773] [Medline: 8800221]
36. Prellwitz M, Tamm M. Attitudes of key persons to accessibility problems in playgrounds for children with restricted mobility: a study in a medium-sized municipality in Northern Sweden. Scandinavian Journal of Occupational Therapy 2009 Jul 12;6(4):166-173. [doi: 10.1080/110381299443645]

XSL•FO
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37. Nabors L, Badawi M. Playground interactions for preschool-age children with special needs. Physical & Occupational Therapy In Pediatrics 2009 Jul 29;17(3):21-31. [doi: 10.1080/j006v17n03_02]
38. Nabors L, Willoughby J, Badawi M. Relations between activities and cooperative playground interactions for preschool-age children with special needs. Journal of Developmental and Physical Disabilities 1999;11(4):4. [doi: 10.1023/A:1021818908388]
39. Schneekloth LH. Play environments for visually impaired children. Journal of Visual Impairment & Blindness 1989;83(4):196-201 [FREE Full text] [doi: 10.1177/0145482x8908300406]
40. Dien L. The use and management of toys and 'loose parts' on a playground for integrating children with and without disabilities: values, problems and possibilities. New York: City University of New York; 1991.
41. Cheung M. The impact of the play environment on the social integration of mentally retarded and nondisabled children. New York: City University of New York; 1989.
42. Veritas Health Innovation. Covidence systematic review software. 2017. URL: http://www.covidence.org [accessed 2021-12-01]
43. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. Int J Surg 2021 Apr;88:105906. [doi: 10.1016/j.ijsu.2021.105906] [Medline: 33789826]
44. Tremblay M, Gray C, Babcock S, Barnes J, Bradstreet C, Carr D, et al. Position statement on active outdoor play. Int J Environ Res Public Health 2015 Jun 08;12(6):6475-6505 [FREE Full text] [doi: 10.3390/ijerph120606475] [Medline: 26062040]
45. Poitras VJ, Gray CE, Borghese MM, Carson V, Chaput J, Janssen I, et al. Systematic review of the relationships between objectively measured physical activity and health indicators in school-aged children and youth. Appl Physiol Nutr Metab 2016 Jun;41(6 Suppl 3):S197-S239 [FREE Full text] [doi: 10.1139/apnm-2015-0663] [Medline: 27306431]
46. Carson V, Lee E, Hewitt L, Jennings C, Hunter S, Kuzik N, et al. Systematic review of the relationships between physical activity and health indicators in the early years (0-4 years). BMC Public Health 2017 Nov 20;17(Suppl 5):854 [FREE Full text] [doi: 10.1186/s12889-017-4860-0] [Medline: 29219090]
47. Brussoni M, Ishikawa T, Brunelle S, Herrington S. Landscapes for play: Effects of an intervention to promote nature-based risky play in early childhood centres. Journal of Environmental Psychology 2017 Dec;54:139-150. [doi: 10.1016/j.jenvp.2017.11.001]
48. Perry MA, Devan H, Fitzgerald H, Han K, Liu L, Rouse J. Accessibility and usability of parks and playgrounds. Disabil Health J 2018 Apr;11(2):221-229. [doi: 10.1016/j.dhjo.2017.08.011] [Medline: 28918095]

Abbreviations

PRISMA-ScR: Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews

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Protocol

Interventions, Participative Role, Barriers, and Facilitators for Involvement in eHealth Communication for People Undergoing Hemodialysis: Protocol for a Scoping Review

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Abstract

Background: eHealth interventions have been shown to offer people living with chronic kidney disease the opportunity of embracing dialysis therapies with greater confidence, the potential to obtain better clinical outcomes and increased quality of life, and diverse and flexible designs and delivery options. eHealth interventions or solutions can offer one-way information without the possibility for dialogue, as with most mobile apps. eHealth interventions intending to enable two-way communication between patients undergoing hemodialysis and health professionals are the focus of this review. eHealth communication interventions that enable two-way communication between patients undergoing hemodialysis and health professionals is an emerging field, but issues relating to participation in eHealth communication for patients undergoing hemodialysis are scarcely described. The current conceptualization of this issue is too scattered to inform the development of future interventions. In this scoping review, we want to assemble and examine this scattered knowledge on participation in two-way eHealth communication for patients undergoing hemodialysis.

Objective: We want to understand the participative role of people living with chronic kidney disease undergoing hemodialysis in available communicative eHealth interventions and to understand which barriers and facilitators exist for patient involvement in eHealth communication with health professionals.

Methods: A scoping review methodology is guiding this study. Peer-reviewed primary studies, including quantitative, qualitative, and mixed methods study designs will be included. A systematic search for published studies, dissertations, and theses at the doctoral level in the English language will be conducted in five databases (MEDLINE, Embase, CINAHL, Scopus, and ProQuest Dissertations and Theses). The included literature will focus on adult (18 years or older) patients undergoing hemodialysis who are involved in eHealth communication with health professionals. Data on the type of eHealth communication interventions, the participative role, and barriers and facilitators for the involvement in eHealth communication for people undergoing hemodialysis will be extracted independently by two reviewers. The extracted data will be collected in a draft charting table prepared for the study. Any discrepancies between the reviewers will be solved through discussion or with a third reviewer.

Results: Results are anticipated by the spring of 2023 and will be presented in tabular format along with a narrative summary. The anticipated results will be presented in alignment with the objectives of the study, presenting findings on the participative role of patients undergoing hemodialysis in eHealth communication interventions.

Conclusions: We anticipate that this study will inform on eHealth communication interventions and the level of patient participation in eHealth communication for patients undergoing hemodialysis. The systematized overview will possibly identify

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research gaps and motivate further development of eHealth communication to ensure patient participation. The findings will be of interest to key stakeholders in clinical care, research, development, policy, and patient advocacy.

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KEYWORDS

chronic disease; decision-making; shared; electronic health records; nephrology; patient advocacy; patient portals; referral and consultation; renal dialysis; renal insufficiency; chronic; patient participation

Introduction

Background

Globally, people living with chronic diseases form a large and expanding group. The number of individuals worldwide with all-stage chronic kidney disease (CKD) reached almost 700 million in 2017 [1]. In 2020, kidney disease has risen from the world's 13th leading cause of death to the 10th [2]. CKD is divided into five stages related to the glomerular filtration rate (GFR). A person with the most advanced stage of kidney disease, CKD5, has a GFR of 15 ml per minute or less, and kidney replacement therapy is needed. At this severe irreversible stage of kidney disease, the kidneys have lost nearly all of their ability to function effectively. The situation is associated with high mortality and comorbidity, including cardiovascular complications, diabetes, anxiety, depression, dietary and fluid restrictions, a comprehensive medication regime, social limitations to prevent infections, fatigue, suicidal ideation, and sexual dysfunction. The patients have an overall ill feeling related to the level of toxicity [3]. The numerous symptoms of CKD5 and the resulting regime of living required to limit the severity of the situation affect the quality of life (QOL) [4].

An estimated three million people with CKD5 receive kidney replacement therapy, either transplantation or various forms of dialysis [1]. There are two forms of long-term dialysis, both advanced and time- and cost-consuming. Peritoneal dialysis (PD) involves cleansing the blood inside the body using the peritoneal membrane and gaining access to the peritoneum through a catheter in the abdomen [5]. However, in-center hemodialysis is the dominant form of dialysis. Hemodialysis is when blood is pumped out of the body to an artificial kidney machine and returned to the body by tubes connecting the patient to the machine [6]. Hemodialysis involves direct access to the patients' circulatory system, and if complications such as severe bleeding, venous thrombosis, infection, or low blood pressure arise, the patients need knowledge and action competence to reduce complications and secure their safety [3]. For decades, the standard schedule for hemodialysis has been 3 sessions a week, 3-4 hours each time [3]. Chuasuwan et al's [7] review points out that patients undergoing hemodialysis showed lower QOL than those undergoing PD. Studies indicate a potential survival advantage with intensive dialysis (an increase in dialysis frequency or duration), a goal that can be reached when dialysis takes place in the patient's home [8]. Due to the high symptom burden and the complexity of their illness and treatment, patients undergoing hemodialysis are dependent on effective and real-time communication with the renal health care professionals for optimal QOL [9]. An increased amount of home hemodialysis (HHD) is an international aim due to patient-centered values of empowerment and QOL. The global increase in CKD poses significant stress on health care systems worldwide, reducing in-center hemodialysis and increasing HHD aimed at reducing both economic burdens and challenges to human resources [10].

Policies and patients' growing demand for patient participation in health-related decision-making for both in-center hemodialysis and HHD call for new and innovative interventions for eHealth communication [11]. Patient participation is increasingly promoted as a way of making health care more responsive to patient needs and ensuring the legitimacy of decisions affecting patient care [12]. Patient participation has both individual and collective dimensions. This review focuses on the individual dimension that refers to enabling patients to have more influence over their health by increasing their capacity to gain more control over issues they define as important. This review also focuses on the collective dimension that refers to patient participation as collective activities in which patients, relatives, service users, or patient representatives are actively engaged in shaping the development of health care services [13]. Thompson [14] has described patient participation as covering five levels of patient-determined participation or involvement: noninvolvement, given information, dialogue, shared decision-making, and autonomous decision-making. Thompson [14] conceived of professionally determined patient involvement as being along a power continuum from a low level of patient power (exclusion) to a high level of patient power (informed decision-making) in patient consultations. For CKD, patient participation has been offered through technological educational interventions offering patients an opportunity to learn about their condition [15] or self-monitoring aspects of their lifestyle such as nutrition [16]. Patient participation is seen in the technological development and use of standardized shared decision-making interventions (eg, treatment choices) [17]. Such interventions aim to enable patients to be informed, learn about, and engage in their own treatment.

Communication is an essential component of patient engagement and the possibility of autonomy. Responsibility for own patient care, transferred from health personnel to patients, can feel like a scary and overwhelming responsibility instead of strengthening patients' rights and autonomy. Patients undergoing hemodialysis need to adhere to a strict regimen, and the patients in HHD accordingly handle advanced machines at home and have access to their own blood system, with possibilities of errors and life-threatening complications. Following Thompson's [14] power continuum when mapping patients' possibilities for participating in eHealth communication will contribute to

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defining and stating patients' self-perceived participation in eHealth dialogue. Whether the alleged contribution from digital solutions provides patients with a feeling of autonomy and flexibility or extra work, burdens, and frustrations can be discussed further throughout the full review.

The World Health Organization defines eHealth as "the cost-effective and secure use of information and communications technologies in support of health and health-related fields, including health-care services, health surveillance, health literature, and health education, knowledge and research" [18]. Sometimes eHealth is referred to as health information technology. Patient participation "requires professionals to engage in two-way communication" [14]. One example of two-way communication is a study evaluating patient and physician perspectives on the key advantages and disadvantages of telephone consultations in a nephrology clinic [19]. Two-way communication might imply the use of computers, mini-computers, and tablets, as well as networks or cloud storage for managing and storing medical records. Mobile health (mHealth) is a narrower concept and refers to the concept of mobile self-care [20], like smartphones and tablet apps used to help people capture data about themselves without assistance or interpretation from health personnel. In recent years, mHealth apps have become increasingly important tools for personalized health care.

eHealth communication is the overarching term used in this review to include communication technologies enabling health professionals and patients to interact, mediated by electronic means [21]. The term incorporates both electronic and digital communication interventions [22]. Many eHealth interventions are multimodal, and definitions may overlap [11]. Examples of communicative eHealth interventions can be related to electronic health records (EHRs) such as care plans. Other examples are patient portals or telehealth solutions such as videoconferencing.

The technological evolution of eHealth communication interventions is claimed to be a paradigm shift for enhanced individuality and patient-centered care, a movement away from the patriarchal traditional health expert–patient relationship. eHealth is predicted to enhance health services and improve care, treatment, effectiveness, and costs, and the development of technology for communication and information sharing has been extensive over the last decades [23]. The COVID-19 pandemic has been a boost for the development and use of eHealth, but the achievement of personalized health care remains an international challenge until there is real data harmonization and interoperability, optimization of data collection, sharing and analytics, and wide acceptance and adoption of innovative digital tools worldwide [23]. Barriers to patients and health professionals participating in eHealth communication could be issues related to the user interface or safety concerns (eg, suboptimal design, technological failure, or invalid data). Facilitators of the use of such technologies are reported to be, for example, systems, programs, education, motivation, patient acceptance and engagement, increased frequency, and quality of interactions with health professionals [11].

Prior Work

Risling et al [24] intended to explore patient participation in the eHealth context in general but ended up exploring patient portals without focusing on two-way communication. They concluded that measurements for patient participation still need to be operationalized, particularly within eHealth intervention contexts [24].

A preliminary search for existing systematic reviews on the current topic in MEDLINE, the Cochrane Database of Systematic Reviews, and JBI Evidence Synthesis revealed two reviews of the use of mHealth technology in CKD. Schrauben et al [25] have explored CKD patients' attitudes to mHealth technology in general. Yang et al [26] have explored the use of mHealth technology for patients undergoing dialysis and found that mHealth technology is mostly used for the self-monitoring of, for example, nutrition or diet. The review also shows that patients undergoing hemodialysis are in special need of real-time monitoring and possibilities for prompt feedback [26]. None of the research questions addressed patient participation, barriers and facilitators, or communication. Digital interaction in the EHR between patients living with hemodialysis and health professionals is unsystematically documented [26]. Unique issues relating to involvement in eHealth communication for patients undergoing hemodialysis were scarcely described in either study. Yang et al's [26] database search ended in October 2018, before the COVID-19 pandemic. The rationale of updating it by means of a scoping review is pertinent, exploring the barriers and facilitators that need to be considered in future interventions. A scoping review methodology is suitable for bringing together literature in disciplines with emerging evidence [27].

Aims and Review Questions

In this scoping review, we aim to systematize and map emerging research on eHealth communication interventions for patients in hemodialysis and their participative role in the interventions, and to identify barriers and facilitators for participation. Based on a preliminary search for literature, we have found structured literature on, for example, mHealth apps and other one-way eHealth solutions. We have on the contrary found scattered literature on patients' access to and measurement of their use of eHealth communication interventions as those intending to enable two-way communication between patients undergoing hemodialysis and health professionals. Therefore we find it relevant to search systematically and broadly. All three authors have clinical experience in nursing and research, and have contributed with ideas and further development of the review questions. The theme and questions have been approved by two user representatives from the Norwegian interest group The Norwegian Kidney Patients Association (Landsforeningen for Nyresyke og Transplanterte). The findings of this scoping review will inspire a process and further studies to develop eHealth communication between patients and nurses in hemodialysis care.

The review will be guided by the following research questions:

- Which type of eHealth communication interventions for patients undergoing hemodialysis and health professionals

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can be identified in the literature and how are they linked to the EHR?
- Which participative role for patients undergoing hemodialysis in eHealth communication with health professionals can be identified in the literature?
- What are the key participative barriers and facilitators to eHealth communication with health professionals encountered by patients undergoing hemodialysis?

Methods

Overview

In this protocol, we predefine the objectives, research questions, and methods, and detail the proposed plan for a scoping review. The proposed scoping review will be conducted according to the Joanna Briggs Institute methodology for scoping reviews [27] and reported following the PRISMA-ScR (Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews) [28].

This protocol was developed in line with the abovementioned methodology and was reported according to the PRISMA-P (Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols) checklist [29].

Eligibility Criteria

We used the PCC (Population, Concept, and Context) mnemonic [27] to construct the review and define inclusion and exclusion criteria.

Population

This review will consider studies that include adult patients (18 years or older) with CKD5 and undergoing hemodialysis. All types of hemodialysis are covered, including prescheduled in-center dialysis, conventional HHD, short daily HHD, and nocturnal HHD. Studies focusing solely on people younger than 18 years, on people living with CKD stages 1-4, on kidney transplants, and on people undergoing PD will be excluded. Studies including these people will be included if they also include patients undergoing hemodialysis.

Concept

This review will consider studies that explore a three-folded concept.

First, we will use a wide definition for interventions. In this review, intervention is a collective term for concepts including, but not limited to, actions, processes, measures, strategies, and initiatives to develop eHealth communication [22]. We will consider all types of eHealth communication interventions or solutions intended to allow two-way communication between patients and health professionals. In this review, we included both electronic and digital technology for oral or written communications (eg, EHRs), including standardized nursing terminology, electronic patient records or portals, electronic conferencing, and mobile written or oral communication mediated by electronic or digital means. Studies on eHealth interventions with no possibility for communication between patients with CKD and health professionals will be excluded (eg, mobile apps for self-efficacy).

Second, patient participation in this review refers to Thompson's [14] definition, stating that patient participation "requires professionals to engage in two-way communication." We will consider the inclusion of studies on all levels of the continuum of patient participation, involvement, and similar concepts.

Third, barriers concerning patient participation in eHealth communication may include but are not restricted to problems, issues, challenges, or obstacles to participation in eHealth communication. Facilitators of patient participation may include but are not restricted to recommendations, interventions or programs, motivation, or experienced results [11].

Context

This review will consider studies focusing on in-center hemodialysis (hospital and satellite units) and HHD contexts.

Information Sources

With no limits on the publication date, we will perform a systematic search for English language articles in the following electronic databases: MEDLINE, Embase, CINAHL, Scopus, and ProQuest Dissertations and Theses Open. We will consider published peer-reviewed primary studies, including quantitative, qualitative, and mixed methods study designs. We will also consider relevant dissertations and theses. Conference abstracts, unpublished studies, literature reviews, and Master's theses will be excluded.

Search Strategy

First, we performed an initial limited search of MEDLINE (Ovid) and CINAHL (EBSCO) to identify articles and search terms on the topic. Text words contained in the titles and abstracts of relevant articles, and the index terms used to describe the articles have been used to develop a full search strategy for MEDLINE (see Multimedia Appendix 1). The search strategy was structured according to PCC (ie, patients undergoing hemodialysis, eHealth interventions with the possibility for written or oral communication, and patient participation). A librarian assisted in developing the search strategy based on the PRESS (Peer Review Electronic Search Strategies) guidelines [30].

Second, the search strategy, including all identified keywords and index terms, will be adapted for each included database. These databases have been discussed and chosen by the authors and the librarian to ensure that a broad overview of published literature within our field will be retrieved by our search. The librarian will assist the search process [30].

Third, the reference list of articles included in the review will be manually searched for additional studies of relevance.

If both a peer-reviewed article and a dissertation are available concerning the same study, we will prioritize the peer-reviewed publication for data extraction. Authors of papers will be contacted to request missing or additional data if required.

Data Management

Following the search, all identified records will be collated and uploaded into the reference management tool EndNote 20 (Clarivate Analytics). Duplicates will be removed. The screening

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software tool Rayyan (Qatar Computing Research Institute) will be used to facilitate the screening process.

Study Selection

Initially, a pilot test will be trialed by the review team to ensure consensus on which articles are considered to meet the inclusion and exclusion criteria. A total of 25 randomly selected articles will be screened by titles and abstracts individually by two reviewers (AD and CFM) and discussed with the third reviewer. Once consensus has been reached, all titles and abstracts will be screened independently by two reviewers for assessment against the inclusion criteria. Potential studies for inclusion will be read in the full text, and studies not meeting the inclusion criteria will be reported with the reason for exclusion. This scoping review is not aimed at making practice recommendations; it rather seeks to provide an overview of the collected data rather than synthesize the evidence [26]. Therefore, methodological quality appraisal of included studies is not pertinent. Any disagreements that arise between the two reviewers at each stage of the selection process will be resolved based on consensus through discussion or with the third reviewer (MSL). The results of the search and the study inclusion process will be detailed and reported in full in the final scoping review and presented in a PRISMA flow diagram [31].

Data Extraction and Collection

A draft charting table (Multimedia Appendix 2) has been developed at this protocol stage by the reviewers, and the data extraction tool will be piloted. The pair of authors (AD and CFM) will individually conduct the data extraction. The data extracted will include specific details about the population, concept, context, methods, and key findings of included articles. Relevant to the review questions, the type of eHealth intervention will be extracted and systemized, and any linking to the EHR will be mapped. The type of participatory role will be determined according to Thompson's [14] taxonomy, and data will be related to the five levels of patient participation described in the taxonomy.

To provide an overview of the collected data, we will use a basic descriptive qualitative coding to identify barriers and facilitators related to participation in eHealth communication interventions [27]. The method of data analysis will also be used to develop and present a narrative description of the data [32].

The draft charting table will be modified and revised as necessary during the process of extracting data from each included paper. Modifications will be detailed in the full scoping review. Any disagreements that arise between the reviewers will be resolved through discussion or with the third reviewer.

Results

The extracted data will be presented in diagrammatic or tabular form in a manner aligned with the objective of the scoping review. The report will also include a narrative summary to accompany the tabulated or charted results. We will present findings on the participative role of patients undergoing hemodialysis in eHealth communication interventions. The collated results will be presented in a systematic scoping review publication related to the review's objective and questions, which is planned to be submitted in the spring of 2023.

Discussion

Contribution to eHealth Communication Development

The anticipated main findings of this study would be a presentation of the types of eHealth communication interventions and patients' experiences with their use of them. A strength of this study is the systematic, precise, and comprehensive process of working out the search strategy in cooperation with the librarian. The rapid and extensive development of eHealth interventions, which is claiming to solve future communication challenges, needs participation from those involved [11]. The anticipated results are expected to show the barriers and facilitators to patient participation and the levels of patient participation.

Conclusions

We are focusing on patient rights by mapping the participative patient role, which can contribute to a further focus on patient participation. The findings can identify research gaps of importance to future research, the development of communicative eHealth interventions, and clinical practice. The systematized knowledge can be transferable to other patient groups, health personnel, researchers, and decision makers in future cocreating processes. The findings from the scoping review can be included as part of the knowledge base for further development of eHealth communication solutions. The knowledge acquired can contribute to developing eHealth interventions to strengthen the relations between service users and service providers. The results will be shared with key stakeholders in the development, use, and policies of eHealth interventions.

Conflicts of Interest

None declared.

Multimedia Appendix 1
Search strategy MEDLINE.
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Multimedia Appendix 2
Draft charting table.

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[DOCX File , 13 KB - resprot_v11i7e38615_app2.docx]

References

1. GBD Chronic Kidney Disease Collaboration. Global, regional, and national burden of chronic kidney disease, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet 2020 Feb 29;395(10225):709-733 [FREE Full text] [doi: 10.1016/S0140-6736(20)30045-3] [Medline: 32061315]
2. The top 10 causes of death. World Health Organization. 2020. URL: https://www.who.int/news-room/fact-sheets/detail/the-top-10-causes-of-death [accessed 2021-12-19]
3. Himmelfarb J, Ikizler TA. Hemodialysis. N Engl J Med 2010 Nov 04;363(19):1833-1845. [doi: 10.1056/NEJMra0902710] [Medline: 21047227]
4. Gadaen R, Kooman J, Cornelis T, van der Sande FM, Winkens B, Broers N. The effects of chronic dialysis on physical status, quality of life, and arterial stiffness: a longitudinal study in prevalent dialysis patients. Nephron 2021;145(1):44-54 [FREE Full text] [doi: 10.1159/000510624] [Medline: 33108785]
5. Peritoneal dialysis: what you need to know. National Kidney Foundation. 2021 Jan 06. URL: https://www.kidney.org/atoz/content/peritoneal [accessed 2021-01-13]
6. Engels N, de Graav G, van der Nat P, van den Dorpel M, Bos W, Stiggelbout A. Shared decision-making in advanced kidney disease: a scoping review protocol. BMJ Open 2020 Feb 27;10(2):e034142 [FREE Full text] [doi: 10.1136/bmjopen-2019-034142] [Medline: 32111615]
7. Chuasuwan A, Pooripussarakul S, Thakkinstian A, Ingsathit A, Pattanaprateep O. Comparisons of quality of life between patients underwent peritoneal dialysis and hemodialysis: a systematic review and meta-analysis. Health Qual Life Outcomes 2020 Jun 18;18(1):191 [FREE Full text] [doi: 10.1186/s12955-020-01449-2] [Medline: 32552800]
8. Miller A, Perl J, Tennankore K. Survival comparisons of intensive vs. conventional hemodialysis: pitfalls and lessons. Hemodial Int 2018 Jan;22(1):9-22. [doi: 10.1111/hdi.12559] [Medline: 28425578]
9. Roberti J, Cummings A, Myall M, Harvey J, Lippiett K, Hunt K, et al. Work of being an adult patient with chronic kidney disease: a systematic review of qualitative studies. BMJ Open 2018 Sep 04;8(9):e023507 [FREE Full text] [doi: 10.1136/bmjopen-2018-023507] [Medline: 30181188]
10. Li P, Cheung W, Lui S, Blagg C, Cass A, Hooi LS, Roundtable Discussion on Dialysis Economics in the 2nd Congress of the International Society for Hemodialysis, Hong Kong, August 2009. Increasing home-based dialysis therapies to tackle dialysis burden around the world: a position statement on dialysis economics from the 2nd Congress of the International Society for Hemodialysis. Hemodial Int 2011 Jan;15(1):10-14. [doi: 10.1111/j.1542-4758.2010.00512.x] [Medline: 21231996]
11. Wang C, Ku E. eHealth in kidney care. Nat Rev Nephrol 2020 Jul;16(7):368-370 [FREE Full text] [doi: 10.1038/s41581-020-0271-z] [Medline: 32238923]
12. Moreira T. The Transformation of Contemporary Health Care: The Market, the Laboratory, and the Forum. Oxfordshire, UK: Taylor and Francis; 2012.
13. Castro E, Van Regenmortel T, Vanhaecht K, Sermeus W, Van Hecke A. Patient empowerment, patient participation and patient-centeredness in hospital care: a concept analysis based on a literature review. Patient Educ Couns 2016 Dec;99(12):1923-1939. [doi: 10.1016/j.pec.2016.07.026] [Medline: 27450481]
14. Thompson A. The meaning of patient involvement and participation in health care consultations: a taxonomy. Soc Sci Med 2007 Mar;64(6):1297-1310. [doi: 10.1016/j.socscimed.2006.11.002] [Medline: 17174016]
15. Lim J, Lim C, Ibrahim I, Syahrul J, Mohamed Zabil MH, Zakaria NF, et al. Limitations of existing dialysis diet apps in promoting user engagement and patient self-management: quantitative content analysis study. JMIR Mhealth Uhealth 2020 Jun 01;8(6):e13808 [FREE Full text] [doi: 10.2196/13808] [Medline: 32478665]
16. Lewis R, Lunney M, Chong C, Tonelli M. Identifying mobile applications aimed at self-management in people with chronic kidney disease. Can J Kidney Health Dis 2019;6:2054358119834283 [FREE Full text] [doi: 10.1177/2054358119834283] [Medline: 30899533]
17. Finderup J, Jensen J, Lomborg K. Shared decision-making in dialysis choice has potential to improve self-management in people with kidney disease: a qualitative follow-up study. J Adv Nurs 2021 Apr;77(4):1878-1887. [doi: 10.1111/jan.14726] [Medline: 33336465]
18. eHealth. World Health Organization. 2022. URL: https://www.emro.who.int/health-topics/ehealth/ [accessed 2022-01-18]
19. Heyck Lee S, Ramondino S, Gallo K, Moist L. A quantitative and qualitative study on patient and physician perceptions of nephrology telephone consultation during COVID-19. Can J Kidney Health Dis 2022;9:20543581211066720 [FREE Full text] [doi: 10.1177/20543581211066720] [Medline: 35024152]
20. mHealth: use of appropriate digital technologies for public health. World Health Organization. 2018. URL: https://apps.who.int/gb/ebwha/pdf_files/WHA71/A71_20-en.pdf [accessed 2022-03-26]
21. Kluge EHW. Framework considerations. In: The Electronic Health Record: Ethical Considerations. Cambridge, MA: Academic Press; 2020:105-133 URL: https://www.sciencedirect.com/science/article/pii/B9780128220450000058
22. Choudhuri A, Chatterjee J, Garg S. Internet of Things in healthcare: a brief overview. In: Balas VE, Son LH, Jha S, Khari M, Kumar R, editors. Internet of Things in Biomedical Engineering. Cambridge, MA: Academic Press; 2019:131-160 URL: https://www.sciencedirect.com/book/9780128173565/internet-of-things-in-biomedical-engineering#book-info

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23. Horgan D, Hackett J, Westphalen C, Kalra D, Richer E, Romao M, et al. Digitalisation and COVID-19: the perfect storm. Biomed Hub 2020;5(3):1341-1363 [FREE Full text] [doi: 10.1159/000511232] [Medline: 33564668]
24. Risling T, Martinez J, Young J, Thorp-Froslie N. Evaluating patient empowerment in association with ehealth technology: scoping review. J Med Internet Res 2017 Sep 29;19(9):e329 [FREE Full text] [doi: 10.2196/jmir.7809] [Medline: 28963090]
25. Schrauben S, Appel L, Rivera E, Lora CM, Lash JP, Chen J, CRIC Study Investigators. Mobile health (mHealth) technology: assessment of availability, acceptability, and use in CKD. Am J Kidney Dis 2021 Jun;77(6):941-950.e1 [FREE Full text] [doi: 10.1053/j.ajkd.2020.10.013] [Medline: 33309860]
26. Yang Y, Chen H, Qazi H, Morita P. Intervention and evaluation of mobile health technologies in management of patients undergoing chronic dialysis: scoping review. JMIR Mhealth Uhealth 2020 Apr 03;8(4):e15549 [FREE Full text] [doi: 10.2196/15549] [Medline: 32242823]
27. Peters M, Marnie C, Tricco A, Pollock D, Munn Z, Alexander L, et al. Updated methodological guidance for the conduct of scoping reviews. JBI Evid Synth 2020 Oct;18(10):2119-2126. [doi: 10.11124/JBIES-20-00167] [Medline: 33038124]
28. Tricco A, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, et al. PRISMA Extension for Scoping Reviews (PRISMA-ScR): checklist and explanation. Ann Intern Med 2018 Oct 02;169(7):467-473 [FREE Full text] [doi: 10.7326/M18-0850] [Medline: 30178033]
29. Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ 2015 Jan 02;350:g7647 [FREE Full text] [doi: 10.1136/bmj.g7647] [Medline: 25555855]
30. McGowan J, Sampson M, Salzwedel D, Cogo E, Foerster V, Lefebvre C. PRESS Peer Review of Electronic Search Strategies: 2015 Guideline Statement. J Clin Epidemiol 2016 Jul;75:40-46 [FREE Full text] [doi: 10.1016/j.jclinepi.2016.01.021] [Medline: 27005575]
31. Page M, McKenzie J, Bossuyt P, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021 Mar 29;372:n71 [FREE Full text] [doi: 10.1136/bmj.n71] [Medline: 33782057]
32. Vaismoradi M, Jones J, Turunen H, Snelgrove S. Theme development in qualitative content analysis and thematic analysis. J Nurs Education Pract 2016 Jan 15;6(5):100-110. [doi: 10.5430/jnep.v6n5p100]

Abbreviations

CKD: chronic kidney disease
EHR: electronic health record
GFR: glomerular filtration rate
HHD: home hemodialysis
mHealth: mobile health
PCC: Population, Concept, and Context
PD: peritoneal dialysis
PRESS: Peer Review Electronic Search Strategies
PRISMA-P: Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols
PRISMA-ScR: Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews
QOL: quality of life

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Protocol

An mHealth App to Promote Adherence to Immunosuppressant Medication and Track Symptoms in Children After Hematopoietic Stem Cell Transplant: Protocol for a Mixed Methods Usability Study

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Abstract

Background: In the United States, poor adherence accounts for up to 70% of all medication-related hospital admissions, resulting in $100 billion in health care costs annually. In pediatrics, adherence is largely dependent on caregivers. In a high-risk hematopoietic stem cell transplant (HSCT) population, caregivers are isolated with their child due to infection risk and must manage challenging treatment regimens at home, often with limited time and support. Complex behavioral interventions, typically employed to address adherence, are difficult to deliver and manage in the context of these daily tasks. The most successful adherence interventions, and thus improved clinical outcomes, have included mobile health (mHealth) reminder approaches and a direct measure of adherence.

Objective: This is a 3-phase project, with this protocol describing phase 2, to determine the usability and feasibility of an mHealth app (BMT4me) designed to promote adherence to immunosuppressant medication and to track symptoms among children who received HSCT.

Methods: This study uses an iterative convergent mixed methods design to develop and assess the usability and feasibility of an adherence digital health intervention. We will recruit 15 caregivers of pediatric patients receiving HSCT to complete user testing. Qualitative and quantitative data will be integrated to enhance and expand upon study findings.

Results: Enrollment began in September 2021 and is ongoing. A total of 7 caregivers have enrolled. We anticipate completion by fall 2022. We anticipate high usability scores and a better understanding of unique features within the app that are needed for HSCT families post transplant. To date, usability scores among enrolled participants are greater than 70%. Feedback from qualitative interviews is being used to further adapt the app by adding specific weekly logs, call provider options, and voice to text.

Conclusions: This protocol describes a mixed methods usability and feasibility study to develop and implement a smartphone app for caregivers of children receiving HSCT. The app was designed to improve immunosuppressant adherence and to track symptoms in the acute phase post discharge. Study findings will inform further refinement of the app and the feasibility of a pilot randomized controlled trial examining efficacy on clinical outcomes.

Trial Registration: ClinicalTrials.gov NCT04976933; https://clinicaltrials.gov/ct2/show/NCT04976933

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International Registered Report Identifier (IRRID): DERR1-10.2196/39098

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KEYWORDS

medication adherence; digital health; mHealth; pediatrics; app; bone marrow transplant; adherence; usability; feasibility; caregivers; children; hematopoietic stem cell transplant; HSCT

Introduction

Background

In the United States, poor adherence accounts for up to 70% of all medication-related hospital admissions [1], resulting in $100 billion in health care costs annually [2]. An estimated 50% to 80% of pediatric patients are nonadherent to medications [3-6]. Reasons for nonadherence are multifactorial. The most important determinants of nonadherence are consistently documented as complexity and duration of treatment regimens, as well as forgetfulness [7-9]. Thus, children undergoing difficult hematopoietic stem cell transplants (HSCTs) who require medication indefinitely are at high risk for medication nonadherence.

HSCT is the transplantation of hematopoietic stem cells derived from bone marrow (ie, "bone marrow transplant" or peripheral blood stem cells). HSCT became the common treatment for life-threatening malignant (eg, leukemia, lymphoma) and nonmalignant (eg, aplastic anemia, sickle cell disease, immune deficiencies) disorders in the mid-1900s. Recipients of bone marrow transplants must adhere to multifaceted outpatient regimens that require strict personal hygiene, environmental restrictions, and complex medication regimens. These include wearing masks, avoiding large crowds, frequent mouth care, and taking multiple time-sensitive medications throughout the day.

Lack of adherence to any of these regimens can be life-threatening [10]. Adherence to immunosuppressant medications during the acute phase (ie, the first 100 days) post transplant is critical to prevent graft versus host disease and avoid graft failure. Studies in children with HSCT report suboptimal adherence rates (52%-78%) that worsen over time [11-13]. Nonadherence to oral medications has been associated with a greater incidence of infections in children during the outpatient HSCT treatment phase [12]. Providers also report adherence as a major concern for outpatient pediatric HSCT recipients [14]. However, no studies have examined adherence specifically to immunosuppressant medications, which are key to engraftment and ultimately survival.

Multiple factors influence adherence, but, ultimately, the final common pathway to adherence is human behavior [15]. For children, caregivers are ultimately responsible for adherence, including refilling prescriptions, retrieving medications, and administering them correctly. In a high-risk HSCT population, caregivers are susceptible to fatigue and stress from being isolated with their child due to infection risk and independently managing complex treatment regimens at home, often with limited time and support. Unfortunately, behavioral interventions employed to address adherence are often difficult to deliver and manage in the context of these daily tasks. Specifically, these interventions can involve 8 to 12 face-to-face sessions, tracking behaviors, practicing skills, and other homework, which can be overwhelming to caregivers.

Alternatively, behavioral economics (BE) theory suggests that small "nudges" can produce and sustain behavior change [16]. A BE approach is a significant paradigm shift from the complex cognitive behavioral theories that inform most adherence interventions. Instead, BE assumes decision-making can be influenced through low-intensity interventions to lead patients to optimal choices [17]. Adherence to medication and exercise programs using BE-designed interventions in adults have some initial promising data [18-21]. Within pediatrics, for example, BE has been successful in increasing fruit consumption and improving vaccination rates [22-24].

With mobile health (mHealth) access nearly ubiquitous and an estimated 250 billion mHealth app downloads in 2022 [25], technology has great potential to improve adherence [26]. mHealth interventions based on BE principles may be ideal, as they provide sophisticated yet simple "nudges" to individuals [27]. Such reminder apps target forgetfulness, a common reason for poor adherence [28,29]. These mHealth interventions are ideally suited for complex HSCT regimens requiring multiple-dose medications that are time sensitive.

A recent systematic review in solid organ transplant reported the most successful interventions, resulting in increased adherence and improved clinical outcomes (eg, complications, hospital admissions, survival) have used mHealth reminders and a direct measure of adherence [30]. Although direct measures of adherence (eg, serum assays) can avoid bias inherent in self- or parent reports, no studies have used direct measures of adherence or mHealth interventions to promote immunosuppression adherence in the acute phase after an HSCT (ie, discharge to day 100). Furthermore, the feasibility, acceptability, and efficacy of BE-designed mHealth interventions have not been examined in the HSCT population. Thus, this study utilizes a BE approach to mHealth app development, as well as an iterative approach of cyclical evaluation and revision, to maximize the usability and adoption of the digital intervention, BMT4me.

BMT4me

BMT4me (Figure 1) is a digital health intervention designed to aid in medication management, optimize adherence, and track symptoms or side effects in real time. The app reminds users of medication doses, records the time medication is taken, and asks reasons for missed doses through pop-up notifications. Medications can be typed in the app by the user or entered using an image-to-text option, which converts the medication label into text. As symptom severity can affect adherence and inform

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the need for medical intervention, it is illustrated by both corresponding emojis and numbers on a 1-to-10 scale to aid understanding and for convenient entry. Additional features include a notes page for recording any details of care to communicate with the provider and the ability to upload pictures. The app can be downloaded to both iOS and Android devices. Currently, availability is limited to the English language, and no clinical data is shared with the medical team during the research study.

Figure 1. BMT4me app wireframes.

Research Aim and Rationale for Mixed Methods Methodology

The overall aim of this mixed methods study is to design and test a theory-driven mHealth app that can virtually assist caregivers of children post HSCT in improving medication adherence, tracking symptoms, and recording pertinent medical information via the journal feature. This app is different from other medication adherence apps available to patients with cancer in several ways: (1) features (eg, reminders, engaging emojis) in the app are designed to support medication adherence by applying BE principles to provide reminders and tailored notifications for caregivers; (2) it is specific to children after an HSCT; and (3) it provides more than medication reminders, with the design encouraging caregivers to engage with the app via symptom tracking and a journal feature that allows uploading of pictures.

Methods

Overall Study Design

The larger mixed methods mHealth app development study consists of 3 phases: (1) prototype development, (2) feasibility and usability, and (3) usability and clinical efficacy (Figure 2). This protocol corresponds to phase 2, feasibility and usability among 15 caregivers immediately upon discharge from the inpatient unit post HSCT. Inclusion criteria include (1) caregiver of child aged 2 to 18 years undergoing allogeneic transplant, (2) access to a smartphone (Android or iOS), and (3) English speaking. Findings from phase 1 informed phase 2, and thus findings from phase 2 will lead to further refinement prior to phase 3. In phase 3, the smartphone app will be compared to usual care in a pilot randomized controlled trial.

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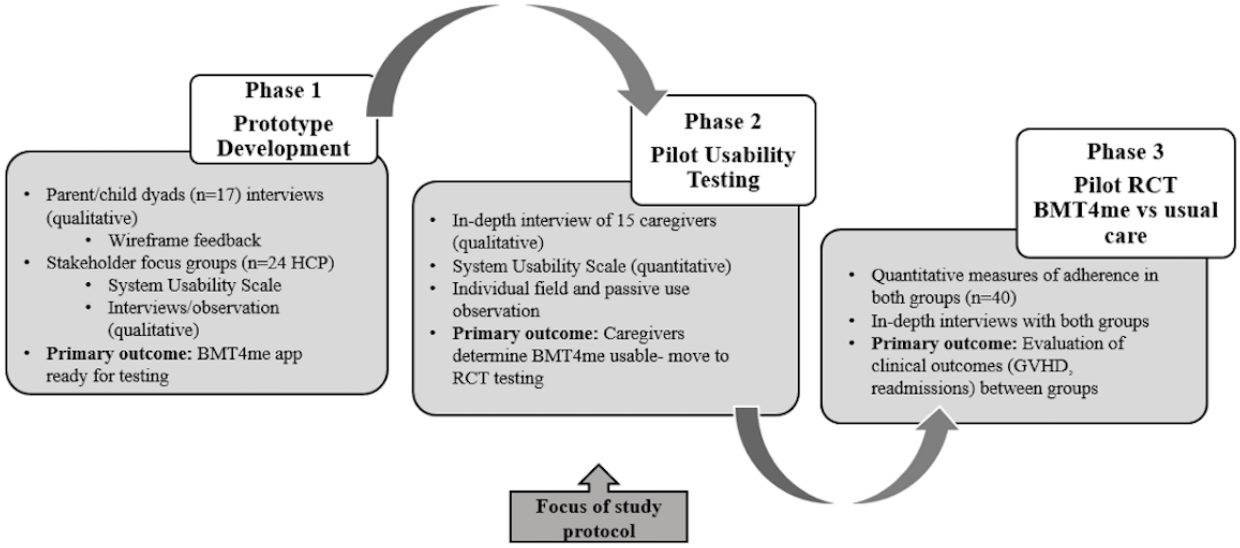
Figure 2. Multiphase mixed methods app design of BMT4me. GVHD: graft vs host disease; HCP: health care practitioner; RCT: randomized controlled trial.



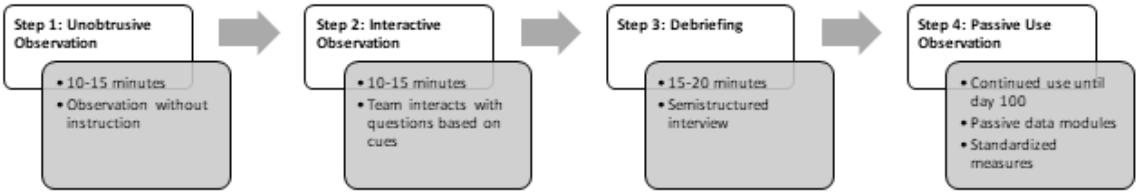
Ethics Approval

All phases of the study have been approved by the Nationwide Children's Hospital Institutional Review Board (approval number STUDY00000910).

Phase 2 Study Design

This is a convergent mixed methods design focused on analysis of quantitative and qualitative data simultaneously collected to obtain feedback on the adherence mHealth app interface, usability, and flow and content of the software. Usability testing is the principal means of determining if the system meets its intended purpose [31]. Purposive sampling will be used to identify caregivers of children across the spectrum of age, sex, and diagnoses of pediatric patients treated with HSCT. Caregivers will be evaluated for engagement and understanding of the app in the following steps (Figure 3):

Figure 3. A stepped approach to usability testing with caregivers.



- *Step 1. Unobtrusive observation to measure the intuitiveness of the interface (10-15 minutes).* Initially, caregivers will be briefly introduced to the program and asked to start interacting with the adherence mHealth app. The design team will not intervene or provide instructions and will observe and record participants' progress.
- *Step 2. Interactive observation (10-15 minutes).* The design team will begin to interrupt individual participants during the interaction by posing questions regarding observed cues that imply success or delay in program use. Caregivers will be encouraged to verbalize their criticisms of the mHealth app. Since discussion will be based on evolving patterns of interaction, pre-prescribed questions are not possible.
- *Step 3. Debriefing (15-20 minutes).* Caregivers will be asked to reflect on their experience with the app and its interface and contents, and to indicate their opinions regarding the strengths and weaknesses of the app. These evaluations will be used to establish criteria for refining the content and interactive app features for future development.
- *Step 4. Passive use observation.* Caregivers will be asked to continue using the mHealth app on their own device until day 100 post HSCT or weaning of the immunosuppressant, whichever occurs first. Passive data modules will be added to the app to capture phone activity (screen on and off times) and will log the participants' use of the app (eg, time, date, duration of use). Changes in app use and phone activity will be descriptively analyzed and plotted. Subjective measures and standard-of-care immunosuppression serum assays will be recorded weekly. Such passive observational effort of app use and adherence, with a mixed method approach, will be one of the first to be reported in an HSCT population.

At the conclusion, caregivers will complete a 15-minute semistructured interview related to participation in the intervention, as well as the System Usability Scale [32]. Open-ended feedback related to suggestions for further app development will undergo qualitative analysis.

Data Collection

Trained research assistants will recruit and onboard eligible participants. The participants will sign written consent forms. The research assistant will then conduct one-on-one audio-recorded sessions, which will include a facilitator and a

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note taker. A project scientist may also participate. The measures listed below will be collected either electronically or in paper-and-pencil form from each caregiver. All participants will receive US $25 at enrollment and US $25 at the conclusion of the study after the exit interview and measures are complete.

The BMT4me App

The BMT4me app will collect daily data on medication-taking (taken or not taken), the time medication was taken, barriers or reasons for missed doses, symptoms, and any notes the caregiver completes. Passive use data on phone activity and app use will be collected.

Demographic Data Form

The caregiver will report on basic background characteristics, including parent and child age, sex, race, ethnicity, education level, and family income.

Medication Adherence Measure

The Medication Adherence Measure (MAM) is a semistructured interview specific to pediatrics, conducted with the parent, to obtain an individual score in each module. The score is represented as percentages of the number of required doses. A total summary score can be calculated across all medications as well separately. This allows for quantification of the degree of adherence on a continuum. MAM has demonstrated adequate convergent validity with MEMS (medication event monitoring system) Caps (r=−0.40, P<.05) [33]. MEMS Caps are electronic monitors that objectively measure adherence. They contain microelectronic circuits that date and time-stamp each instance the container is opened for a dose of medication. Data from the MEMS Caps will be downloaded using cloud- or computer-based software at each study visit [34,35].

System Usability Scale

The System Usability Scale is a 10-item questionnaire routinely used to evaluate the functionality and acceptability of mHealth apps [32,36]. Items are rated on a 5-point scale and scores range from 0 to 100 [36]. Reliability (0.91) and validity (0.81 correlation with a 7-point scale of “user-friendliness”) have been well established [37]. A score of >68% is considered above average [36].

Caregiver Satisfaction

Satisfaction will be assessed via semistructured interviews and electronic surveys with caregivers. Caregivers will be asked for feedback regarding participation in the intervention, benefits, burden, barriers, suggested modifications, and overall satisfaction. Suggested modifications to the app and advice to the health care team will also be solicited.

Medication Level Variability Index

The medication level variability index is the calculation of the standard deviation of serum assays of immunosuppressants that has been shown to correlate with adherence and clinical outcomes in the solid organ transplant population [38]. Immunosuppressant serum assays are collected weekly during the acute phase. The degree of variation among levels will also be calculated.

Data Analysis

All interviews will be transcribed verbatim. During qualitative analysis, investigators will use an iterative process of reading, summarizing, and rereading data. The qualitative team is composed of 3 individuals with formal research training in psychology, behavioral health, and nursing. The interview transcripts will be organized and coded using NVIVO software (QSR International). In-vivo coding will occur as new themes emerge from the data. The data will be triangulated by comparing and integrating quantitative survey data with qualitative findings.

Quantitative data will be summarized with descriptive statistics (frequencies, means, and SDs). During the passive use observation period, passive data modules will capture phone activity and caregivers’ application use (eg, time, date, duration of use). Descriptive statistics will be used to analyze phone activity. Correlation analysis will be used to investigate use behavior over time. Acceptability will be assessed by averaging total scores from the System Usability Scale. Consistent with the literature [36], scores >68% on the System Usability Scale will be considered acceptable. The proportion of participants that enroll and complete the study will be examined to assess study feasibility.

The nature of the study is exploratory rather than confirmatory. Thus, the objective of the analysis is effect size estimation, rather than formal hypothesis testing. Threats to power (eg, participant attrition due to patient death, early taper of immunosuppressant medication) are not a primary concern. We will compute pre-post effect sizes (eg, a standardized mean difference) to inform the future randomized controlled trial (phase 3) assessing the efficacy of the intervention.

Results

Enrollment of caregivers of children post HSCT from the free-standing Midwestern Children’s Hospital began in September 2021 and is ongoing. Findings from phase 2 will be used to inform further development and refinement of the app for testing in the pilot randomized controlled trial (phase 3) anticipated to begin in fall 2022. We anticipate high usability scores and a better understanding of unique features within the app that are needed for HSCT families post transplant. To date, usability scores among enrolled participants are greater than 70%. Feedback from qualitative interviews is being used to further adapt the app by adding specific weekly logs, call provider options, and voice to text. The results of this study will be disseminated through presentations at scientific conferences and publication in peer-reviewed journals.

Discussion

To our knowledge, this is one of the first studies to use a systematic, phased approach to the development of a digital health intervention and evaluation of usability and feasibility to improve outcomes in pediatric HSCT. From this study, we anticipate high usability scores and a better understanding of unique features within the app that are needed for HSCT families post transplant. The long-term goal of this research is to develop

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novel digital interventions to increase adherence and ultimately improve clinical outcomes for these high-risk children. In addition, there is potential to adapt our work for children with other chronic conditions.

The strengths of the mixed methods approach and proposed digital health intervention include constructs from behavioral health and BE theory that drive data collection and analysis, as well as the use of multiple methods of data collection and multiple data sources to gain a comprehensive understanding of patient needs. The development of the intervention has undergone multiple iterations based on feedback from multiple stakeholders, including pediatric patients, caregivers, physicians, and nurses, each offering unique and important perspectives.

Potential limitations of the study include the use of 1 pilot recruitment site; however, there is a diverse group of patients requiring HSCT at this institution. A small number of patient caregivers will be recruited, and a larger user population could yield additional data. At this time, only English-speaking caregivers are eligible; opportunities to increase diversity by adding additional languages are planned in future iterations.

This protocol describes the second phase of a multiphase, theory-driven digital health app intervention to improve adherence and symptom tracking in children post HSCT. The study findings will provide important knowledge regarding the feasibility of testing in a larger randomized controlled trial. The goal of the entire project is to improve adherence and clinical outcomes in children post HCST, which may have important implications for improving adherence in other clinical populations.

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Authors' Contributions

MS conceived and designed the study. MS wrote the initial draft of the manuscript. MS, ES, JS, WL, AP, and CG made substantial contributions to the planning and design of the study and contributed to the revision of the manuscript. All authors read and approved the final version of the manuscript.

Conflicts of Interest

None declared.

Multimedia Appendix 1
Peer-review report by the National Institute of Nursing Research Initial Review Group (NRRC) (National Institutes of Health, USA).
[PDF File (Adobe PDF File), 151 KB - resprot_v11i7e39098_app1.pdf]

References

1. Bissonnette JM. Adherence: a concept analysis. J Adv Nurs 2008 Sep;63(6):634-643. [doi: 10.1111/j.1365-2648.2008.04745.x] [Medline: 18808585]
2. Drotar DD, Crawford P, Bonner M. Collaborative decision-making and promoting treatment adherence in pediatric chronic illness. PI 2010 Mar;2:1-7. [doi: 10.2147/pi.s8820]
3. Drotar D. Strategies of adherence promotion in the management of pediatric chronic conditions. J Dev Behav Pediatr 2013;34(9):716-729. [doi: 10.1097/DBP.0b013e31829f6781] [Medline: 24247913]
4. McGrady M, Hommel KA. Medication adherence and health care utilization in pediatric chronic illness: a systematic review. Pediatrics 2013 Oct;132(4):730-740 [FREE Full text] [doi: 10.1542/peds.2013-1451] [Medline: 23999953]
5. Fiese B, Everhart RS. Medical adherence and childhood chronic illness: family daily management skills and emotional climate as emerging contributors. Curr Opin Pediatr 2006 Oct;18(5):551-557. [doi: 10.1097/01.mop.0000245357.68207.9b] [Medline: 16969171]
6. Landier W. Age span challenges: adherence in pediatric oncology. Semin Oncol Nurs 2011 May;27(2):142-153. [doi: 10.1016/j.soncn.2011.02.006] [Medline: 21514483]
7. Shemesh E, Shneider BL, Savitzky JK, Arnott L, Gondolesi GE, Krieger NR, et al. Medication adherence in pediatric and adolescent liver transplant recipients. Pediatrics 2004 Apr;113(4):825-832. [doi: 10.1542/peds.113.4.825] [Medline: 15060234]

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8. Quine L, Steadman L, Thompson S, Rutter DR. Adherence to anti-hypertensive medication: proposing and testing a conceptual model. Br J Health Psychol 2012 Feb;17(1):202-219. [doi: 10.1111/j.2044-8287.2011.02034.x] [Medline: 22107150]
9. Varni JW, Wallander JL. Adherence to health-related regimens in pediatric chronic disorders. Clin Psych Rev 1984 Jan;4(5):585-596. [doi: 10.1016/0272-7358(84)90046-1]
10. Hoodin F. Psychological and behavioral correlates of medical adherence among adult bone marrow transplant recipients (Dissertation). Detroit, MI: Wayne St. University; 1993.
11. Phipps S, DeCuir-Whalley S. Adherence issues in pediatric bone marrow transplantation. J Pediatr Psychol 1990 Aug;15(4):459-475. [doi: 10.1093/jpepsy/15.4.459] [Medline: 2258795]
12. Pai AL, Rausch J, Drake S, Morrison CF, Lee JL, Nelson A, et al. Poor adherence is associated with more infections after pediatric hematopoietic stem cell transplant. Biol Blood Marrow Transplant 2018 Feb;24(2):381-385 [FREE Full text] [doi: 10.1016/j.bbmt.2017.10.033] [Medline: 29102720]
13. McGrady ME, Williams SN, Davies SM, Pai AL. Adherence to outpatient oral medication regimens in adolescent hematopoietic stem cell transplant recipients. Eur J Oncol Nurs 2014 Apr;18(2):140-144 [FREE Full text] [doi: 10.1016/j.ejon.2013.11.007] [Medline: 24361039]
14. Skeens M, Akard TF, Gilmer MJ, Garee A, Miller A. Toward a better understanding of pediatric BMT adherence: an exploration of provider perceptions. Bio Blood Marrow Transplant 2014 Feb;20(2):S315. [doi: 10.1016/j.bbmt.2013.12.553]
15. Patel MS, Volpp KG, Asch DA. Nudge units to improve the delivery of health care. N Engl J Med 2018 Jan 18;378(3):214-216. [doi: 10.1056/nejmp1712984]
16. Linnemayr S, MacCarthy S, Kim A, Giguere R, Carballo-Dieguez A, Barreras JL. Behavioral economics-based incentives supported by mobile technology on HIV knowledge and testing frequency among Latino/a men who have sex with men and transgender women: Protocol for a randomized pilot study to test intervention feasibility and acceptability. Trials 2018 Oct 05;19(1):540 [FREE Full text] [doi: 10.1186/s13063-018-2867-1] [Medline: 30290851]
17. Stevens J. Behavioral economics as a promising framework for promoting treatment adherence to pediatric regimens. J Pediatr Psychol 2014 Sep;39(10):1097-1103. [doi: 10.1093/jpepsy/jsu071] [Medline: 25216661]
18. van Mierlo T, Hyatt D, Ching AT, Fournier R, Dembo RS. Behavioral economics, wearable devices, and cooperative games: results from a population-based intervention to increase physical activity. JMIR Serious Games 2016 Jan 28;4(1):e1 [FREE Full text] [doi: 10.2196/games.5358] [Medline: 26821955]
19. Mitchell MS, Goodman JM, Alter DA, John LK, Oh PI, Pakosh MT, et al. Financial incentives for exercise adherence in adults: systematic review and meta-analysis. Am J Prev Med 2013 Nov;45(5):658-667. [doi: 10.1016/j.amepre.2013.06.017] [Medline: 24139781]
20. Angellotti E, Wong JB, Pierce A, Hescott B, Pittas AG. Combining Wireless Technology and Behavioral Economics to Engage Patients (WiBEEP) with cardiometabolic disease: a pilot study. Pilot Feasibility Stud 2019 Jan 15;5(1):7 [FREE Full text] [doi: 10.1186/s40814-019-0395-8] [Medline: 30675374]
21. Chang LL, DeVore AD, Granger BB, Eapen ZJ, Ariely D, Hernandez AF. Leveraging behavioral economics to improve heart failure care and outcomes. Circulation 2017 Aug 22;136(8):765-772. [doi: 10.1161/circulationaha.117.028380]
22. Malo TL, Hall ME, Brewer NT, Lathren CR, Gilkey MB. Why is announcement training more effective than conversation training for introducing HPV vaccination? A theory-based investigation. Implement Sci 2018 Apr 19;13(1):57 [FREE Full text] [doi: 10.1186/s13012-018-0743-8] [Medline: 29673374]
23. Opel DJ, Taylor JA, Zhou C, Catz S, Myaing M, Mangione-Smith R. The relationship between parent attitudes about childhood vaccines survey scores and future child immunization status: a validation study. JAMA Pediatr 2013 Nov 01;167(11):1065-1071 [FREE Full text] [doi: 10.1001/jamapediatrics.2013.2483] [Medline: 24061681]
24. Taylor NK, Buttenheim AM. Improving utilization of and retention in PMTCT services: can behavioral economics help? BMC Health Serv Res 2013 Oct 10;13(1):406 [FREE Full text] [doi: 10.1186/1472-6963-13-406] [Medline: 24112440]
25. Barth S, de Jong MD, Junger M. Lost in privacy? Online privacy from a cybersecurity expert perspective. Telemat Inform 2022 Mar;68:101782. [doi: 10.1016/j.tele.2022.101782]
26. Camacho E, LoPresti M, Appelboom G, Dumont ELP, Taylor B, Connolly ES. The ubiquitous role of smartphones in mobile health. BBIJ 2014 Sep 27;1(1):14-19. [doi: 10.15406/bbij.2014.01.00004]
27. Asch DA, Muller RW, Volpp KG. Automated hovering in health care — watching over the 5000 hours. N Engl J Med 2012 Jul 05;367(1):1-3. [doi: 10.1056/nejmp1203869]
28. Skrabal Ross X, Gunn KM, Suppiah V, Patterson P, Olver I. A review of factors influencing non-adherence to oral antineoplastic drugs. Support Care Cancer 2020 Sep 25;28(9):4043-4050. [doi: 10.1007/s00520-020-05469-y] [Medline: 32335731]
29. Unni E, Sternbach N, Goren A. Using the Medication Adherence Reasons Scale (MAR-Scale) to identify the reasons for non-adherence across multiple disease conditions. PPA 2019 Jun;Volume 13:993-1004. [doi: 10.2147/ppa.s205359]
30. Duncan S, Annunziato RA, Dunphy C, LaPointe Rudow D, Shneider BL, Shemesh E. A systematic review of immunosuppressant adherence interventions in transplant recipients: Decoding the streetlight effect. Pediatr Transplant 2018 Feb 07;22(1):e13086 [FREE Full text] [doi: 10.1111/petr.13086] [Medline: 29218760]

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31. Alwashmi MF, Hawboldt J, Davis E, Fetters MD. The iterative convergent design for mobile health usability testing: mixed methods approach. JMIR Mhealth Uhealth 2019 Apr 26;7(4):e11656. [doi: 10.2196/11656]
32. Fedele DA, Cushing CC, Fritz A, Amaro CM, Ortega A. Mobile health interventions for improving health outcomes in youth: a meta-analysis. JAMA Pediatr 2017 May 01;171(5):461-469 [FREE Full text] [doi: 10.1001/jamapediatrics.2017.0042] [Medline: 28319239]
33. Hommel KA, Davis CM, Baldassano RN. Objective versus subjective assessment of oral medication adherence in pediatric inflammatory bowel disease. Inflamm Bowel Dis 2009 Apr;15(4):589-593 [FREE Full text] [doi: 10.1002/ibd.20798] [Medline: 18985746]
34. Quittner AL, Modi AC, Lemanek KL, Ievers-Landis CE, Rapoff MA. Evidence-based assessment of adherence to medical treatments in pediatric psychology. J Pediatr Psychol 2008 Oct 18;33(9):916-36; discussion 937 [FREE Full text] [doi: 10.1093/jpepsy/jsm064] [Medline: 17846042]
35. Ingerski LM, Hente EA, Modi AC, Hommel KA. Electronic measurement of medication adherence in pediatric chronic illness: a review of measures. J Pediatr 2011 Oct;159(4):528-534 [FREE Full text] [doi: 10.1016/j.jpeds.2011.05.018] [Medline: 21722917]
36. Lewis JR, Sauro J, editors. The Factor Structure of the System Usability Scale. Berlin, Heidelberg: Springer; 2009.
37. Bangor A, Kortum PT, Miller JT. An empirical evaluation of the system usability scale. International Journal of Human-Computer Interaction 2008 Jul 30;24(6):574-594. [doi: 10.1080/10447310802205776]
38. Shemesh E, Bucuvalas JC, Anand R, Mazariegos GV, Alonso EM, Venick RS, et al. The Medication Level Variability Index (MLVI) predicts poor liver transplant outcomes: a prospective multi-site study. Am J Transplant 2017 Oct 22;17(10):2668-2678 [FREE Full text] [doi: 10.1111/ajt.14276] [Medline: 28321975]

Abbreviations

BE: behavioral economics
HSCT: hematopoietic stem cell transplant
MAM: Medication Adherence Measure
MEMS: medication event monitoring system
mHealth: mobile health

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