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Contents

Protocols

Original Papers

Viewpoint

Protocol

The OnTrack Diabetes Web-Based Program for Type 2 Diabetes and Dysphoria Self-Management: A Randomized Controlled Trial Protocol

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Abstract

Background: The prevalence of type 2 diabetes is rising with the majority of patients practicing inadequate disease self-management. Depression, anxiety, and diabetes-specific distress present motivational challenges to adequate self-care. Health systems globally struggle to deliver routine services that are accessible to the entire population, in particular in rural areas. Web-based diabetes self-management interventions can provide frequent, accessible support regardless of time and location

Objective: This paper describes the protocol of an Australian national randomized controlled trial (RCT) of the OnTrack Diabetes program, an automated, interactive, self-guided Web program aimed to improve glycemic control, diabetes self-care, and dysphoria symptoms in type 2 diabetes patients.

Methods: A small pilot trial is conducted that primarily tests program functionality, efficacy, and user acceptability and satisfaction. This is followed by the main RCT, which compares 3 treatments: (1) delayed program access: usual diabetes care for 3 months postbaseline followed by access to the full OnTrack Diabetes program; (2) immediate program: full access to the self-guided program from baseline onward; and (3) immediate program plus therapist support via Functional Imagery Training (FIT). Measures are administered at baseline and at 3, 6, and 12 months postbaseline. Primary outcomes are diabetes self-care behaviors (physical activity participation, diet, medication adherence, and blood glucose monitoring), glycated hemoglobin A1c (HbA1c) level, and diabetes-specific distress. Secondary outcomes are depression, anxiety, self-efficacy and adherence, and quality of life. Exposure data in terms of program uptake, use, time on each page, and program completion, as well as implementation feasibility will be conducted.

Results: This trial is currently underway with funding support from the Wesley Research Institute in Brisbane, Australia.

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Conclusions: This is the first known trial of an automated, self-guided, Web-based support program that uses a holistic approach in targeting both type 2 diabetes self-management and dysphoria. Findings will inform the feasibility of implementing such a program on an ongoing basis, including in rural and regional locations.

Trial Registration: Australian and New Zealand Clinical Trials Registration number: ACTRN12612000620820; https://anzctr.org.au/Trial/Registration/TrialReview.aspx?ACTRN=12612000620820 (Archived by WebCite at http://www.webcitation.org/6a3BeXC5m).

Introduction

Diabetes mellitus affects an estimated 346 million people globally and type 2 diabetes accounts for 85% to 90% of all cases [1]. In Australia, type 2 diabetes affects 4% of the population [2]. Diabetes constitutes the eighth-highest burden of disease in Australia and type 2 diabetes accounts for 92% of this burden [3]. With the rapidly rising prevalence of diabetes, the effects of inadequate diabetes self-management continue to increase and resulting diabetes complications and premature mortality become more urgent to address. Diabetes is the leading cause of blindness, end-stage renal disease, and lower limb amputation in the world [1]. Moreover, the effects of diabetes on quality of life, mental health, work productivity, and other intangible losses are substantial and add further to the diabetes-related burden to society.

Depression [4,5] and anxiety [6] are significantly more prevalent in people with diabetes than in the general population. Comorbid mental health conditions are barriers to effective diabetes self-care [7] and further increase diabetes-related expenditures [8]. Dysphoria complicates the achievement of adequate glycemic control through multiple pathways. Comorbid depression and/or anxiety with diabetes predisposes individuals to diabetes-specific distress [9,10] and affects glycemic control [11] both directly (via physiological mechanisms [8-10]) and indirectly by reducing motivation for adequate self-management [12-14]. Even subclinical manifestations, such as dysphoria, are associated with clinically deleterious outcomes, including reduced self-care [7], poorer glycemic control [15,16], increased incidence and progression of diabetes complications [17,18], and greater disability [19]. Stress contributes to other common physical comorbidities in diabetes patients, including metabolic syndrome and cardiovascular disease [20]. Diabetes-specific distress (DSD)—the emotional and psychological burden posed by diabetes [21]—accounts for a high proportion of variance in depression [22] and further impedes self-management [23]. Combined effects of inadequate glycemic control and dysphoric mood in diabetes [21,22] thus call for urgent intervention.

Prior research indicates the need for behavioral diabetes self-management interventions to incorporate psychological and emotional support components for optimum efficacy [23]. Improvements in diabetes self-care are strongly associated with improved glycemic control [24,25], so behavioral interventions to support diabetes self-care might also improve clinical outcomes [26]. However, improvements in glycemic control do not generally result in significant improvements in mood [23], nor do psychological treatments for depression and anxiety in people with diabetes reliably produce improvements in glycemic control [27]. Despite the limited impact of single-focused interventions in diabetes [28], self-management interventions typically fail to address both issues. Furthermore, trials on self-management interventions often only follow-up participants for relatively short periods (eg, ≤6 months [29]) so that long-term effects remain undetermined.

There are many barriers to adequate treatment of type 2 diabetes within health systems, including a shortage of health professionals, inadequate availability of services, limited access in rural and remote regions, practitioner/patient communication problems, time pressures in medical consultations, and limitations in the skills and confidence of health professionals in the provision of psychological interventions [30]. Patients often struggle to manage the complexity of type 2 diabetes treatment regimens [31], to recognize dysphoria symptoms [32,33], acknowledge their need for support, and find the motivation to overcome barriers to a healthy lifestyle [34]. Shortcomings in health care services particularly affect patients at risk of psychological comorbidities and the number of these patients will escalate sharply as the incidence of diabetes increases [4].

Recent evidence demonstrates that Web-based diabetes self-management interventions have potential efficacy, feasibility, user acceptability, and uptake [29]. Web programs have demonstrated significant improvements in clinical, behavioral [35-37], psychological, emotional, and psychosocial outcomes [38], as well as a strong uptake and acceptability by both mature [39] and novice users [40].

Recently trialed Web-based diabetes self-management programs based on social cognitive theory (SCT) [41] have demonstrated efficacy [35,42,43]. Central tenets of SCT include self-efficacy, or one's belief in their capabilities to execute desired courses of action, and outcome expectancies, or personal predictions of likely outcomes resulting from certain courses of action [41]. SCT encompasses the key recommendations in national practice guidelines for diabetes management [44]. These include encouraging patient empowerment (promoting self-efficacy), ongoing monitoring of target outcomes (self-evaluation), and providing diabetes education (instructions). Therefore, SCT provides a theoretical avenue by which to address both behavioral self-management and emotional issues [45].

Self-efficacy has significant positive associations with behavioral outcomes including physical activity participation [46,47], nutrition intake [48,49], weight loss [50], and diabetes self-care [51], as well as with emotional outcomes, including depressive symptoms [52], in people with diabetes.

Despite the growth in supportive evidence on Web-based diabetes programs for self-management, there are some inconsistencies in their results and further data are needed on their potential to improve glycemic control [53]. Lorig et al [54] trialed a diabetes self-management intervention that included modules to assist users in coping with emotional challenges both related and unrelated to diabetes. Although improvements were found in self-efficacy, patient activation, and glycated hemoglobin (HbA$_{1c}$) at 6 months postenrollment, there were no significant improvements in health behaviors, including exercise participation. Emotional outcomes and effects on long-term glycemia were not determined. On the other hand, Glasgow and colleagues [36] reported that their Internet-based diabetes education program (D-Net) did not significantly improve mood or glycemic control, but produced significant improvements in behavioral and psychosocial outcomes. Although current trials show that Web-based diabetes programs have substantial promise, there remains a need to enrich available data on their effects on both mood and glycemia. Given the close mutual influences between dysphoria and diabetes self-management, including the challenging context of psychosocial [55] and emotional stressors [56] in which self-management is attempted, a Web intervention that utilizes a holistic approach to diabetes self-management is required. Such a program would allow users to address both the behavioral and emotional challenges of diabetes in context.

Developing and maintaining commitment to any significant behavior change is challenging. Over the last 30 years, motivational interviewing [57] has demonstrated an ability to enhance motivation, particularly in addictive disorders (where it began), but also in some other behavioral domains [58]. However, until now, its effects on behavior change and glycemic control in diabetes have been inconsistent with only a minority of trials having significant differential effects [59]. Recently, a new approach to eliciting motivation, which uses a motivational interviewing style but trains participants to use motivational imagery in their everyday life, has been advanced [60]. This approach, Functional Imagery Training (FIT), applies 10 years of theoretical and empirical work on the nature and modulation of desires [61]. Personalized multisensory imagery about the benefits of health maintenance behaviors, past successes, and effective strategies is elicited. This is described as television advertisements in which the participant is the actor and is

reliving an event or imagining a future event. Participants are asked to practice this imagery when they undertake a routine everyday task and to set electronic reminders for times when they need to undertake a health routine or avoid a dysfunctional behavior. Imagery is cued using photos taken by the participant and is refreshed using new events that illustrate actual gains and effective strategies. Commitment and social support for the goal is elicited by sharing a brief recorded statement about the goal, why it was adopted, how it will be done, and why it will be successful; this recording is replayed if motivation is fading. Brief phone calls by the therapist remind the participant to practice their imagery and help them solve problems by using it.

The study described subsequently comprises a randomized controlled trial (RCT) involving the OnTrack Diabetes program, an automated Web-based intervention aimed to achieve and maintain improvements in type 2 diabetes self-management and dysphoria symptoms. It compares delayed and immediate access to the program, and immediate access supplemented by FIT-based coaching.

Methods

The OnTrack Diabetes Program

The development of OnTrack Diabetes is described in a companion paper [62] (see Figure 1 for screenshot). The program targets physical activity participation, nutrition, adherence to health routines, and mood disturbance (depression, anxiety, and diabetes-related everyday stressors). Specifically, the program includes informational resources: goal setting, planning, and creating routines for self-care behaviors; feeling confident and problem solving via interactive tools; goal attainment scaling via self-monitoring tools, quizzes, and automated feedback graphs; relaxation and mindfulness audios; and an electronic diary. Access to health care providers is also promoted by encouraging users to establish a diabetes care team. Further, the program addresses the independent effects of depression, anxiety, and diabetes-specific distress by enabling users to provide personalized responses in the emotional support tools regarding both diabetes-specific and nonspecific emotional challenges. Although program sections appear in an ordered structure, users can choose to undertake segments in any order—a feature intended to foster user empowerment [63]. Both provided and entered text is minimized with extensive use of icons and pictures and simple sentences and vocabulary so that reading requirements do not exceed Year 7 educational levels.

Figure 1. Screenshot of the OnTrack Diabetes home page.

Design and Setting

A pilot trial of the program is initially implemented to test for program functionality and to provide an indication of program efficacy, user acceptability, and satisfaction. Following the pilot, a RCT with the participant as the unit of randomization is implemented. The trial is conducted Australia-wide and access is ongoing. The research team is based at the Mitsubishi Centre for Rural and Remote Health at the Wesley Research Institute in Brisbane.

The RCT evaluates the efficacy of the OnTrack Diabetes program in improving the primary outcomes glycemic control (HbA$_{1c}$ level) and diabetes-specific distress symptoms, and the secondary outcomes of depression, anxiety, physical activity participation, diet, blood glucose self-monitoring, and medication taking. User acceptability, ease of use, utility, program satisfaction, and implementation feasibility are also assessed.

It is hypothesized that at 3 months postbaseline, the immediate access plus FIT condition will show the greatest improvements in primary and secondary outcomes compared with the immediate access and the delayed access conditions. Results of the immediate access and the delayed access conditions are expected to be similar at 6 months when both conditions will have received the full intervention. A CONSORT flow diagram for the trial is shown in Figure 2.

Figure 2. CONSORT flow diagram of the OnTrack Diabetes main randomized controlled trial.
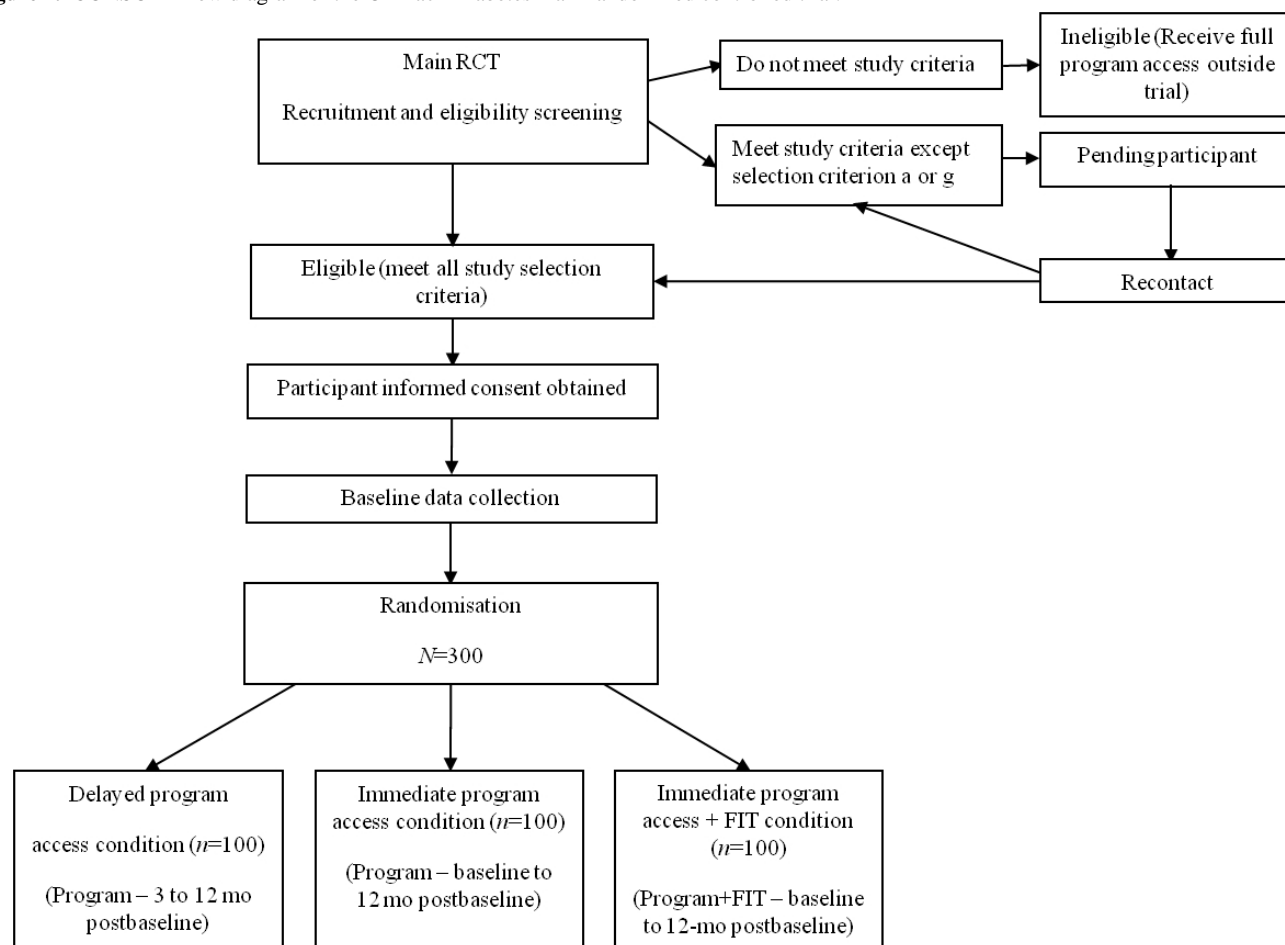
Recruitment and Sample

Recruitment strategies for the trial are primarily community-based: newspaper advertisements, health organization newsletters, radio broadcasts, notice board postings, bulletins, emails, and online advertisements. Targeted methods include the distribution of study flyers and posters to medical centers, letters to health institutions, pharmacies and health professionals, and featuring the OnTrack Diabetes website URL on statewide Diabetes Australia research Web pages. Attendance at diabetes-related expos and events allows in-person recruitment and further promotion of the project to health professionals.

The trial aims to enroll at least 210 participants. Selection criteria include (1) type 2 diabetes diagnosis (by a medical doctor and according to World Health Organization criteria) of at least 3 months duration, (2) age 18 years or older, (3) living in Australia without plans to leave within 12 months, (4) regular computer and Internet access, (5) contactable by phone, (6) clear command of written English (at least Year 5 education), and (7) stable diabetes pharmacotherapy (medication dose stable ≥4 weeks; medication type stable ≥3 months). Study exclusion criteria include (1) current diagnosis of mental disorder other than depression or anxiety (participant is asked if a condition has been diagnosed and if so they are informed that they will receive access to the program but not be included in the trial), (2) current suicidal risk (assessed via suicide risk assessment), (3) significant cognitive disorder (eg, from head trauma or dementia), (4) currently on steroid medication or likely to

commence it in the next 12 months, and (5) pregnant or likely to become pregnant in the next 12 months.

All participants are asked to undertake a medical assessment by their general practitioner prior to study enrollment. Individuals with physical limitations or concurrent physical disorders are advised of the need to exercise caution in setting physical activity goals according with their doctor's advice.

Measures

Primary outcomes include diabetes self-care behaviors, HbA_{1c} level, and diabetes-specific distress. Secondary outcomes include depression, anxiety, (medication taking, nutrition intake, physical activity, and blood glucose self-monitoring), quality of life, and user evaluations of the program. Measures are administered at baseline and the 3-, 6-, and 12-month follow-up time points. Table 1 in Multimedia Appendix 1 lists the measures.

Procedure

Participants register interest on the study website and select a time to undertake an eligibility screening appointment by phone. Eligible individuals undertake baseline measures by email and phone interview at their selected appointment time. Individuals who satisfy all criteria except inclusion criterion time since diagnosis or stable medication are asked if they wish to be recontacted for future screening; if so, they are categorized as "pending." Individuals who are ineligible are allowed to use the program without being enrolled in the trial.

Following baseline measures, all participants who are randomly allocated to the immediate access or the immediate access plus FIT interventions receive a secure username and password with which to log on to the program. Those enrolled in the delayed access condition are informed that they will receive program access details in 3 months. Computer-generated randomization occurs automatically. One week before the due date for follow-up study measures, participants receive an email notification with a link to the online survey and a preset time for the timeline follow-back procedure phone interview. The email requests that participants email the researcher if the phone interview time does not suit them.

Delayed Access

In this condition, participants undertake their usual diabetes care with no Web-based program access. Following 3-month follow-up study measures, they receive access to the full OnTrack Diabetes program. Their access to the program is actioned by a member of the research team after which they receive an email that contains an exclusive username and password to access the program.

Immediate Access

Participants receive access to the full OnTrack Diabetes program from baseline as described in the companion paper about the development of OnTrack Diabetes [62]. This includes access to extensive information resources, a nutrition module (Eating Well and Feeling Healthy), a module focused on adherence to health regimens (Health Routines), an emotional well-being module (Thinking Well and Feeling Fine), and a maintenance module (Keeping On Track). The first section of each module includes a series of interactive tools that incorporate guided imagery, planning goal implementation, goal setting, and confidence building. The planning tools guide participants in proceeding toward their own personalized goals in incremental steps. The second section of each module is entitled "More on..." (eg, More on Health Routines) and involves setting a weekly schedule to increase participation in desired health behaviors and pleasurable activities, and tools for problem-solving challenges. A printable summary is provided on completion of each interactive tool. These summaries can be accessed on future occasions and participants can also complete tools or modules repeatedly if they wish. Self-monitoring tools allow daily monitoring of highest and lowest blood glucose levels, best and worst mood, and the degree that physical activity and nutrition goals were met. Automated feedback graphs on progress are provided for the past week, month, or 3 months. Mindfulness audios are playable on the computer or can be downloaded to an MP3 player.

Immediate Access Plus Functional Imagery Training

In addition to content received in the immediate access condition, participants in this condition receive regular therapist support phone calls wherein FIT techniques are utilized. The therapist is a provisionally registered psychologist who contacts participants twice in the first week of study enrollment and once in the second and third week of enrollment followed by biweekly calls. Calls last for an average of 30 to 40 minutes until the participant has been enrolled for 1 month, after which they last

approximately 20 minutes. Participants are encouraged to practice FIT at home every day. The approach assists them to develop and maintain personalized changes to their diabetes self-care behaviors, alcohol use, smoking, or lifestyle. The therapist reinforces the imagery-based activities already included in the OnTrack Diabetes program and extends these by encouraging additional imagery rehearsal to further enhance motivation.

Statistical Analyses

Preliminary analyses assess for baseline differences and subsequent analyses control for any observed differences. The primary analyses will comprise multiple regressions, predicting posttreatment and follow-up results from baseline measures and treatment contrasts with multiple imputation being used to predict missing data. Mixed-model ANOVAs with repeated measures will also be applied to confirm whether effects are still obtained without imputations. Both methods allow an intention-to-treat approach to the data. Repeated measures ANOVAs will be used to evaluate differences in change scores between the study time points among the 3 study conditions.

User satisfaction, perceived ease of use, and usefulness are examined with ANOVAs and program reach, acceptability, implementation feasibility, and outreach are assessed using the Reach Effectiveness Adoption Implementation Maintenance (RE-AIM) framework [64]. This will be operationalized using the OnTrack Diabetes Evaluation Questionnaire, which asks about users' perceptions of the program's acceptability, issues with feasibility, and outreach (ie, ability to access the program and barriers to access including poor broadband network availability). The inclusion of residents of rural and regional areas enriches this evaluation as will quantitative data about participants' exposure to the program.

Sample Size and Retention

The sample of 210 enables detection of a small effect size of f^2=.046 in the multiple regressions. Although the study uses all allocated participants in the outcome analyses, efforts are made to maximize retention by maximizing rapport at the baseline assessment and collecting multiple means to contact participants, including email, landline, and mobile phone contact details, and by assertive follow-up. With these strategies, the study is aimed to have at least 70% retention at 12 months.

Ethics

Ethics approval to conduct this project was granted by the Uniting Care Health Human Research Ethics Committee (#Cassimatis9111) and the Queensland University of Technology Human Research Ethics Committee (#1100000783).

Results

This trial is currently underway with funding support from the Wesley Research Institute in Brisbane, Australia.

Discussion

Results from this trial will provide information on the efficacy, practicality, and user perspectives on the effects of such a

program and the success of its dissemination within the Australian context. A 12-month follow-up period will provide data on the maintenance of effects from the programs as well as patterns of usage over time and the relationship of these variables to study outcomes.

Previous trials of diabetes self-management Web-based programs have indicated that a common limitation of such programs is reduced user engagement over time [36,54,64]. It is expected that ongoing access to interactive tools and self-monitoring that users can apply to issues with self-management and dysphoria as they arise will help to maximize engagement and retention. Fortnightly email reminders may also assist users to keep on track of their program usage and prompt continued user engagement with the program [65]. Follow-up assessments during the trial will ask about usage of other treatments and website resources, but the validity of those reports cannot be guaranteed.

Results will provide information about the effectiveness of using a self-guided approach to a Web-based type 2 diabetes self-management intervention. Limitations to generalizability that commonly affect studies conducted within specific clinical or experimental settings are avoided [64] by providing nationwide access and enabling the intervention to be conducted at any location from which access to the Web via a computer is possible. As well as assessing whether the OnTrack Diabetes program will improve type 2 diabetes self-management and dysphoria, this trial is intended to serve as a source of information about the successes and shortcomings entailed in implementing such a program. Results will provide information on which future trials of Web-based cognitive behavioral therapy interventions can build in terms of processes that enhance and those that impede the practicality and rigor of research in this domain.

Conflicts of Interest

MC and DK wrote the Web-based program evaluated in this study, but they do not obtain commercial gain from its use. All other authors have no competing interests to declare.

Multimedia Appendix 1

Measures used in trial.

[PDF File (Adobe PDF File), 31KB - resprot_v4i3e97_app1.pdf]

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Abbreviations

FIT: Functional Imagery Training
RCT: randomized controlled trial
SCT: social cognitive theory

Protocol

Efficacy of a Multicomponent Positive Psychology Self-Help Intervention: Study Protocol of a Randomized Controlled Trial

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Abstract

Background: Positive psychology interventions have been found to enhance well-being and decrease clinical symptomatology. However, it is still unknown how flourishing can also be increased. Although multicomponent interventions seem to be necessary for this purpose, different formats can be used. A cost-effective approach could be a positive psychology-based self-help book with tailored email support to reach large target groups and to prevent dropout.

Objective: This study will evaluate the efficacy of a comprehensive multicomponent self-help intervention with or without email support on well-being and flourishing, and will seek to determine the working mechanisms underlying the intervention.

Methods: In this 3-armed, parallel, randomized controlled trial, 396 participants with low or moderate levels of well-being and without clinical symptomatology will be randomly assigned to (1) a self-help book condition with weekly email support, (2) a self-help book condition without email support but with a weekly information email, or (3) a waiting list control condition. Online measurements will be assessed at baseline, at post-test (3 months after baseline), and at 6 and 12 months after baseline.

Results: The primary outcomes are well-being and flourishing (ie, high levels of well-being). Secondary outcomes are the well-being components included in the intervention: positive emotion, use of strengths, optimism, self-compassion, resilience, and positive relations. Other measures include depressive and anxiety symptoms, personality traits, direct medical and non-medical costs, life-events, and client satisfaction.

Conclusions: This study will add knowledge to the efficacy and cost-effectiveness of a multicomponent positive psychology intervention. We will also explore who can benefit most from this intervention. If the intervention is found to be effective, our results will be especially relevant for public mental health services, governments, and primary care.

Trial Registration: The Netherlands Trial Register NTR4297; http://www.trialregister.nl/trialreg/admin/rctview.asp?TC=4297 (Archived by WebCite at http://webcitation.org/6Uwb5SUUM).

KEYWORDS

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Introduction

Background

Since the introduction of positive psychology in 1998 [1], the proportion of published studies on this topic has grown rapidly each year compared to the entire field of psychological research [2]. Researchers have argued that the study of positive psychology is more capacious than the field of psychopathology because its primary focus is not on dysfunction but on well-being and optimal functioning [3]. Recent evidence indicates that positive mental health and mental illness are related but different continua [4-6]. This so-called two-continua model implies that individuals can experience positive outcomes such as life-satisfaction, meaning, and personal growth when mentally ill, and that the absence of mental illness does not automatically imply high levels of positive mental health [7,8]. As a consequence, researchers have underscored the importance of enhancing positive mental health in addition to preventing and treating mental illness, in clinical populations as well as in the general population [3,9].

A central aim in positive psychology is to increase the amount of flourishing worldwide [1,10]. Flourishing is defined as the presence of high levels of the affective or "feeling good" dimension of well-being (ie, hedonic well-being) in combination with high levels of the psychological functioning or "living well" dimension of well-being (ie, eudaimonic well-being) [4,9,11]. Compared to "languishers" (ie, people at the lowest levels of hedonic and eudaimonic well-being) and individuals with depression, research has shown that flourishers experience the least emotional distress and psychosocial impairment, have hardly any lost work days, and are most likely to survive [4,8]. Keyes and colleagues [12] have found initial support for the hypothesis that an increase in well-being protects against the development of mental illness. More specifically, they found that the risk for having a mental disorder was equally lowest for individuals who were flourishing in 1995 and in 2005, and for individuals who were flourishing in 2005 but not in 1995 [12]. The same study also indicates that it is possible to enhance the amount of flourishing [12]. However, there seems to be significant room for improvement because epidemiological studies using the same operationalization of flourishing have found that there were only 17% flourishers in the United States [4], 20% flourishers in South Africa [13], and 37% flourishers in The Netherlands [14]. Some researchers theorize that even small improvements in the level of well-being in the general population could generate large preventive effects on the amount of psychopathology [9,15]. Yet, little is known about how the amount of flourishing can be increased. The present study will evaluate a theory- and research- based positive psychology intervention (PPI) on efficacy, specific working mechanisms, and cost-effectiveness for enhancing well-being and flourishing in the general population.

Positive Psychology Interventions

A large number of theories have been used to develop interventions and exercises within the positive psychology movement, as can be found in the Key Competence Happiness Database [16]. Two meta-analyses have shown that PPIs significantly enhance well-being and alleviate depression in the short term, although effect sizes were relatively small [17,18]. These small effect sizes might be a result of the nature and intensity of the included interventions, which were mostly single-component interventions (ie, one or more individual exercises targeting one component of well-being). Examples are "the three good things exercise" or "savoring" targeting positive emotion, and "using one's strengths in new ways" to increase flow. However, since well-being is a multifaceted construct [10,19] it might be more efficacious to promote well-being and flourishing with a multicomponent intervention that contains a variety of evidence-based individual exercises targeting 2 or more theoretically relevant hedonic and eudaimonic well-being components. For example, the well-being theory of Seligman [10] states that the components of positive emotion, engagement, relationships, meaning, and accomplishment (PERMA) are all necessary for flourishing. Also, multicomponent interventions are higher intensity, target more resources of well-being in an individual, and are often of longer duration than single-component interventions, which may increase their efficacy.

In the last decade, some multicomponent PPIs have been investigated, including different face-to-face interventions. Examples are (1) Positive Psychotherapy, a structured 14-session program developed for individual or group therapy in clinical settings based on Seligman's well-being theory [10,20,21], (2) Well-being therapy, an individual psychotherapeutic strategy of 8-12 sessions that is based on Ryff's model of psychological well-being [19] and therefore contains strategies and therapeutic techniques to influence the components self-acceptance, environmental mastery, positive relations with others, personal growth, autonomy, and purpose in life [22], and (3) the Working for Wellness Program, a structured 6-week group-based program for employees with a strong focus on strengths, flow, and social relationships [23]. The efficacy of these multicomponent PPIs on mental illness and positive mental health have been demonstrated in a wide variety of studies—including randomized controlled trials (RCTs)—although most of these studies used small samples [20,22,23]. However, the need for trained therapists in these intensive face-to-face PPIs is a disadvantage that may limit their feasibility, cost-effectiveness and dissemination.

Positive psychology exercises have the advantage of being relatively small and easy-to-implement in daily life, and are therefore well-suited for self-administered interventions. Recently, some Web-based multicomponent PPIs have been developed to increase the reach of PPIs. For example, Schueller and Parks [24] selected 6 exercises from the Positive Psychotherapy intervention (active-constructive responding, gratitude visit, life summary, three good things, savoring, and strengths) and randomly assigned participants to a 6-week program containing all 6 exercises, 4 of the exercises, or 2 of the exercises. The 2- and 4-exercise programs resulted in significantly larger effects on depressive symptomatology than the control group and the 6-exercise program, although participants in the latter program practiced the exercises on significantly more days than participants in the 2- or 4-exercise programs [24]. Another, more comprehensive intervention is

Psyfit. This intervention contains 6 modules, each with 4 lessons, about goal setting, positive emotion, positive relations, mindfulness, optimism, and mastery [25]. An RCT showed significant but small effects on well-being and depressive symptomatology, although most participants completed less than 4 lessons of 1 or more modules [25]. While these and other Web-based multicomponent PPIs have shown that they can reach many individuals, their cost-efficacy seem to be limited by low adherence rates [24-27], which could be due to the lack of human contact and coaching [27,28].

Self-Help Book With Email Support

Another, possibly cost-effective approach could be to intertwine the advantages of the aforementioned formats by using an accessible self-help book in combination with email support to reach and stimulate large groups of individuals at minimal costs. Meta-analyses have shown that the use of self-help books—also called bibliotherapy—with or without support are effective in the treatment of depression [29,30] and the treatment of alcohol problems [31]. Also, research on guided self-help in the form of email support in combination with face-to-face therapy or online therapy has shown promising results [32,33]. Besides, there are some indications that tailored email support is more effective than no support or automated email support [32,34]. More important, promising findings have been found for the use of positive psychology-based self-help books without any support [35-37] or with email support [38]. For example, Parks and Szanto [37] compared a PPI group of students who received the book "The How of Happiness" [39] to a group of students who received a cognitive behavioral self-help book to cope with depression and a control group. Results showed that both intervention groups were equally effective in reducing depressive symptoms at post-test compared to the control group, and that significant increases in life-satisfaction were found only for the PPI compared to the control condition at the 6-month follow-up. Another study used a multicomponent self-help book based on acceptance and commitment therapy in a sample with mild to moderate depressive symptomatology [38]. One intervention group received the book with extensive and tailored email support on progress and process, while another group received the book with minimal email support on progress. Results revealed significant increases in well-being and mindfulness and significant decreases in depressive, anxiety, and fatigue symptomatology for both intervention groups at 3-months follow-up compared to a waiting list control group [38]. In this study, we will use a version of the extensive email support similar to that used in the latter study [38]. That is, participants will be guided through the self-help book by tailored email feedback from trained counselors, but we will compare it to receiving an information email instead of minimal email support.

This Study

This study will examine a comprehensive multicomponent positive psychology-based self-help book with email support. The self-help book is entitled, "This is your life" (TL) [40] and targets 6 key components in positive psychology: positive emotion, use of strengths, optimism, self-compassion, resilience, and positive relations. We will compare a condition wherein

participants receive the book with weekly asynchronous and tailored email support (TL-E) to a condition wherein participants receive the book with a weekly email with information (TL-I). Both groups will be compared to a waiting list control condition (WL). Our research aim is to evaluate the efficacy of the multicomponent self-help book with or without email support in terms of well-being and flourishing in an RCT (NTR4297) and to evaluate which of the included well-being components in the self-help book contribute to its efficacy. We expect that TL-E will be equivalent or superior to TL-I and superior to WL at post-test and 6 months follow-up, and that the effects will be sustained at 12 months follow-up.

This study will add to current knowledge in 3 ways. First, it will be conducted in a sample with low or moderate levels of well-being without moderate or severe clinical symptomatology, which is a potential "happiness-seekers" group [41] that has not previously been studied in PPIs [17,18,27]. Second, this study will gain insight into the working mechanisms underlying the intervention by evaluating which of the included well-being components in the self-help book (ie, positive emotion, use of strengths, optimism, self-compassion, resilience, and positive relations) contribute to its efficacy and by examining individual differences in demographic characteristics, number of life events, personality traits, and adherence rates. Third, this study will examine if the innovative format used in this study (ie, self-help book with relatively inexpensive email support) is a cost-effective approach for enhancing well-being and flourishing compared to a waiting list control group, since little is known about the cost-effectiveness of PPIs [26].

Methods

Study Design

This study is a parallel RCT with 3 groups: a group receiving the self-help book with weekly asynchronous and tailored email support (TL-E); a group receiving the self-help book without email support but with a weekly information email (TL-I); and a waiting list control group (WL). Outcomes will be assessed at baseline (T0), post-test (around 3 months after baseline; T1), and at 6 (T2) and 12 months (T3) after baseline. All measurements will be self-reported and gathered via email with a link to a personal questionnaire built with Qualtrics software [42]. The design and procedures of this study were approved by the Ethics Committee of the University of Twente in The Netherlands (no. 13212).

Participants

Participants will be recruited from the general population in The Netherlands using newspaper advertisements. The recruitment messages will be positively framed: (1) "Get the best out of yourself and improve your resilience and well-being with a free self-help course", and (2) "Become happy and stay happy? Improve your resilience and well-being with a free self-help course".

Interested participants will be directed to a website with extensive information about the study and an application form. After applying, participants will be sent a personal link to a screening questionnaire on their specified email address.

Participants who open the personal link will be asked to give online informed consent. If no informed consent is given, participants will be diverted to the information website and will not be able to participate in the study. If informed consent is given, participants will fill out the screening questionnaire before the start of the study. Figure 1 shows the intended flow-chart of participants.

Adults aged 18 or above with low or moderate levels of well-being without moderate or severe clinical symptomatology are eligible for this study because previous studies have shown that these individuals might search for happiness [41] and could boost their mental health by elevating the level of well-being [7,8]. Other inclusion criteria are a sufficient internet connection, a valid email address, and a willingness to invest an average of 4 hours per week for 8-12 weeks. In the screening questionnaire, the Mental Health Continuum Short Form (MHC-SF) will be used to assess the level of well-being and the Hospital Anxiety and Depression Scale (HADS) will be used to assess the level of clinical symptomatology. Participants will be excluded from the study if they score 4 or 5 (range 0-5) on at least 1 of the 3 emotional well-being items in combination with a score of 4 or 5 (range 0-5) on at least 6 of the 11 social and psychological well-being items of the MHC-SF, which is operationalized as flourishing (ie, high levels of well-being) [13,43]. Participants will also be excluded if they score 10 or higher (range 0-21) on the depression scale and/or on the anxiety scale of the HADS, which indicates individuals with moderate or severe clinical symptomatology [44]. Participants who will be excluded from the study will be notified by email because, (1) they are already flourishing, or (2) they probably have at least moderate depression or anxiety symptoms. The latter group will receive their specific scores and their meaning on the HADS and will be advised to talk to their general practitioner when symptoms persist or increase. After screening, the remaining participants receive a personal email link to the baseline questionnaire.

Figure 1. Design of the study and intended flow-chart of participants.
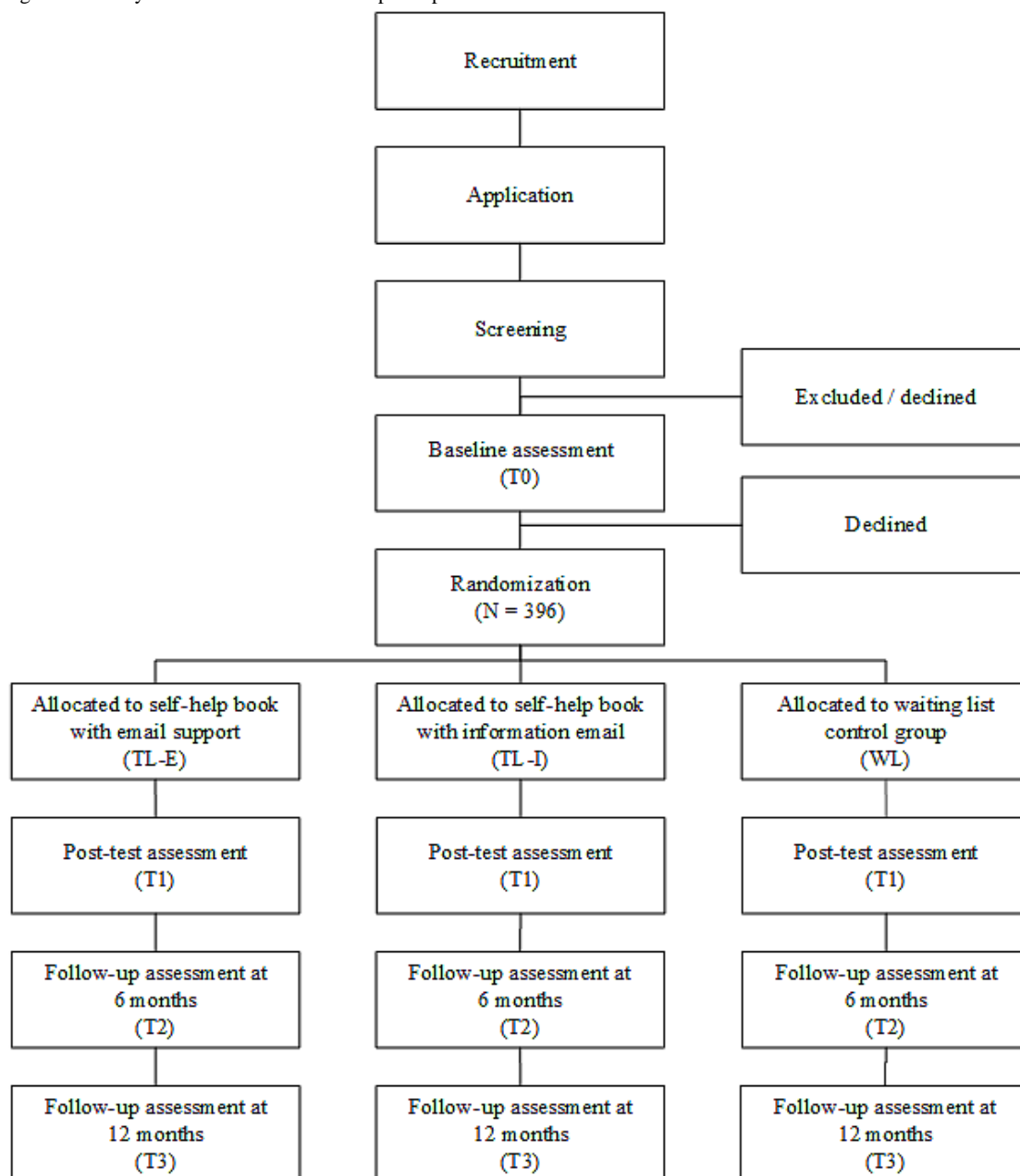
Randomization

Randomization will be conducted after all eligible participants complete the baseline questionnaire, with 396 participants being randomly assigned to 1 of the 3 groups (allocation ratio, 1:1:1). Randomization will be stratified by gender and educational level (ie, low, medium, high) using a computerized random number generator created with Excel. This is an automated process with no interference from the investigators.

Interventions

This study will use the self-help book, "This is your life" [40] in both experimental conditions. This book is mainly based on the overarching and comprehensive well-being theory of Seligman [10] and Ryff's theory of psychological well-being [19]. The book consists of 8 modules on 6 key components in positive psychology: positive emotion; discovering and using strengths; optimism and hope; self-compassion; resilience and post-traumatic growth; and positive relations (Table 1). Each module contains psycho-education derived from specific theories and empirical evidence in positive psychology and related research areas. Each module also contains a number of positive psychology exercises, ranging from 3-10 per module. Most of these exercises are evidence-based, such as the "three good things exercise" [17,18] and "imagine your best possible self" [45-47]. All modules are, in theory, effective independent strategies for enhancing well-being. Participants in the experimental groups will receive the self-help book by regular mail, accompanied by a time schedule for reading the book and practicing the recommended exercises (see Table 1). Participants will be instructed to read one module per week—except for module 2, which can be spread out over two weeks—in sequential order, and to practice the recommended exercises of that module. If the participant has more time, he or she can re-read the module and practice other exercises of that module. Participants will be encouraged to invest the most time in the exercises that feel most beneficial to them. Participants will have 8-12 weeks to complete the 8 modules of the book to take holidays and other circumstances into account. When participants in the TL-E group need more than 9 weeks to complete the book, in consultation with the counselor, they will not receive email support in the weeks they are not in the position to work on a module. Participants in the TL-I group will receive weekly information emails during the first 9 weeks and will be asked to read the emails in chronological order in the weeks they actually work on a module. On average, participants in the experimental groups will be expected to invest 4 hours per week during the intervention period.

Table 1. Content of "This is your life" and recommended exercises for participants in the experimental conditions.

Module	Recommended exercises	Theoretical background
1. Positive emotions	• Diary of pleasant emotions: What happened, who was there, what did you feel, what did you thought? • Three good things: Think about three things that went well today and savor those moments.	Fredrickson, 1998 [48]; Fredrickson, 2001 [49]; Fredrickson, 2009 [50]
2. Discovering strengths	• Overview of your strengths: Which of the 47 strengths do you have and which of these give you energy and pleasure? • Identify your strengths I: Answer the 10 questions (ie, who inspires you?) that will help you to discover your strengths. • Identify your strengths II: Which strengths do you recognize in answering the 10 questions? • Vision of others: Ask 3-5 people about your top 5 strengths with examples from daily life. • Top 5 strengths: Based on all previous exercises, choose your top 5 strengths that also give you energy and pleasure.	Linley et al., 2010 [51]; Linley and Harrington, 2006 [52]
3. Use of strengths, flow	• Change "must" into "want": Make a list of things you don't like but must do. What are underlying intrinsic motivations? • Flow: Have you experienced flow and why? • Flow at the moment: How much flow did you experience the preceding week? When, how? • Challenge yourself: How can you create more flow in your life? Use your strengths in a new way.	Csikszentmihalyi, 2001 [53]
4. Optimism, hope	• ABC-Diary: What do you think and do when something negative happens? How can you challenge favorite pessimistic thoughts? • Imagine your best possible self: Visualize yourself in the personal, relational, and professional domain.	Carver et al., 2010 [54]; Scheier and Carver, 1992 [55]; Seligman, 1990 [56]
5. Self-compassion	• Wish yourself something good: Be mindful and identify your greatest need at this moment. Use your inner voice to repeat your compassionate wish. • Develop a compassionate inner voice: Write 5 minutes about situations in the preceding week wherein you showed self-compassion.	Gilbert, 2009 [57]; Neff, 2003 [58]; Neff and Germer, 2012 [59]
6. Resilience	• Coping style: Take the test to identify your prominent coping style(s). • Expressive writing: Write 15 minutes on at least 4 days about emotions, thoughts, and feelings around a negative or positive event. • Needs: What are your specific needs at this moment? Who should know your needs?	Joseph, 2011 [60]; Joseph and Linley, 2006 [61]; Tedeschi and Calhoun, 2004 [62]

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Module	Recommended exercises	Theoretical background
7. Positive relations (I)	• Active-constructive responding: Respond positively to good news shared by others. Use active communication skills, how does the other react? • Listen compassionately: Try to use elements of compassionate listening, such as "What feelings and needs does the other express?" • Expressing gratitude: Write a gratitude letter and/or read it aloud to the person you are thankful to.	Gable et al., 2004 [63]; Reis and Gable, 2003 [64]; Reis et al., 2010 [65]; Rosenberg, 2009 [66]
8. Positive relations (II)	• Relaxation/meditation: Relax by doing a "body scan", physical exercise, or "stand like a tree". • Reflect on your needs: What are your intrinsic goals, needs and motives? Do you live those needs and why (not)? • Acts of kindness: Rejoice somebody by performing an unexpected act of kindness or by doing volunteer work.	Bloom, 2011 [67]; Otake et al., 2006 [68]

Email Support

The TL-E group will receive weekly email support from a personal counselor. These counselors will be 5 senior positive psychology students of the University of Twente who completed a course on email counseling in which they are trained to guide a fellow student on using the self-help book "This is your life". Each of these will guide 25 participants and the remaining participants will be guided by the first author (MS). Participants will be randomly assigned to 1 of the 6 counselors in the same manner as the randomization procedure outlined above (eg, stratified by gender and educational level). Additional training will be given in a 1-day workshop and via weekly supervision by authors MS and EB and a clinical psychologist. In these meetings, random emails of the counselors will be discussed to increase treatment integrity, and counselors can ask specific questions to the supervisors. The personal counselors will introduce themselves in an initial email sent the day participants receive the self-help book. The participants will be asked to introduce themselves before the email sessions start. Participants will be instructed to send a weekly email on Sunday or Monday wherein they write about their experiences with the scheduled module. Every Wednesday, the personal counselors will answer the emails.

The main goal of the email support is to encourage the participants to read the scheduled modules and practice the recommended exercises. The email support will be more process-oriented than content focused, and will be flexible within the boundaries of the structured time schedule. The personal counselors will be instructed to provide tailored feedback on progress and process using positive reinforcement, paraphrasing, and motivational interviewing techniques (eg, "I read that you have invested quite some time in the recommended exercises of this week."; "Could it be helpful for you to practice this exercise more regularly?"; "What have you discovered when you performed the exercises?"). Specifically, counselors will use positive reinforcement for signs of awareness, insights, improvement and change (eg, "This seems a valuable experience for you, how exactly did you achieve that?; "What will be a

next sign of progress?"; "That seems like a helpful thought to me."). When there are reasons to assume that a participant has serious complaints, the participant will be referred to a general practitioner or a health care specialist. In an attempt to reduce intervention dropout, reminders will be sent to participants who do not send an email to their counselor. The first 2 reminders will be sent by the personal counselor, followed by up to 3 additional reminders sent by the researcher (MS). If a participant has completed more than 3 modules of the book, he or she will only receive reminders from their personal counselor. A final email with overall feedback on the process of the participant will be sent to all participants who complete at least 3 modules. This final email will be sent when the participant has completed all modules (between 8 and 12 weeks), when the maximum of 3 reminders has been reached by the personal counselor, or when participants are in week 12 of the study without completing all modules.

Email With Information

The TL-I group will receive a weekly email from the investigator that contains additional information about the self-help book or the study. A frequently-asked-questions (FAQs) format will be used for this email (eg, "Q: How can I find the time to practice the recommended exercises?" "A: Select a good moment in your daytime routine, so that practicing the exercises can become a habit. For example, during lunch time, directly after work or half an hour before bed time."). The information emails will be a work-in-progress during the study because FAQs by participants in the TL-E group will also be integrated into the information emails. Participants will be instructed to read the weekly emails and not to respond to the investigator.

Control group

Participants in the control group will be on a waiting list for the first 6 months of the study and will receive the self-help book after they complete the 6-month follow-up assessment. For the sake of comparison at the long-term follow-up, the control group will also receive the information emails in the same way provided in the TL-I group.

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Measures

For a brief overview of all outcome measures and assessment times, see Table 2. Because one of our aims is to examine the working mechanisms underlying the intervention, which requires assessing all included positive psychology components, measures are selected on brevity and availability in the Dutch language.

Table 2. Intended questionnaires and assessment times.

Questionnaire	Measurement	Screening	T0 Pre-test	T1 Post-test	T2 Follow-up[a]	T3 Follow-up[b]
MHC-SF	Well-being/ flourishing	X	X	X	X	X
FS	Social-psychological well-being		X	X	X	X
HADS	Symptoms of depression and anxiety	X			X	X
m-DES	Positive and negative emotions		X	X	X	X[d]
SUS	Use of strengths		X	X	X	X[d]
LOT-R	Optimism		X	X	X	X[d]
SCS-SF	Self-compassion		X	X	X	X[d]
BRS	Resilience		X	X	X	X[d]
SPR	Positive relations		X	X	X	X[d]
EPQ-RSS	Extraversion and neuroticism		X			
NEO-FFI	Conscientiousness		X			
MCQ	Direct medical consumption costs		X	X[c]	X[c]	X
PCQ	Non-medical productivity costs		X			X
Brugha Life-events	Positive and negative life-events		X	X	X	X
CSQ-8	Client satisfaction			X[d]		
Process evaluation	Invested time, adherence, positive changes			X[d]		X[e]
	Level of (continued) use					X
Demographics	Gender, age, education, marital status, living situation, ethnicity, daily activities	X				

[a] 6 months after T0.

[b] 12 months after T0.

[c] Only medical health care costs are assessed, not medication costs.

[d] Only assessed in the experimental groups, not the control group.

[e] Only assessed in the control group, not the experimental groups.

Primary Outcome

Well-being is the primary outcome of this study, measured with the 14-item MHC-SF and the 8-item Flourishing Scale (FS). The items of the MHC-SF can be divided into 3 subscales: emotional well-being (3 items), social well-being (5 items), and psychological well-being (6 items). All items can be answered on a 6-point answer scale from 0 (never) to 5 (almost always). A mean score will be computed separately for the total scale and the 3 subscales. The MHC-SF has excellent psychometric properties [5,13]. The FS measures social-psychological well-being with 8 positively formulated items. Participants rate the items on a 7-point scale from 1 (strongly disagree) to 7 (strongly agree). Total summed scores can range from 8-56. The FS has demonstrated good internal consistency and construct validity [69].

Secondary Outcomes

The MHC-SF is also used to measure the amount of flourishing [13,43]. Flourishers score 4 or 5 on 1 or more items on the emotional well-being subscale in combination with a score of 4 or 5 on 6 of the 11 remaining items. Languishers are those with scores of 0 or 1 on these subscales, and individuals who are neither flourishing nor languishing are labelled as moderately mentally healthy.

Depressive and anxiety symptoms will be measured with the HADS [44]. Each subscale consists of 7 items, 14 items in total. Answer categories differ per item, but all items have 4 answer categories with scores ranging from 0-3. Item scores are summed into a total scale score for anxiety (range 0-21) and depression (range 0-21). The HADS is a widely validated instrument and can be used as a screening instrument in different populations [70,71]. A cut-off score of 10 and above on each subscale is

generally used to identify individuals with at least mild depressive or anxiety symptomatology [44,70].

Positive and negative emotional states will be assessed with the modified Differential Emotions Scale (m-DES), which measures 8 groups of positive emotions and 8 groups of negative emotions on a 7-point scale (1 = not at all, 7 = very intense). Total mean scores will be computed. Although the DES is validated and widely used, the m-DES has not yet been validated [72].

The Strength Use Scale (SUS) is a 14-item scale to assess participants' use of their strengths in a variety of settings [73]. Scores range from 1 (strongly disagree) to 7 (strongly agree) with a total summed score of 14 to 98. The SUS possesses high internal consistency and long-term stability [74].

Optimism will be assessed with the 10-item Life Orientation Test-Revised (LOT-R) [75,76]. Items are rated on a 5-point scale ranging from 0 (strongly disagree) to 4 (strongly agree) and indicate participants' evaluation of positive expectations about the future. There are 4 filler items which are excluded from analysis. Scores on the 6 items are summed into a total optimism score ranging from 0-24. The LOT-R has shown predictive and discriminant validity [75].

Self-compassion will be assessed with the Self-Compassion Scale-Short Form (SCS-SF), which consists of 12 items. Participants rate the items on a 7-point scale ranging from 1 (rarely or never) to 7 (almost always) with a total summed score ranging from 12-84. The SCS-SF has proven to be a valid equivalent of the long-form version [77] developed by Neff [78].

The 6-item Brief Resilience Scale (BRS) [79] will be used to evaluate the level of resilience, which is the ability to bounce back and cope with stress or negative life-events. Items are rated on a 5-point scale from 1 (strongly disagree) to 5 (strongly agree) with total mean scores ranging from 1 to 5. The psychometric properties are good [79].

Although positive relations will be assessed with 1 item of Ryff's scales of psychological well-being [19] in the MHC-SF, we will also measure the original Subscale of Positive Relations (SPR) as proposed by Ryff [19]. This subscale contains 9 items and a 6-point scale ranging from 1 (strongly disagree) to 6 (strongly agree) [80] and a total summed score that range of 9-54.

Tertiary Outcomes

The personality traits extraversion and neuroticism will be assessed with the Eysenck Personality Questionnaire-Revised Short Scale (EPQ-RSS) [81-83] and conscientiousness with the NEO Five Factor Inventory (NEO-FFI) [84]. These personality surveys are widely used and validated. Direct medical and non-medical costs will be measured with the Dutch Medical Consumption Questionnaire (MCQ) [85] and 5 items from the Productivity Cost Questionnaire (PCQ) [86]. Other variables that will be assessed are positive and negative life-events with a scale based on the Brugha Life-events section [87], and the socio-demographics of gender, age, educational, marital status, living situation, ethnicity, and daily activities.

Process Outcomes

The Client Satisfaction Questionnaire-short form (CSQ-8) [88,89] will be used to determine overall satisfaction. Additional questions will be asked about time spent with the intervention and self-help book modules, adherence to each module, and significant positive changes since they started with the intervention. The latter question is based on the Client Change Interview Protocol [90]. All email correspondence between participants and personal counselors will be retrieved and saved for content analysis.

Sample Size

Well-being is the primary outcome used for the power calculation. We expect to detect a significant effect on well-being between the experimental groups TL-E and TL-I compared to the WL group. Based on recent meta-analyses [17,18] and a previous comparable study [38], we expect to find a standardized effect size on well-being of 0.40 or larger. The targeted sample size is 99 participants per group (297 in total) to provide a statistical power of $(1 - \beta)$ = 80% and a 5% significance level (two-tailed). To allow a study dropout rate of 25%, we need 132 participants in each condition and 396 participants in total for the trial.

Statistical Analyses

The Consolidated Standards of Reporting Trials (CONSORT) statement [91] will be used to report the results. Independent t tests and Chi-square statistics (X^2) will be used to examine baseline differences between the study groups. Non-significant socio-demographic differences at baseline will indicate successful randomization. Internal consistency of the constructs will be determined using Cronbach's alpha. To examine the efficacy of the intervention, intention-to-treat analyses will be conducted by including all participants in the analyses who have been randomized. The Expectation Maximization (EM) method will be used to impute all missing data on the continuous measures of T1, T2 and T3. This method imputes the data by maximum likelihood estimation using the observed data in an iterative process [92]. The intention-to-treat analysis will be compared with a completers-only analysis.

To examine significant differences between the 3 groups, we will perform repeated measures ANOVA in a 3 (group) x 3 (time) design with well-being (MHC-SF and FS) as the primary dependent variable and positive/negative emotions (mDES), the use of strengths (SUS), optimism (LOT-R), self-compassion (SCS-SF), resilience (BRS), and positive relations with others (SPR) as the secondary dependent variables. Significant time x group interactions will be tested with Tukey' post hoc tests. Within-group effects (Cohen's d) will be calculated by subtracting the mean post-test or follow-up score from the mean baseline score and dividing the difference by the pooled standard deviation. Between-group effects (Cohen's d) will be calculated by subtracting the mean post-test or follow-up score of the experimental group from the mean post-test or follow-up score of the control group, and dividing the difference by the pooled standard deviation [93]. These effect sizes are used to gain insight into the relevance of the significant effects. To examine changes in the amount of flourishers, languishers, and

moderately mentally healthy (MHC-SF), descriptive statistics will be used. Changes in categories will be tested with X^2-statistics.

Mediator and moderator analyses will be performed as described by Hayes [94,95]. Mediator analyses will be conducted to investigate which of the specific components of the intervention—positive emotion, use of strengths, optimism, self-compassion, resilience, and positive relations—contribute to its efficacy and mediate overall well-being. Moderator analyses will be conducted to examine which specific subgroups will improve most (or least) on well-being and flourishing from participation in one of the experimental groups. The independent variables of gender, educational level, life-events, personality traits, level of adherence to the intervention, and participation satisfaction will be entered as moderators in regression analyses.

A cost-effectiveness analysis will be conducted from a societal perspective. For each condition, the mean annual health care costs (MCQ), costs due to productivity losses (PCQ), and intervention costs will be calculated on an annual per capita basis for the reference year 2014. All costs will be expressed in Euro (€). The incremental cost-effectiveness ratio (ICER) will be calculated using a bootstrap approach. Then, a cost-effectiveness acceptability curve will demonstrate the probability of the cost-effectiveness of TL-E and TL-I compared to WL, for a range of willingness-to-pay (WTP) ceilings. All tests will be two-sided and will use alphas of 0.05. All data-analyses will be performed with SPSS version 21.0 or higher.

Results

The data collection will be completed in June 2015.

Discussion

This study will investigate the short- and long-term efficacy of a multicomponent PPI (ie, self-help book with tailored email support) on well-being and flourishing. Mediator and moderator analyses will be conducted to explore which theoretically relevant hedonic well-being and eudaimonic well-being components included in the self-help book appear to contribute to its efficacy, and who will benefit most from the intervention. The study will be conducted in The Netherlands in a sample with low or moderate levels of well-being without moderate or severe clinical symptomatology. The results from this study will contribute to the knowledge of evidence-based PPIs, in particular multicomponent PPIs, and will be valuable for public mental health services and governments who are increasingly interested in enhancing well-being in the general population [96,97].

There could be several limitations that need to be considered in advance. First, our results might not be generalizable to the general Dutch population, since we will use a self-selected sample and apply exclusion criteria on the level of well-being and clinical symptomatology. It is not unlikely that our open recruitment with advertisement in national newspapers will attract mostly highly-educated women. However, we will use a randomization procedure stratified by gender and education,

which will create equal distribution of these characteristics to each group and therefore not harm the internal validity of our study. Second, non-adherence to the intervention and drop out from assessments (incomplete data) could occur. Both types of attrition are closely related and may bias our results [98]. Reasons for non-adherence and dropout could be related to individual characteristics (ie, low-educated individuals might find the intervention and/or assessments too difficult), characteristics of the intervention (ie, individuals in the experimental conditions receive the self-help book after baseline and are unaware of the content of the book and type of exercises when they apply for the study), and characteristics of the study (ie, participants will be given instructions and a time schedule) [98]. To gain insight on adherence in our study, participants will be asked about time spent on each module, and the personal counselors will gather reasons for non-adherence mentioned in the email correspondence. Although we expect to find higher adherence rates for individuals in the TL-E condition than has previously been found for Web-based multicomponent PPIs [24,25,27], it could be lower than in face-to-face multicomponent PPIs [20,22,23]. However, our study can only draw conclusions about the comparison of the self-help book with email support to the self-help book without email support. Differences in adherence and efficacy between face-to-face support, email support, and no support warrant attention in future research. Furthermore, to prevent low power due to drop out, we have taken into account an attrition rate of 25% in our power analysis. We will also conduct dropout analysis to identify any selectiveness or characteristics of attrition that may be relevant for real-life implementation of the intervention. Third, the use of senior positive psychology students for the email support can be a risk for the professionalism of our intervention because these students are unexperienced psychologists. We will try to reduce this risk by providing extensive supervision from experienced psychologists and by only selecting students who are thoroughly trained in email support and who have practiced the self-help book. On the other hand, the guidance is primarily process-oriented and advanced clinical counseling skills are therefore not considered necessary. The benefit of using students as counselors is that the intervention costs will be very low. If proven effective, it could be even more effective when implemented in a mental health service with experienced and professional counselors, although this could be disadvantageous for its cost-effectivity. Nevertheless, this needs to be tested in future research.

Our study will be the first to investigate the efficacy and working mechanisms of a theory- and research- based multicomponent PPI in the form of a self-help book with email support to enhance well-being and flourishing in the general population. Our study will add to the existing knowledge in that we (1) focus on well-being and flourishing instead of mental illness, (2) use a multicomponent intervention instead of a single-component intervention, (3), integrate some advantages of face-to-face multicomponent PPIs with web-based multicomponent PPIs by using a self-help book with asynchronous and tailored email support, (4) examine the intervention in a population with low or moderate levels of well-being without moderate or severe clinical symptomatology instead of a population with at least moderate clinical

symptomatology without any criteria on the well-being dimension of the two-continua model of mental health, and (5) measure and analyze each specific well-being component that is included in the self-help book: positive emotion, use of strengths, optimism, self-compassion, resilience, and positive relations. Taken together, our results will contribute to a new field of multicomponent PPIs for enhancing well-being and flourishing in the general population and highlight a new target population for mental health promotion. If proven effective, our results can be specifically of interest for public mental health and primary care because these health care fields are expanding, while specialist mental health care is diminishing, at least in The Netherlands.

Conflicts of Interest

None declared.

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Abbreviations

ANOVA: analysis of variance
BRS: Brief Resilience Scale
CONSORT: Consolidated Standards for Reporting Trials
CSQ-8: Client Satisfaction Questionnaire-short form
EM: expectation maximization

EPQ-RSS: Eysenck Personality Questionnaire–Revised Short Scale
FS: Flourishing Scale
HADS: Hospital Anxiety and Depression Scale
ICER: incremental cost-effectiveness ratio
LOT-R: Life Orientation Test-Revised
MCQ: Medical Consumption Questionnaire
m-DES: modified Differential Emotions Scale
MHC-SF: Mental Health Continuum-Short Form
NEO-FFI: NEO Five Factor Inventory
PCQ: Productivity Cost Questionnaire
PERMA: positive emotion, engagement, relationships, meaning and accomplishment
PPI: positive psychology intervention
RCT: randomized controlled trial
SCS-SF: Self-Compassion Scale-Short Form
SPR: Subscale of Positive Relations
SPSS: Statistical Package for the Social Sciences
SUS: Strengths Use Scale
TL: "This is your life"
TL-E: "This is your life" with email support
TL-I: "This is your life" with an information email
WL: waiting list control condition
WTP: willingness-to-pay

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Original Paper

The Walking Interventions Through Texting (WalkIT) Trial: Rationale, Design, and Protocol for a Factorial Randomized Controlled Trial of Adaptive Interventions for Overweight and Obese, Inactive Adults

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Abstract

Background: Walking is a widely accepted and frequently targeted health promotion approach to increase physical activity (PA). Interventions to increase PA have produced only small improvements. Stronger and more potent behavioral intervention components are needed to increase time spent in PA, improve cardiometabolic risk markers, and optimize health.

Objective: Our aim is to present the rationale and methods from the WalkIT Trial, a 4-month factorial randomized controlled trial (RCT) in inactive, overweight/obese adults. The main purpose of the study was to evaluate whether intensive adaptive components result in greater improvements to adults' PA compared to the static intervention components.

Methods: Participants enrolled in a 2x2 factorial RCT and were assigned to one of four semi-automated, text message–based walking interventions. Experimental components included adaptive versus static steps/day goals, and immediate versus delayed reinforcement. Principles of percentile shaping and behavioral economics were used to operationalize experimental components. A Fitbit Zip measured the main outcome: participants' daily physical activity (steps and cadence) over the 4-month duration of the study. Secondary outcomes included self-reported PA, psychosocial outcomes, aerobic fitness, and cardiorespiratory risk factors assessed pre/post in a laboratory setting. Participants were recruited through email listservs and websites affiliated with the university campus, community businesses and local government, social groups, and social media advertising.

Results: This study has completed data collection as of December 2014, but data cleaning and preliminary analyses are still in progress. We expect to complete analysis of the main outcomes in late 2015 to early 2016.

Conclusions: The Walking Interventions through Texting (WalkIT) Trial will further the understanding of theory-based intervention components to increase the PA of men and women who are healthy, insufficiently active and are overweight or obese. WalkIT is one of the first studies focusing on the individual components of combined goal setting and reward structures in a factorial design to increase walking. The trial is expected to produce results useful to future research interventions and perhaps industry initiatives, primarily focused on mHealth, goal setting, and those looking to promote behavior change through performance-based incentives.

Trial Registration: ClinicalTrials.gov NCT02053259; https://clinicaltrials.gov/ct2/show/NCT02053259 (Archived by WebCite at http://www.webcitation.org/6b65xLvmg).

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Introduction

Overview

Walking is a low-cost, widely accepted physical activity (PA) associated with significant health benefits [1,2]. However, a meta-analysis by Conn et al [3] found that PA interventions showed improvements of only 14.7 minutes/week (about 2 minutes/day), suggesting more potent interventions are needed. Goal setting is a key component of behavioral theories [4,5] and PA interventions [6]. Though step goals are a key modality to increase PA, differing implementation strategies impede definitive conclusions [7]. Also, inconsistencies in reward structures for goal attainment further impair best practices for behavior change. Principles of operant learning and behavioral economics have the potential to concurrently refine goal setting and incentive strategies in the behavioral sciences [8].

Percentile Shaping: Adaptive Versus Static Goal Setting

Goal setting approaches are often fixed over time, though typically vary from researcher-assigned [9-12] to participant-selected [7,13,14]. If goals include participant input, it is often to set a starting goal from a baseline value [7]. A review of goal setting approaches for weight loss using PA and diet interventions found mixed results, noting the presence of extensive methodological issues and confounders in most studies [15]. Traditionally, fixed or static goals are the same across individuals (eg, walk 10,000 steps or exercise 30 minutes daily), affording the investigator a simple but insensitive threshold to promote behavior change. A major limitation of static goals is the inherent inflexibility to accommodate the myriad influences on day-to-day behavior (eg, illness, major life events, daily, or other cyclical schedules [16]).

Adaptive goals that adjust frequently and uniquely to an individual's recent performance may be a more realistic approach to developing flexible yet challenging and attainable goals, but the task remains to standardize treatment dose across participants. Recently, intensively adaptive interventions have gained attention [16,17]. Intensively adaptive interventions require intensive (eg, daily) repeated measures of the tailoring variable(s) and target behavior. Concepts from percentile shaping may be one solution to standardize treatment dose [16,18] and through technology can be coupled with intensive repeated measures to produce intensively adaptive interventions [16,17].

Percentile shaping uses a moving window of recent performance (eg, last 9 observations or days) and a rank-order percentile algorithm to produce adaptive goals that can adjust systematically up or down daily, both within and between individuals, and over time. Percentile shaping capitalizes on the natural variation in behavior to produce personalized goals. Percentile shaping also generates inherently specific, measurable

goals that can be explicitly rewarded. Only a handful of studies have tested the use of a percentile shaping approach by providing adapting goals to increase physical activity, and none have orthogonally compared goals derived from percentile schedules with immediate versus delayed reinforcement [16,19,20].

Reinforcement Schedule: Immediate Versus Delayed

Rewarding small changes in behavior over time is important; however, types and dimensions (eg, latency, schedule) of reinforcement for goal attainment vary widely across interventions [15,16,21-23]. Principles of operant psychology [8] and behavioral economics [24] posit a temporal inconsistency in reward structures for healthy versus unhealthy behaviors. Specifically, "less healthy" behaviors tend to deliver an immediate reward (eg, physical comfort for sedentary behavior), with deleterious effects in the future (eg, lowered physical fitness contributing to heart disease). However, "more healthy" behaviors typically require an immediate cost (eg, physical discomfort for intense exercise) and require a sustained effort to experience delayed rewards (eg, improved physical fitness). As the benefits of healthier behaviors are inherently delayed, the immediate benefit of the less healthy response often wins in the economics of behavior. Interventions that attempt to tip the balance of reward in favor of healthy behaviors through immediate rewards are likely to produce more favorable and longer-term behavior change [16,24-26].

Purpose and Aims

The purpose is to present the rationale and methods from the Walking Intervention Through Texting (WalkIT) trial—a 4-month, 2x2 factorial randomized controlled trial (RCT) for inactive, overweight, and obese adults. We used a semi-automated text message system to deliver adaptive versus static goals and immediate versus delayed reinforcement. The primary aim was to evaluate whether adaptive goals and immediate reinforcement resulted in a greater change in objectively measured PA compared to the static intervention and delayed reinforcement groups. Daily step counts were measured by a Fitbit device over the course of the 4-month study to evaluate the primary aim. We hypothesized that participants in the adaptive goals and immediate reinforcement groups would increase their average steps/day more than participants in the static goals or delayed reinforcement groups. Secondary aims were to evaluate the effectiveness of the adaptive goal and immediate reinforcement interventions to improve psychological measures, aerobic fitness, and cardiometabolic risk factors.

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Methods

Overview

The WalkIT trial was a 2x2 factorial RCT conducted over 4 months. Following a 10-day baseline phase to assess usual PA levels measured by Fitbit Zip accelerometers, participants underwent simple randomization using a computerized random number generator for assignment into one of four treatment groups. Main effects of the treatment included Goal Type (adaptive vs static goals) and Reinforcement Type (immediate vs delayed reinforcement). In brief, adaptive goals and immediate reinforcement were based on a percentile-shaping algorithm that adjusted each participant's goal up and down daily based on their previous nine valid observations (usually the last 9 days) of Fitbit-measured steps. Static goals were set to the recommended 10,000 steps per day and did not change over the course of the study. Participants in the immediate reinforcement group received praise feedback and one reward point each time they met a daily goal, whereas those in the delayed reinforcement group received monthly incentives. All participants received a walking intervention with semi-automated text message–based components. Researchers monitored the text message system for non-standard messages from participants (eg, when a participant asked a question, the research staff was notified), and staff responded through the system.

The Arizona State University Institutional Review Board approved the intervention trial and all the procedures used in data collection. The study is registered as a clinical trial (NCT02053259). See Multimedia Appendix 1 for the CONSORT EHEALTH checklist [27].

Inclusion and Exclusion Criteria

Participants were generally healthy, inactive, 18-60 years old, with a body mass index (BMI) of 25-55 kg/m^2 (see Table 1 for complete list of inclusion and exclusion criteria). Initially, criteria were 18-45 years and BMI 25-45 kg/m^2, but these were increased due to interest and to meet recruitment goals. Attempts were made to contact those previously ineligible who met the expanded criteria. The criteria for determining an inactive participant was defined in two ways. First, physical activity level was screened online with the International Physical Activity Questionnaire (IPAQ) short form. We addressed the limitations of using the IPAQ (eg, recall and social desirability bias) as a pre-screening method by inviting those with ≤1300 metabolic equivalents (MET)-min/week to make an appointment for the office visit. Then, in the 10-day baseline phase prior to randomization, we provided participants with a masked Fitbit (to limit participant reactivity) and monitored wear and steps/day remotely. Inactive participants, defined as those who did not accumulate ≥10,000 steps/day on ≥5 days/week, were randomized to one treatment group. Participants were required to have basic computer literacy, daily access to a personal computer for study-related software, a mobile phone with short message service (SMS, or text) capabilities, and be willing to receive up to 3-5 text messages per day. These criteria were imperative to receiving the mobile health (mHealth) related intervention components.

Table 1. Inclusion and exclusion criteria for the WalkIT trial.

Participants	Criteria
All participants	
Home residence	Live in Maricopa County, Arizona.
Age	Between 18-60 years.
Body Mass Index	Between 25-55 kg/m^2.
Inactive	Not meeting or exceeding physical activity (PA) recommendations (ie, ≥10,000 steps/day on ≥5 days/week).
Health	No contraindicated condition(s) as assessed via Physical Activity Readiness Questionnaire (PARQ+).
Medication use	No medication(s) use that prohibits a moderate intensity physical activity program or testing.
Pregnancy status	Not currently pregnant or planning to become pregnant in the next 4 months.
Staying within study area	Not planning to leave for ≥10 days or live outside of Maricopa County in the next 4 months.
Concurrent program	Not currently in a physical activity, diet, or weight loss program (eg, Weight Watchers).
Computer access	Access to personal Windows or Mac machine on a daily basis.
Internet access	Access to email and the Internet daily.
Mobile phone access	Has mobile phone with text messaging; willing to send and receive up to 3-5 texts per day.
For vascular subset measures	
Vaso-active medications	No supplements or over-the-counter medications (eg, calcium, non-steroidal anti-inflammatories) at least 4 days prior to visits.
Female menstrual phase	Within 7 days of onset of menses or >12 months post-menopause at time of visits.

Recruitment and Setting

Recruitment emails and paper fliers included a brief study overview, notice of compensation for participating, and instructions on how to receive more information and begin the screening process. Local businesses, government agencies, social networking groups, retail outlets, and university departments were contacted to send the email notice and some elected to post physical fliers for their employees or patrons. Focused recruitment of minority populations was conducted through a free online social group advertisement.

Interested participants were directed to a secure online survey system (Qualtrics, LLC) for a pre-screening step, where they found a brief description of the study and completed the eligibility survey. Those determined to be eligible at pre-screening were contacted via phone and email for a telephone follow-up screening. Written (via online survey check box) and verbal informed consent (via the phone) were obtained at the initiation of each screening, respectively. Over the phone, the study was described in detail to participants, who were then offered opportunities to ask questions about participating and asked to clarify responses from their pre-screening responses to further assess eligibility. Qualified individuals were invited to schedule an appointment at the research office to review the study, provide written informed consent, complete baseline measures, and participate in accelerometer training.

Participants were required to reside in Maricopa County, Arizona, and to agree to make two visits to the research office located in Phoenix, Arizona, for pre- and post-intervention measurements. Rolling recruitment occurred February-August 2014 with data collection completed in December 2014. Weather was anticipated to be an influential confounder as the study occurred chiefly in the warmer months and over a monsoon season. Phoenix has a subtropical dry arid desert climate at low latitude (Köppen climate BWh). Wide variation in seasonal temperatures (eg, average high temperatures: July 41.2°C/106.2°F, December 18.9°C/66.0°F), along with monsoons (which include dust storms and flash floods), may drastically limit outdoor activity on very hot or hazardous days.

The 2013 median annual household income in Maricopa County was US $53,596 [28]. Maricopa County's majority is white, non-Hispanic (58%), with those identifying as Hispanic or Latino (30%), black (8%), and Asian (4%) being the largest racial/ethnic minority groups [28]. Statewide, 93% of households have access to at least one vehicle [28] and since 2/3 of the state population lives in the recruitment area (ie, Maricopa County), this indicates heavy reliance on car travel within our study area.

Intervention Groups

Figure 1 shows how intervention groups varied by goal type (ie, adaptive vs static goals) and reinforcement type (ie, immediate vs delayed reinforcement) in a 2x2 design. This design allowed all participants to receive a form of the treatment in an effort to reduce attrition and improve compliance over the duration of the study. During the intervention phase, all participants were asked to self-report steps nightly (ie, before midnight) via the study's interactive text messaging system that acknowledged their report and provided differential feedback based on group status and performance. The factorial design efficiently tested how each component influenced PA without the use of a "no-treatment" control group. All participants were told their ultimate target behavior was 10,000 steps on ≥5 days per week and that daily goals sent via SMS were good for 1 day only.

Figure 1. Illustration of 2x2 factorial design.
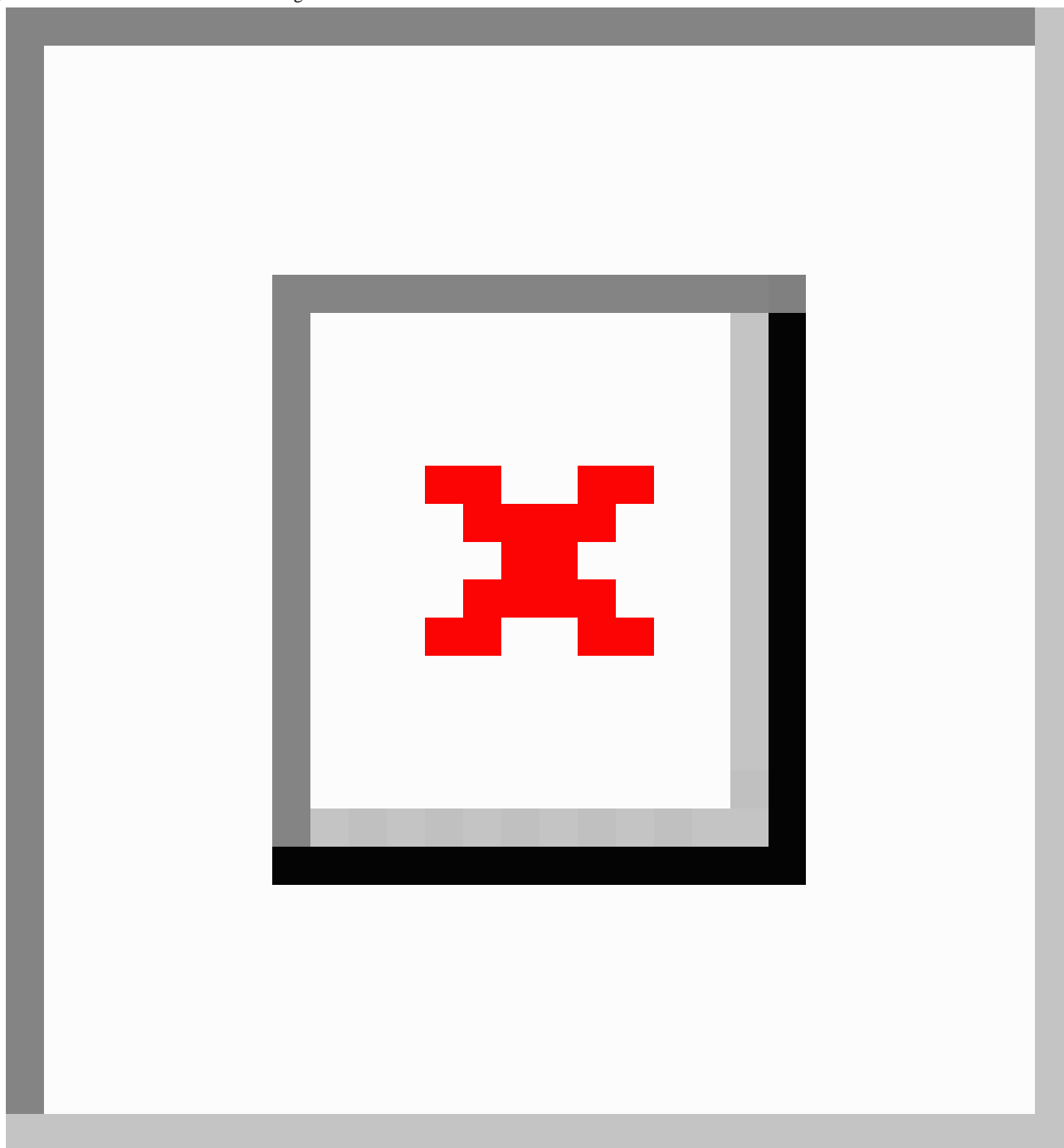
Experimental Components

Goal Setting

Participants received a goal by text message each day they self-reported their steps. The static intervention groups received the standard 10,000 steps per day goal, with immediate or delayed reinforcement for goal attainment. Participants assigned to the adaptive goal group received performance-based goals based on an algorithm developed by the research team. This algorithm was adapted from recent developments in basic science around percentile schedules of reinforcement [18,29]. The preceding nine observations (typically last 9 days) of data were used to derive a rank-ordered percentile goal. The percentile algorithm requires (1) continuous and repeated measurements of PA, (2) ranking of a sample of behavior (steps/day) from lowest to highest, and (3) calculation of a new goal based on an nth percentile criterion.

To illustrate, if a participant's step count for the preceding 9 days was 1000, 1500, 2600, 4500, 5000, 5700, 6300, 8000, 11,000, rank-ordered from lowest to highest, using a 60th percentile criteria, then 5700 steps becomes the participant's next goal. The baseline phase provides data for the first goal and then a 9-day "moving window" adapts in each new day's step count to calculate the next goal. The newest step count observation replaces the oldest step count observation. The 60th percentile was chosen based on previous PA research by Adams [16,20].

It is important to highlight that prescribed adaptive goals always fall within each participant's recent abilities due to the moving window of the last 9 days. This is distinct from the static intervention group, which receives the commonly recommended goal of at least 8000-10,000 steps 5 days/week, which may be well beyond their current abilities. Because adaptive goals adjust daily, participants were informed that each new goal is good for only one day. We believe this encourages participants to send in step reports daily unprompted.

Praise Messages

Several health behavior theories indicate that it is critical to praise improvements to develop new behavior or strengthen a habit [8,30,31]. The combination of goals and feedback was expected to provide a strong PA-shaping program. Delayed reinforcement participants did not receive contingent praise for achieving goals but did receive incentives on a monthly basis. Participants assigned to the immediate reinforcement groups received contingent differential feedback depending on whether a daily goal was met. Participants who did not meet the goal were provided a simple confirmation that steps were entered correctly and provided their next day's goal (eg, "Steps Received. Goal for 4/1/14 is 4525 steps"). This approach avoids negative messages that could be discouraging. Each time a participant met a goal, a single message from the pool of praise messages was sent to the participant (eg, "Well done! You're steps closer to good health. Goal for 4/1/14 is 4525"). Some messages used the participant's first name for enhanced personalization.

Reward Points and Incentives

Participants assigned to the delayed reinforcement groups received progressively increasing incentives each month for participating in the study (month 1=$5; months 2 and 3=$10 each; month 4=$20; total $45). Participants assigned to the immediate reinforcement groups received a point-based incentive each time they met a step goal. They had the opportunity to earn a point once per day (110 points possible) when a goal was met by the end of the day. Points were automatically exchanged for incentives ($5 for every 5 points earned) during the study. Participants self-selected their incentive from a list of retail options (eg, Amazon, iTunes, Target) or a charity (ie, the United Way), and all incentives were sent as electronic gift cards. To prevent habituation or satiation, they were allowed to change their choice at any time. Incentive amounts for delayed reinforcement groups approximate the total amount made available to the immediate reinforcement groups to control for cumulative amount of incentives.

Additional Intervention Components

Overview

All four groups received the following: (1) Fitbit Zip, (2) SMS based self-monitoring and reporting of steps per day, (3) brief health information, and (4) text message prompts. Random allocation was performed by a researcher who did not have contact with participants during screening or assessments and who knew them only by participant identification number.

Objectively Measured Physical Activity

Participants in all four groups received a commercially available accelerometer (Fitbit Zip, Fitbit Inc.) to wear for the 4-month duration of the study. Participants wore the accelerometer for at least 10 days prior to randomization to an intervention group and continued wearing for the remaining approximately 110 days. The Fitbit clips on clothing near the hip and has a small and unobtrusive form factor, thus accommodating various clothing styles to minimize non-wear. Participants were asked to wear the Fitbit during all waking hours (ie, at least 10 hours) every day for the duration of the study (ie, both the baseline and intervention phases), removing it for sleeping or in circumstances that might submerge it in water (eg, swimming). Fitbit accelerometers have excellent reliability and validity for measuring steps compared to direct observation and Actical accelerometers [32,33]. The Fitbit recorded steps and transmitted the data to the study team via the Internet to verify participants' texted step reports. The accelerometer's display was masked during baseline (to avoid participant reactivity) and then unmasked at randomization. Participants were also asked to sync their Fitbit each day using a personal computer connected to the Internet and the Fitbit sync dongle. Instructions on how to install the software were provided and demonstrated in the lab. The study team initiated and created study-managed accounts on the Fitbit website so participants were *not* able to access or view activity history, nutrition trackers, "badges" earned, social media interfaces, and other online tools that could have acted as potential confounders. To further limit access to the Fitbit website, we did not allow participants to sync their Fitbit using Fitbit's mobile phone app because this required logging into the study-managed account. Fitbit, Inc. allowed researcher access to their Application Programming Interface (API) but otherwise was not involved with this project.

Text Message System

The study's software engineer developed a proprietary automated text message system with the principal investigator. The texting system was the "front end" for participants to interact with the study and used a commercial SMS gateway service (Twilio) with a designated study SMS phone number. Participants in all four groups were instructed to send a "step report" text message to this number each night after 8 p.m. The "step report" is a daily step count in a specified format (eg, "5555 today"). The system was fully automated to recognize step reports, in a pre-determined set of natural language patterns, from all other types of messages. All SMS traffic was logged in a server database. Automated feedback was provided as per the participant's intervention assignment when a step report was obtained. Participants in the immediate reinforcement groups received a US $5 incentive email automatically from the system upon meeting a daily goal when the 5th point was earned.

Text messages were sent to all participants daily through this same study SMS number. Participants could text message "goal" at any time to receive an automated reminder of their step goal for that day. When a message was not recognized by the system (eg, "I lost my Fitbit"), it was immediately forwarded to the on-duty researcher's mobile device with a prefix of the

participant's study identification number. The system facilitated researcher-initiated messages to participants through the system's phone number (ie, all messages appeared to come from the SMS phone number regardless of the mobile device it originated from). Researchers could send texts to a specific participant or to all participants as group (see Figure 2 for a diagram of the system).

Figure 2. Schematic for intensive adaptive intervention system.
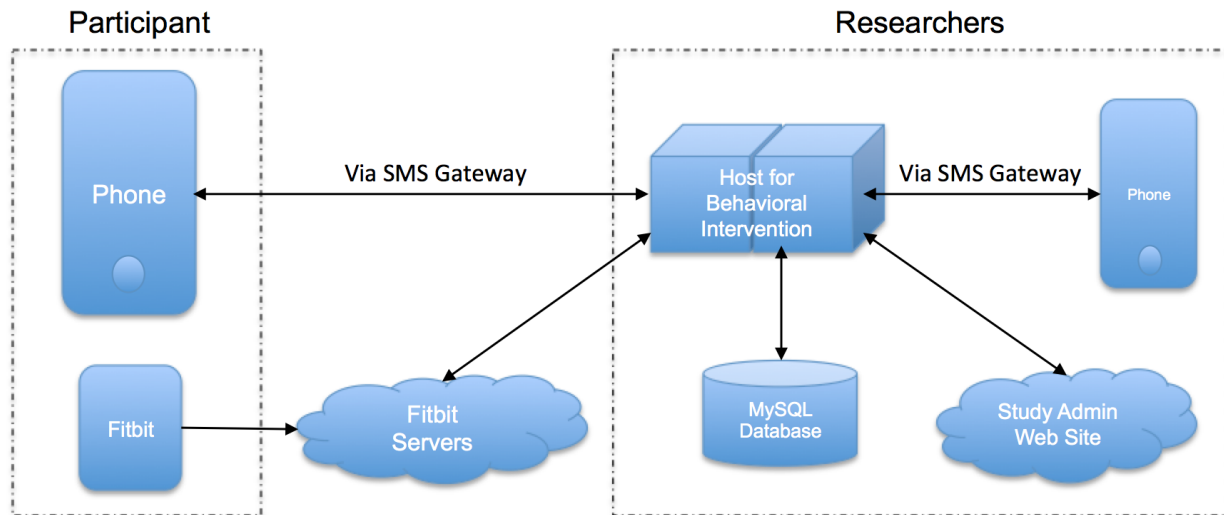
Health Information Brochures

Upon randomization, participants in all four groups were sent two brochures on PA via email. A US Health and Human Services brochure [34] presents information on overcoming barriers to being active, initiating a PA routine, and recommendations on quantity of PA to evoke health benefits. An America on the Move Foundation brochure [35] suggests 100 ways to increase steps (eg, "take your dog for a walk") throughout the day. Participants in all groups received the same materials on the first intervention day only.

Text Message Prompts

All participants in the intervention phase received daily text message prompts (≤160 characters) to encourage PA, except when Ecological Momentary Assessment (EMA) questions were administered (see Table 2). A randomly selected message (or EMA question) was sent at a random time of day between the hours of 8 a.m. and 6 p.m. local time. The research team developed a pool of messages that complemented or expanded on the health information brochures. The prompts included motivational quotes, health risks of inactivity, benefits of PA,

and encouragement to be active (eg, "It doesn't matter how old you are – it's never too early or too late to become physically active so start today; only then will you start to see results!"). Acknowledging that maintaining participation over a 4-month study is often difficult, these unvalidated prompts were primarily a mechanism to remind participants of their involvement and served as somewhat of a disguise for the experimental components under manipulation (ie, the goal-setting and reinforcement types).

Office Visits and Secondary Outcome Measures

Eligible participants visited the laboratory twice for about 2 hours each time. The initial visit included the written informed consent, physical activity PAR-Q+, the pre-measures as listed in Table 2, and training on the Fitbit and the texting system. At the second visit, the participant returned the Fitbit, completed post-measures (similar to pre-, except where noted in Table 2 [36-49]), and was debriefed regarding the study purpose. Data collection staff were blinded to treatment allocation at pre- and post-measures. However, it was impossible to blind participants as treatment groups were explained in the consent process.

Table 2. Secondary outcome measures.

Measure	Description	Pre-post	Once	Other
		Frequency		
Self-administered computerized surveys				
IPAQ long form	IPAQ long form; 31-item survey designed to capture details on domain-specific physical activity with acceptable test-retest ($r=.8$) and criterion validity ($r=.3$) [36] and intraclass correlation coefficient=.27-.71 [37].	x		
Neighborhood	Neighborhood Environment Walkability Scale abbreviated; 54-item survey to measure neighborhood characteristics [38-40].		x[b]	
Monetary choice	Delayed discounting protocol using 27-item self-administered questionnaire [41,42].		x[c]	
Satisfaction	Consumer satisfaction style questionnaire for rating experience and providing feedback; question number and type differed by intervention assignment.		x[c]	
Self-Efficacy	Single-item Ecological Momentary Assessment (EMA) of self-efficacy (0-9 Likert-type scale) delivered via SMS on 21 random intervention days. Item language based on previous work [43,44].			x
Researcher performed laboratory measures				
Height and weight	Measured using digital stadiometer and scale (Seca 284 measuring station, Seca GmbH & co. KG).	x		
Aerobic fitness	Aerobic capacity (VO_{2peak}) estimated using a submaximal continuous treadmill ramp protocol (modified Balke) and the Foster equation [45-47].	x		
Body composition[a]	Dual-energy x-ray absorptiometry (Lunar iDXA, GE Healthcare).	x		
Blood pressure[a]	Brachial and central blood pressure assessed during pulse wave analysis using Sphymocor XCEL (AtCor Medical Inc) [48,49].	x		
Arterial stiffness[a]	Carotid-femoral pulse wave velocity assessed using Sphymocor XCEL (AtCor Medical Inc) [48,49].	x		
Biochemical[a]	Venous blood samples for cardiovascular risk and inflammatory markers; post-centrifugation samples archived in aliquots at -80°C.	x		

[a]Measured in the vascular subset of participants.

[b]Measured once at initial visit; second done at follow-up only if moved during study.

[c]Measured at follow-up visit only.

Statistical Analysis

Power and Sample Size Determination

To estimate the sample size required to test the main aim of changes to steps/day, we conducted a set of simulations using a SAS macro developed by Psioda [50] and effect size estimates derived from findings reported by Adams et al [16]. Across the simulation runs, we varied the number of participants (Ns of 60-96), the magnitude of change from baseline to intervention Phase (1200 vs 1600 steps/day), magnitude of Goal Type (Static vs Adaptive) x Phase interaction effect (800 vs 1200 steps/day between-group difference in the magnitude of the Phase effect; compare to 1130 steps/day difference reported by Adams et al [16]), magnitude of Reinforcement Schedule (Delayed vs Immediate) x Phase interaction (300 vs 500 steps/day between-group difference in the magnitude of the Phase effect), and the Goal x Reinforcement x Phase interaction (150 vs 300 steps/day difference in Phase effect over and above the main effects and 2-way interaction effects). The simulations revealed that under the most conservative sets of assumptions (ie, sets comprising combinations of the smallest effect magnitudes) and an assumed attrition rate of 20%, a total initial sample size of N=100 participants (n=25 per group) would be required to have power of .80 or greater to detect hypothesized interaction effects.

Data Analysis

We plan to first examine univariate and bivariate statistics to evaluate distributional properties of outcome measures and to identify potentially relevant confounders and covariates. We will also evaluate psychometric properties (eg, internal consistency) of self-report multi-item measures of psychosocial variables. Where warranted, we will apply transformations (eg, natural log) to normalize distributions of outcome measures. We will examine main effects of and interactions among Phase (Baseline vs Intervention), Goal Type (Static vs Adaptive), and Reinforcement Type (Delayed vs Immediate) using a generalized linear mixed (ie, random effects or multilevel regression) modeling approach, with repeated assessments of PA (ie, both steps/day and minutes above various step/min cadence levels) treated as nested within persons. To minimize collinearity among interaction terms and constituent linear effects, we will use effect-coded indicators (ie, -1/1) as opposed to dummy coded (ie, 0/1) indicators for dichotomous predictors. In all models, we will account for (1) effects of covariates identified in preliminary analyses, (2) linear, quadratic, and cyclical (weekly, monthly) time effects, (3) random variation in person-level intercepts, and (4) autocorrelation among residuals. All analyses will be conducted using mixed modeling procedures in SAS 9.4 (eg, PROC MIXED, PROC GLIMMIX) and R (eg, lme4).

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We will model the main effect of each intervention component (either Goal Type or Reinforcement Type) on changes in PA (steps/day and cadence) from baseline to 4 months via Intervention x Phase (Baseline vs Intervention) interactions. The interaction between interventions will be examined via a Goal Type x Reinforcement Type x Phase interaction effect, with planned contrasts comparing PA change in the Adaptive Goal + Immediate Reinforcement condition to PA change in the other groups. Secondary analyses will be dependent on the specific research question and the most appropriate statistical methods for the design.

Missing Data

Given the potential for non-ignorable missingness in our outcome data, we will explore various strategies for mitigating potential biases in estimates and loss of statistical power due to missing data, including standard intent-to-treat approaches, full information maximum likelihood-estimated models, and analysis of multiply-imputed datasets, to be followed by sensitivity analyses assessing robustness of conclusions drawn from each approach.

Results

This study completed data collection in December 2014, but data cleaning and preliminary analyses are still in progress. We expect to complete analysis of the main outcomes in late 2015 to early 2016.

Discussion

Principal Considerations

This study integrates measures of behavior change and physiological outcomes to evaluate intervention strategies and mechanisms that improve health through adoption of walking behaviors over 4 months in an inactive, overweight/obese adult sample. The study examines the effects of two experimental factors: (1) percentile shaping to produce performance-based adaptive goals, versus typical static goals of 10,000 steps/day, and (2) reward structure using principles of behavioral economics (ie, US $1 per daily goal achieved, obtained immediately as goal achievement is reported), versus a delayed incentive. The group with a combination of static goals and delayed reinforcement approximates procedures found in practical settings (eg, a physician offering a PA brochure, recommending 10,000 steps/day, and giving a pedometer to a patient) with the difference being a predetermined monthly reward for continuing with the study—a common approach in many research studies [16,20,51,52].

Our factorial study design allows examination of the independent and joint effects of these components and explores the promise of percentile shaping and small immediate rewards to optimize behavioral interventions. Our work will contribute to the field by testing specific methodologies that link behavior change theory to practical applications. The limited body of research on shaping to improve PA shows complementary results, even with differing methodological approaches [16,19,20]. Further, employing mHealth strategies, such as SMS for treatment delivery and reward mechanisms, and wearable activity monitoring with feedback and wireless upload, enhance the overall treatment and theoretical fidelity [53] while capitalizing on the omnipresence of mobile technology.

Limitations

Potential limitations of this study include limited generalizability due to convenience sampling, although random allocation to the treatment group improves internal validity and reduces selection bias. Inclusion criteria may also limit generalizability as only generally healthy persons with a BMI classification as overweight or obese were included. Further limitations include a 4-month intervention length, which may not be long enough for some individuals to fully adopt successful walking routines. Also, without a post-intervention period follow-up, we will not be able to determine behavioral maintenance.

Strengths include the relatively large sample size, especially considering the extensive laboratory visits (approximately 2 hours each). The intensive repeated measures design is important for monitoring PA behavior to provide continual performance-based feedback via percentile shaping. We also included a large number of pre-menopausal women in the physiological measures, which is important due to underrepresentation in studies that limit inclusion to men and post-menopausal women when assessments involve biomarkers such as biochemical assays and arterial stiffness. Increasing time spent in PA is independently beneficial to health [54] especially for inactive populations and regardless of weight status [55-57]. We aim to better elucidate the link between behavior change and mediators of physiological and cardiometabolic health markers.

Conclusion

The Walking Interventions Through Texting (WalkIT) trial will further the understanding of theory-based intervention components to increase the PA of men and women who are healthy, insufficiently active, and are overweight or obese. With the overwhelming number of options interventionists have to use in health promotion, it is useful to look mechanistically at specific intervention components to optimize the treatment with economical, scalable mHealth methods. Though many studies have investigated walking interventions through a variety of methods, WalkIT is among the first directing the focus to the individual components of combined goal setting and reward structures in a factorial design to increase walking. The WalkIT trial is expected to produce results useful to future research interventions and perhaps industry initiatives, primarily focused on mHealth, goal setting, and those looking to promote behavior change through performance-based incentives.

Conflicts of Interest

None declared.

Multimedia Appendix 1

CONSORT-EHEALTH checklist V1.6.2 [27].

[PDF File (Adobe PDF File), 141KB - resprot_v4i3e108_app1.pdf]

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Abbreviations

API: Application Programming Interface
EMA: Ecological Momentary Assessment
IPAQ: International Physical Activity Questionnaire
MET: metabolic equivalents
PA: physical activity
PARQ+: Physical Activity Readiness Questionnaire
RCT: randomized control trial
SMS: short message service
WalkIT: Walking Interventions Through Texting

Treatment of Basal Cell Carcinoma Using a One-Stop-Shop With Reflectance Confocal Microscopy: Study Design and Protocol of a Randomized Controlled Multicenter Trial

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Abstract

Background: Basal cell carcinoma (BCC) is the most common cancer diagnosed in white populations worldwide. The rising incidence of BCC is becoming a major worldwide public health problem. Therefore, there is a need for more efficient management.

Objective: The aim of this research is to assess the efficacy and safety of a one-stop-shop (OSS) concept, using real-time *in vivo* reflectance confocal microscopy (RCM) (Vivascope 1500; Lucid Technologies, Henrietta, NY, USA) as a diagnostic tool, prior to surgical management of new primary BCCs.

Methods: This is a prospective non-inferiority multi-center RCT designed to compare the "OSS concept using RCM" to current standards of care in diagnosing and treating clinically suspected BCC. Patients ≥ 18 years attending our outpatient clinic at the Department of Dermatology, Academic Medical Center, University of Amsterdam, and the Department of Dermatology, the Netherlands Cancer Institute-Antoni van Leeuwenhoek Hospital (Amsterdam, The Netherlands) with a clinically suspected new primary BCC lesion will be considered for enrollment using predefined inclusion and exclusion criteria, and will be randomly allocated to the experimental or control group. The main outcome parameter is the assessment of incomplete surgical excision margins on the final pathology report of confirmed BCC lesions (either by punch biopsy or RCM imaging). Other outcome measures include diagnostic accuracy (sensitivity and specificity) of RCM for diagnosing BCC and dividing between subtypes, and throughput time. Patient satisfaction data will be collected postoperatively after 3 months during routine follow-up.

Results: This research is investigator-initiated and received ethics approval. Patient recruitment started in February 2015, and we expect all study-related activities to be completed by fall 2015.

Conclusions: This RCT is the first to examine an OSS concept using RCM for diagnosing and treating clinically suspected BCC lesions. Results of this research are expected to have applications in evidence-based practice for the increasing number of patients suffering from BCC and possibly lead to a more efficient disease management strategy.

Trial Registration: ClinicalTrials.gov: NCT02285790; https://clinicaltrial.gov/ct2/show/NCT02285790 (Archived by WebCite at http://www.webcitation.org/6b2LfDKWu).

Introduction

Basal Cell Carcinoma

Basal cell carcinoma (BCC) is the most common cancer diagnosed in white populations worldwide. The rising incidence of BCC is becoming a major worldwide public health concern [1,2]. Between 1973 and 2009, the European standardized rate quadrupled from 40 to 165 per 100,000 person-years for men and from 34 to 157 for women, most likely because of more intensive UV exposure [3]. This is supported by previous published epidemiological literature indicating that ultraviolet radiation is an important risk factor for BCC, with a significant increase among outdoor workers [4,5]. Despite the low mortality from BCC, multiple and recurring tumors confer a high morbidity and considerable burden for health care providers and health budgets. Although BCC does not seem to have a strong effect on patients' quality of life, patients suffering from BCC are definitely interested in efficacy, low recurrence rates, and cosmetic outcomes of their treatment [6]. Meanwhile, resources available at hospitals have not increased proportionally, and therefore, optimizing the effectiveness of present treatment modalities in daily dermatologic practice is necessary [7].

Clinically, BCC are characterized by small, translucent, or pearly papules, with raised teleangiectatic edges [8]. Most BCC occur in sun-exposed skin of the head and neck areas [9,10]. Sensitivity and positive predictive value of the clinical diagnosis of BCC by dermatologists have been reported to be 95.4% and 85.9%, respectively [11]. However, dividing between BCC subtypes is not always possible upon clinical assessment. To date, histological analysis of punch biopsy remains the gold standard to confirm the clinical diagnosis of BCCs and divide between the following subtypes: superficial (sBCC), nodular (nBCC), micro nodular (mnBCC) and infiltrating (iBCC). Of those, nBCC and sBCC have a less aggressive growth pattern in comparison to mnBCC and iBCC. Additionally, mixed type BCC (mtBCC) can be defined as a combination of subtypes and is frequently composed of aggressive subtypes [12]. Surgical excision remains the standard of treatment, with Mohs micrographic surgery typically utilized for high-risk lesions [13]. Based upon the histological growth pattern, BCC are surgically removed with a margin of either 3 mm (nBCC and sBCC) or 5 mm (mnBCC and iBCC) in accordance with current Dutch guidelines.

Reflectance Confocal Microscopy

The use of real-time *in vivo* reflectance confocal microscopy (RCM) has proven successful to noninvasively diagnose BCC. Various studies have demonstrated that RCM is safe and accurate (sensitivity and specificity) to diagnose BCC [14-18]. Reported sensitivity and specificity for RCM in diagnosing BCC range from 83%-100% and 79%-97%, respectively [19-25]. Furthermore, Peppelman et al and Longo et al recently reported on RCM features that might divide between nodular, micronodular, superficial, and infiltrative subtypes of BCC [24,26,27].

One-Stop-Shop

In 2012, van der Geer et al reported on the feasibility of a one-stop-shop (OSS) concept for the treatment of skin cancer patients [28]. One-stop-shop implies that on the day of the initial outpatient clinic consultation, diagnosis and treatment planning both take place. In their study, preoperative frozen section histology was used to confirm BCC diagnosis and subtype. The mean throughput time was 4 hours and 7 minutes, no complications were observed, and patient satisfaction was high [28]. Incorporating RCM as a noninvasive diagnostic tool in a BCC OSS concept for lesions suitable for conventional surgical excision might further reduce the time between clinical diagnosis and treatment, administrative workload, and costs.

Aims and Objectives

The aim of our study is to assess the efficacy and safety of the OSS concept, using real-time *in vivo* RCM (Vivascope 1500; Lucid Technologies, Henrietta, NY, USA) as a diagnostic tool, prior to the surgical management of new primary BCC, of all subtypes, in the general population. We hypothesize that compared to current standards of care, the OSS concept using RCM will not result in a significant increase of incomplete surgical excision margins on the final pathology report of confirmed BCC lesions. It is further hypothesized that in this OSS concept, RCM will have acceptable diagnostic accuracy (sensitivity and specificity) for diagnosing BCC and dividing between subtypes, throughput time will not increase, and patient satisfaction will be higher for participating subjects.

Methods

Recruitment, Screening, and Enrollment

Patients will be recruited from the outpatient clinics of the Department of Dermatology, Academic Medical Center, University of Amsterdam (AMC), and the Department of Dermatology, the Netherlands Cancer Institute-Antoni van Leeuwenhoek Hospital (AVL), second-line and third-line reference centers. Consecutive patients with clinically suspected new primary BCC will be prospectively enrolled and randomly assigned to either the experimental (RCM-OSS) or control (standard of care) group during times the study associates will be available. Clinical assessment will be performed by an experienced, board-certified dermatologist. Clinical and dermoscopy pictures of the BCC lesion will be taken by a medical photographer. Patients with multiple clinically suspected new primary BCC lesions will be included for only the lesion most suitable for conventional surgical treatment according to the following order: (1) chest, (2) extremities, and (3) head and neck area.

The inclusion criteria are the following:

1. patient with clinically suspected new primary BCC as assessed by an experienced board certified dermatologist,

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(2) age ≥18, (3) patient is willing and able to give written informed consent, (4) BCC lesion is suitable for conventional surgical excision under local anesthetics, and (5) BCC lesion has been present for at least 1 month.

2. The exclusion criteria are the following: (1) BCC lesion in a high-risk location of the face (H-zone and ears), (2) contra-indication for conventional surgical excision (primary surgical closure seems not achievable), (3) recurrent BCC lesion (BCC that has been previously unsuccessfully treated), (4) macroscopic ulcerating BCC lesions (not feasible for RCM analysis due to technical reasons), (5) patient with basal cell nevus syndrome, (6) patient treated with hedgehog inhibitor medication, (7) patient with a history of hypersensitivity and/or allergy to local anesthesia, (8) patient unavailable in the following 6 weeks (for example due to holidays or sports), and (9) patient not able to understand the procedures involved.

The investigators will enrol subjects at both study locations (AMC and AVL). Included patients with clinically suspected new primary BCC lesions will be randomly allocated to the different diagnostic procedures. The investigators will obtain the patient's consent. Each consecutive patient will be assigned a randomization number according to a computer-generated randomization list (ALEA) using random block sizes of 2, 4, 6, and 8 to ensure treatment concealment. Randomization will take place between the control and experimental group. This study will have an open label set-up. The patient and local investigator will not be blinded.

The randomization will be blinded. The pathologists analyzing the final excision specimen will be blinded to the patient's history and to the results of RCM imaging. Whenever the histology of the punch biopsy is not required in the diagnostic process of the final excision specimen, the pathologist will also be blinded for those results. After initial RCM diagnosis by the study associates (DK and YE), two independent outcome assessors (M. Ulrich, Charite Berlin in Germany and C. Longo, Modena and Reggio Emilia in Italy) analyzing the RCM images will be blinded to the patient's history and to the results of the final pathology report (reference standard).

We chose a cutoff of 95% as an acceptable radical BCC excision rate with standard of care based on our experience. Using the Miettinen and Nurminen confidence interval around the risk difference (24), with two groups of 38 patients, we will have 80% power to assess noninferiority of the OSS concept with RCM over usual care, considering an expected radical BCC excision rate of 95% in both arms, a noninferiority limit (delta) of 15%, and a one-sided alpha of 0.05.

Outcome Measures

Incomplete surgical excision on the final pathology report of a routinely processed tissue specimen of confirmed BCC lesions (either by punch biopsy or RCM imaging) is the main outcome parameter. Assessment will be performed by an experienced board-certified pathologist. The number of incomplete excisions will be compared between the experimental and control group. Other assessments of included subjects with confirmed BCC lesions (either by punch biopsy or RCM imaging) will include the following:

1. Diagnostic accuracy (sensitivity and specificity) of the RCM for BCC diagnosing and subtyping will be separately analyzed by comparing RCM diagnosis and subtype with final pathology reports of the experimental group. This will be performed by using unidentifiable saved RCM images of all included lesions of the experimental group to analyze inter and intraobservership variability in the interpretation of RCM imaging. The study associates (DK and YE) and two independent outcome assessors (MU and CL) will be blinded to the patient's history and to the results of the final pathology report (reference standard).

2. Throughput time will be assessed by the study associates and compared between the experimental and control group.

3. Patient satisfaction will be assessed postoperatively 12 weeks after excision by using a standardized web-based questionnaire for patient reported outcomes in the management of skin diseases. An adjusted version of this web-based questionnaire has previously been published to assess patient satisfaction among patients suffering from psoriasis [29]. The outcome of the questionnaire will be compared between the experimental and control group.

4. The frequency of and reasons for exclusions will be documented.

5. The frequency of interpretable, indeterminate, and intermediate tests will be documented.

6. Adverse events during the procedure will be documented.

Study Procedures

BCCs will be divided into 5 main subtypes based on the histopathological growth pattern of the final excision specimen: superficial (sBCC), nodular (nBCC), micronodular (mnBCC), infiltrating (iBCC), and basosquamous (bBCC). In the case of mixed-type diagnosis, defined as two or more single growth patterns, the histology will be classified into single subgroups determined by the most aggressive component of the pathological feature according to the descending gradation from bBCC, iBCC, mnBCC, nBCC, to sBCC. The most aggressive component will determine the excision margin (5 mm versus 3 mm).

After obtaining written informed consent, the screening will be completed. Patients with clinically suspected new primary BCC lesions will be randomly allocated to the following regimes:

1. Experimental group (N=38): Clinically suspected new primary BCC lesions will be diagnosed and divided into subtypes using RCM imaging (Vivascope 1500; Lucid Technologies, Henrietta, NY, USA) according to a standardized protocol [24,26,27] (Table 1). After diagnosis, excision of BCC lesions with adequate margins will be performed on the same day at the Department of Dermatology according to the one-stop-shop concept. Clinically suspected primary BCCs that are not confirmed by RCM will also receive surgical treatment with a margin of 3 mm.

2. Control group (N=38): Clinically suspected new primary BCC lesions will be diagnosed and divided into subtypes according to current standards of care. A conventional 3 mm punch biopsy will be performed in the most elevated part of the lesion using local anesthetics (1%

xylocaine/adrenaline). A biopsy specimen will be analyzed by a pathologist (within 2 weeks). After diagnosis, excision of the BCC lesions with adequate margins will be performed within the following 4 weeks according to current standards of care. Clinically suspected primary BCCs that are not confirmed by punch biopsy will also receive surgical treatment with a margin of 3 mm.

The study design incorporated five parts. First, screening took place. Second, intake involved the following steps: written informed consent, intake, randomization, and photo documentation. Third, allocation to the experimental or control group consisted of (1) assessment of diagnosis and subtyping of clinically suspected new primary BCC, and (2) assessment of surgical margins. Fourth, surgical excision of the lesion took place: the excised surgical specimen was assessed by the pathologist and an assessment of throughput time was conducted. Finally, a routine 12-week postoperative control visit was conducted, involving an assessment of patient satisfaction using the web-based questionnaire (Multimedia Appendix 1).

Table 1. Expected RCM features of different BCC subtypes as previously reported in the literature.

Subtype	Epidermis	DEJ[a]	Upper dermis
sBCC	Epidermal streaming	• cords connected to the epidermis that may occasionally display clefting and peripheral palisading of nuclei OR • dark silhouettes embedded in stroma of thickened collagen • dilated blood vessels coursing parallel to en-face plane of imaging	thin blood vessels parallel to the en-face plane of RCM imaging
nBCC	Possible ulceration	• increase in vascular diameter without cords connected to the epidermis	rounded to polycyclic basaloid bright tumor islands (*large in size*) with peripheral palisading of nuclei and surrounding dark clefting; stroma of thickened collagen
mnBCC	Possible ulceration	• increase in vascular diameter without cords connected to the epidermis	rounded to polycyclic basaloid bright tumor islands (*smaller in size*) with peripheral palisading of nuclei and surrounding dark clefting; stroma of thickened collagen
iBCC		• increase in vascular diameter without cords connected to the epidermis	the absence of small or big tumor islands
bBCC		• no features previously reported	no features previously reported

[a]dermal epidermal junction

Data Analysis

Data will be recorded on data entry forms and will be entered in a computer system for subsequent tabulation and statistical analysis. The data will be handled confidentially and anonymously. Furthermore, all information relevant to the treatment will be recorded in the electronic medical file.

All data will be collected and transferred to a Microsoft Excel database. The statistical analysis will be performed at the AMC using SPSS version 21.0. We will calculate the observed difference as the proportion of radical BCC excisions in the care-as-usual arm minus this proportion in the OSS with RCM arm, and calculate a one-sided 95% (or two-sided 90%) confidence interval for this difference using the Miettinen and Nurminen method [30]. The inferiority hypothesis will be rejected when the upper limit of this confidence interval does not exceed 15%. Side effects will be described per item.

Results

This is an investigator-initiated unfunded prospective open-label noninferiority randomized controlled multicenter trial.

Development of the project commenced in fall 2012, and the study protocol has been approved by the ethics committee at the coordinating center (AMC, METC 2014_244) and by the local Institutional Review Board at the participating center (AVL) in fall 2014. This trial has also been registered publically at ClinicalTrials.gov (identification number: NCT02285790). Patient recruitment started in February 2015, and the expected date of completion is fall 2015.

The study is being conducted according to the principles of the Declaration of Helsinki (Fortaleza, Brazil, October 2013) and in accordance with the Medical Research Involving Human Subjects Act (WMO) and other relevant guidelines, regulations, and acts.

Discussion

BCC is the most prevalent skin cancer, and its prevalence is increasing [1]. Histological analysis of punch biopsy remains the gold standard to confirm a clinical diagnosis of BCC and dividing subtypes. However, due to the rising incidence of BCC, there is a need for more efficient, noninvasive methods of

diagnosis. Incorporating RCM as a noninvasive diagnostic tool in a BCC OSS concept for lesions suitable for conventional surgical excision, in concordance with current Dutch guidelines, might reduce time between clinical diagnosis and treatment, administrative workload, and costs. Surgical treatment of BCC is generally performed under local anesthesia, which makes it suitable for an OSS approach.

Subjects participating in the study will be informed and will have to provide written informed consent prior to enrollment. Study participation will not result in additional follow-up visits other than clinically required 3 months postoperative.

Real-time *in vivo* RCM uses a confocal microscope to noninvasively image a thin surface of the skin at high resolution directly without the need for invasive biopsies. The diagnostic procedure itself is painless and no side effects have been reported. Outcome measures involve routinely processed surgical specimens after excision, patient satisfaction, calculation of throughput time, and analyzing diagnostic accuracy of the RCM procedure in subtyping BCC lesions. The overall burden of the study is minimal. A possible inconvenience for participating patients in the experimental group is that

specific features for BCC subtyping are still being established. Therefore, a potential side effect for those patients may be less accurate subtyping of BCCs resulting in less adequate surgical margins. At the same time, RCM imaging may be of additional value in scanning the complete lesion, which potentially could prevent missing a more aggressive part of a tumor in contrast to a biopsy.

Thus, there is a potential benefit for the participating subject, namely noninvasive confirmation of clinically suspected BCC lesions followed by direct surgical treatment. Considering the relatively quick and simple procedure, noninvasiveness of the diagnostic method, and the one-stop-shop concept of diagnosing and treating BCC at the same consultation, the balance between burden, possible side effects, and prospect for improvement might be very favorable.

This RCT is the first to examine an OSS concept using RCM for diagnosing and treating clinically suspected BCC lesions. Results of this research are expected to have applications in evidence-based practice for the increasing number of patients suffering from BCC, and possibly lead to a more efficient disease management strategy.

Conflicts of Interest

None declared.

Multimedia Appendix 1

Patient satisfaction questionnaire.

[PDF File (Adobe PDF File), 59KB - resprot_v4i3e109_app1.pdf]

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Original Paper

Dietary Advanced Glycation End Products Consumption as a Direct Modulator of Insulin Sensitivity in Overweight Humans: A Study Protocol for a Double-Blind, Randomized, Two Period Cross-Over Trial

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Abstract

Background: Advanced glycation end products (AGEs) are formed during the processing, storage, and cooking of foods. As part of a western diet, AGEs are consumed in excess and impair glucose metabolism in patients with type 2 diabetes. In the absence of diabetes, AGE-mediated decreases in insulin sensitivity and signaling have been postulated. However, randomized studies to test this relationship in humans are limited.

Objective: The primary aim of this trial is to determine whether dietary consumption of AGEs will decrease insulin sensitivity in healthy overweight adults. A secondary aim is to determine the effects of dietary AGEs on insulin secretion, circulating soluble receptor for AGEs (sRAGE), and inflammation markers.

Methods: Overweight, but otherwise healthy, non-diabetic adults (N=20) aged 18-50 years old will complete a randomized cross-over design intervention study alternating low and high (4-fold increase) AGE diets (2-week duration). At baseline, participants will undergo a medical review including an intravenous glucose tolerance test (IVGTT), a hyperinsulinemic-euglycemic clamp, and anthropometric measures and questionnaires assessing diet, physical activity, and general wellness. Each test diet will be followed for 14 days, followed by a 4-week washout period before commencement of the second alternate dietary period. Energy, macronutrient, and AGE intake will be calculated for each dietary period. Additionally, the AGE content of foods used in the study will be measured by ultra performance liquid chromatography mass spectrometry. All measurements will be repeated at the beginning and end of each dietary period. Primary and secondary outcomes will be expressed as a change over the dietary period for insulin sensitivity, secretion, anthropometric parameters, sRAGE, and inflammation markers and compared by paired t test and analysis of variance (ANOVA).

Results: The study will be completed in early 2016.

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Conclusion: The proposed trial will provide much needed clinical evidence on the impact of excess dietary AGE consumption on insulin sensitivity and will indicate whether lowering dietary AGE intake can improve insulin sensitivity and/or secretion, thereby decreasing risk for type 2 diabetes.

Trial Registration: Clinicaltrials.gov NCT00422253; https://clinicaltrials.gov/ct2/show/NCT00422253 (Archived by Webcite at http://www.webcitation.org/6ZXLhT89c)

Introduction

In both developed and developing countries, the consumption of highly processed foods has increased dramatically over the past 30 years [1]. This change in diet has been associated with increased exposure to advanced glycation end products (AGEs), which are formed in foods by processes such as non-enzymatic browning (Maillard reaction). AGEs and Maillard reaction products are important for flavor and color and increase the shelf-life of treated foods [2]. While foods high in sugar and protein are most susceptible to AGE formation, long-term storage, heating, and physical or chemical processes may also produce AGEs even in foods regarded as healthy such as fruit juice, milk, and cereals. In addition, foods high in fat and sugar can also facilitate in vivo formation and deposition of AGEs within tissues [3,4]. Cooking temperature with promotion of surface browning is also a critical factor: baking, roasting, frying, and grilling are potent promoters of advanced glycation [5]. High levels of AGEs are thus found in many common foods such as heated milk and other dairy foods, baked breads, biscuits and cookies, toasted breakfast cereals, grilled steak, brewed beer, and roasted coffee beans.

Type 2 diabetes is a global health problem and in many developed countries it has already reached epidemic proportions over the past few decades [6]. There is accumulating evidence from animal studies indicating that high dietary AGE consumption contributes to increased insulin levels, insulin resistance, defects in first phase insulin secretion, and type 2 diabetes [7-9]. Interestingly, low AGE diets can protect against declining insulin sensitivity and the onset of type 2 diabetes in animal models, even in the context of high fat intake and marked weight gain [7,8]. This suggests that it is the high AGE content in high fat diets and not the fat content per se, as was previously thought, that impairs glucose metabolism. In addition, successive generational feeding of a high AGE diet to rodents results in descendants with increased adiposity, insulin resistance, impaired insulin signaling, and a proinflammatory phenotype [10], which further implicates dietary AGEs in the etiology of type 2 diabetes.

In humans, one clinical trial demonstrated an association between the low dietary consumption of AGEs and improvement in insulin sensitivity in patients with type 2 diabetes [11]. Similar results were seen in another trial in people without diabetes [12], although macronutrients were not matched in these studies. Both trials used a homeostasis model assessment (HOMA-IR), which is an indirect measure of insulin sensitivity. HOMA-IR is unable to reliably differentiate between the insulin sensitivity and insulin secretion (HOMA-β) because both are calculated from fasting glucose and insulin concentrations. No studies have used gold standard measurements of insulin sensitivity and secretion to investigate the metabolic effects of high and low AGE diets. In particular, there is a paucity of data testing the effects of dietary AGEs on insulin secretion in both animals and humans. We have recently shown in rodents that changes in insulin secretion following long-term exposure to AGEs [13,14] can be prevented with AGE-lowering therapy [13]. In addition, there is a suggestion that an AGE-RAGE interaction could mediate β-cell failure from cell [13,15] and animal studies [16].

To date, there have been no human trials investigating the impact of a dietary AGE intervention on direct measures of insulin sensitivity and insulin secretion or on the development of type 2 diabetes. Therefore, our aim is to compare the effects of high and low AGE diets, followed for 2 weeks, on direct measures of insulin sensitivity and insulin secretion in healthy yet overweight or obese individuals without diabetes. We also plan to assess the contribution of AGE receptors and chronic low-grade inflammation to the changes in insulin sensitivity and secretion observed during the trial.

Methods

Study Design and Setting

Overview

This study has a randomized, two period double-blind cross-over design (Figure 1). We aim for 20 overweight but otherwise healthy normoglycemic adults, aged 18-50 years to complete the trial. Participants will commence the study after a 2-week run-in on their habitual diet, but with restricted intake of alcohol, fast food, and coffee. Test diets will then each be followed for 2 weeks, separated by a 4-week washout period (return to habitual diet). Usual levels of physical activity will be continued throughout the study. Overweight participants will be selected for enrolment in this study as they represent the average Australian population, are generally more insulin resistant, more sedentary, and have higher levels of inflammatory markers, all factors that increase their risk for type 2 diabetes [17,18]. Participants will be sought using a number of advertising strategies including posters, flyers, newspaper, and online advertising and email newsletters from the Alfred Hospital in Melbourne, Australia.

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Figure 1. Trial protocol.
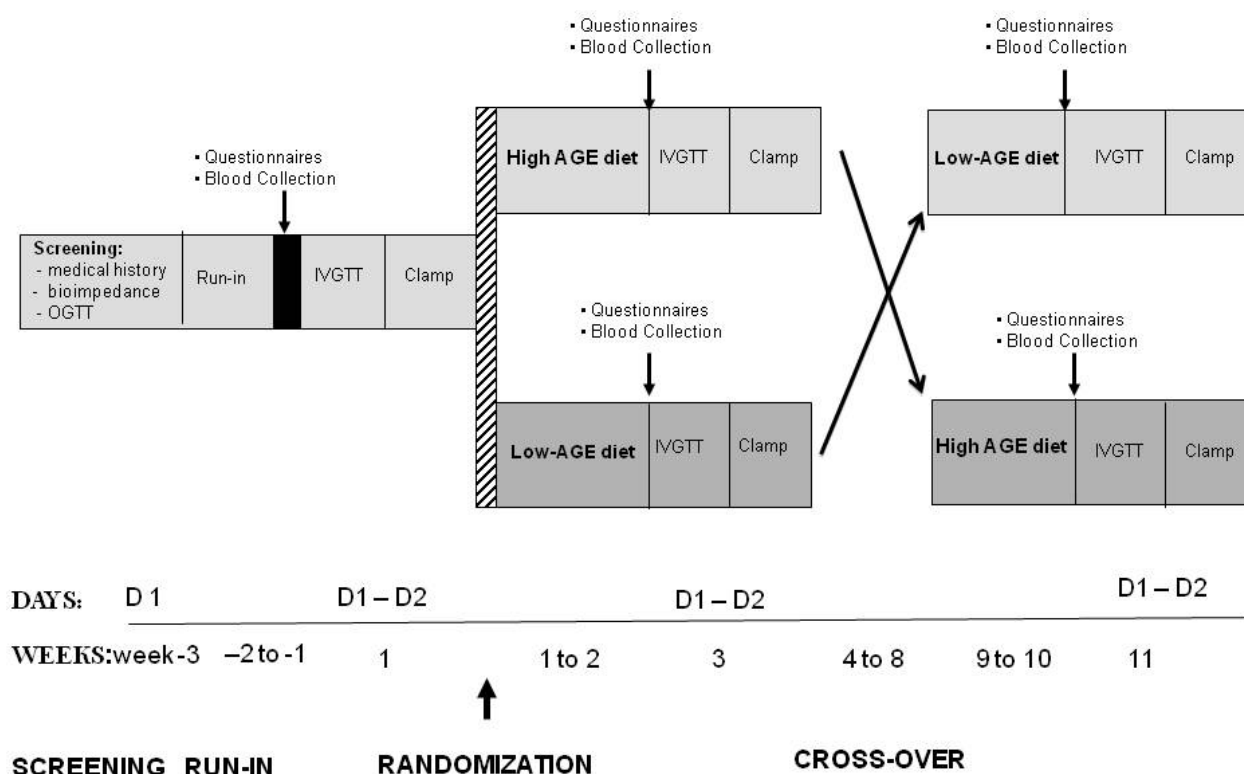
Inclusion Criteria

Inclusion criteria for the study will include the following (1) aged 18-50 years, (2) free of diabetes (previously diagnosed or on the basis of the screening OGTT), (3) generally healthy upon medical screening, (4) overweight or obese but not morbidly obese (body mass index (BMI)>25 kg/m^2 but <40 kg/m^2), and (5) stable body weight, having exhibited a weight change <5 kg in the preceding year with no intention to lose weight or change physical activity during the trial.

Exclusion Criteria

Exclusion criteria will include (1) substance abuse including smoking and high alcohol use (>4 and >2 standard drinks per week for males and females, respectively), (2) known allergies, (3) use of medications including vitamin supplements and hormonal contraceptives, (4) any renal, cardiovascular, hematological, respiratory, gastrointestinal, endocrine or central nervous system diseases, psychiatric disorders, active cancer within the preceding 5 years, or the presence of acute inflammation or infection based on the medical history and the physical and laboratory examinations obtained at recruitment, and (5) women in menopause, or pregnant and/or lactating.

Statistical Considerations

Sample Size Calculation

The sample size is estimated on the basis of the primary hypothesis including being able to detect a 20% difference in insulin sensitivity following dietary AGE modification using G*Power, an online tool to compute statistical power analyses. This effect size is clinically significant and similar to that seen after a 6-month intervention period using troglitazone, an insulin sensitizing therapy. Troglitazone improved insulin sensitivity as measured by glucose clamp in obese, non-diabetic individuals [19] whose initial glucose disposal rate was 8.1 (+2.0) mg/kg/min. To detect a 20% difference in insulin sensitivity in a cross-over design by paired t test, we will require complete data from 20 individuals (power 80%, alpha 5%, SD 1.0).

Data Analysis

Descriptive analysis will be performed on baseline characteristics and covariates. We will use paired t test to determine the significance of the change in measured parameters during test diets. Multiple regression will be used to assess the determinants of insulin secretion after adjusting for covariates. Dietary order will be included in multiple regression models as a between participant variable. Carryover effects will be tested in an expanded model including diet and period interaction when evaluating the effects of diet over the 2 test periods. Period effects refer to a change between intervention and measurement periods and within subjects, which would have occurred independently from any diet given. Plausible period effects in diet-based trials might arise from behavioral changes by participants as a result of enrolment in a dietary-based trial

Adjustment to P values for multiple comparisons will be performed using the Holm method, and statistical significance will be assumed when $P<.05$.

Screening

The study timelines are presented in Figure 1. Female participants will be required to commence metabolic testing while they are in the follicular phase of their menstrual cycle

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and a urine pregnancy test will be performed to exclude pregnancy. At visit 1, screening will be undertaken by a registered medical practitioner who will collect the medical history and perform a physical examination including measurement of blood pressure, height, body weight, and waist and hip circumference using the methods outlined in the following sections.

At the second visit, participants will undergo an OGTT with measurement of fasting and 2-hour glucose levels to exclude diabetes according to the World Health Organization (WHO) 1999 criteria [20]. Blood samples will be analyzed by a single accredited laboratory for full blood count, kidney and liver function, lipid profile, and C-reactive protein (CRP) as a marker of inflammation. Participants will also be given a 3-day food diary to record their habitual dietary intake and this will be returned on their next visit where it will be used to aid the dietitian in the development of individualized test diets (as following).

Baseline Assessment

Baseline assessments will commence at the third visit which will involve measurement of blood pressure and body composition by bioimpedance. At the fourth and fifth baseline visits, an intravenous glucose tolerance test (IVGTT) and a hyperinsulinemic euglycemic clamp will be performed (detailed below in Data Collection and Analyses). Participants will complete the International Physical Activity Questionnaire (IPAQ) questionnaire to assess habitual physical activity [21].

Randomization and Blinding

Following successful screening and baseline assessment, subjects will be randomized by a computer program to commence the study with either the high or low AGE diet. Randomization will be done in blocks of four by gender using a relevant computer program to ensure balance in each test group and will be conducted by a researcher from within our department who is not involved in the trial data collection, analysis, or reporting. Diet type will be coded as (red or blue) by the dietitian, so that participants and blinded investigators remain unaware of which dietary period they are undertaking or how diet might affect glucose metabolism. Clinical and laboratory investigators will also be masked to diet allocation.

Intervention

Using Australian food composition data in addition to data on the AGE, N-carboxymethyllysine (CML), N-carboxyethyllysine (CEL), and methylglyoxal-derived hydroimidazolone (MGH1) content of common foods [3], a set of carefully matched alternative food choices has been designed with each alternate food choice having similar macronutrient and total energy content but differing greatly in AGE (referred to as the "Food List") [9].

To ascertain dietary AGE content, food items used in the study were obtained from local supermarkets and prepared according to the instructions of the study. To prevent neo-formation of CML during acid hydrolysis, a reduction step with sodium borohydride was used. Food items containing <20% fat were mixed and subsequently deproteinized with 1000 μl cold (4°C)

TFA. Food items >20% fat were mixed and subsequently deproteinized with a mixture of chloroform:methanol (2:1, v/v) [22]. After centrifugation (4300 g, 4°C, 20 min), the supernatant (TFA) or lower phase (chloroform) was carefully removed. For validation experiments, 25 μL of a standard solution (six point calibration curve; 5250-0 nmol/L CML, 6250-0 nmol/L CEL and 14749-0 nmol/L MGH1) was added. Samples were then hydrolyzed by adding 500 μl 6N HCl and incubated for 16 hours at 100°C. After hydrolysis, 40 μL hydrolysate and 20 μL internal standard (containing 1432 nmol/L ^{2}H2-CML, 1378 nmol/L ^{2}H4-CEL, and 1322 nmol/L ^{2}H3-MGH1) were mixed in a reaction vial. The mixture was evaporated to dryness under a stream of nitrogen gas at 70°C. To increase sensitivity during electrospray ionization and increase retention time using reversed phase chromatography, samples were subsequently derivatized with 100 μL 1-butanol:HCl (3:1, v/v) for 90 minutes at 70°C. After derivatisation, the samples were evaporated to dryness under nitrogen, redissolved in 300 μL water, mixed, and subsequently centrifuged at 20,000 g for 20 minutes. AGE-free adducts in foods were measured.

Using the 3-day diet diary recorded by each participant during the "run-in" period, the dietitian will help participants select foods for their first test diet from the "Food List", guided by their individual preferences and energy requirements. The content of their second test diet will comprise the alternate paired foods. Food choices on the high-AGE diet thus will approximate a typical Australian diet, while the isoenergetic low AGE diet, matched for macronutrient content, will have reduced AGE content through altered cooking techniques [23] and use of differently processed foods. All food required for both test diets will be provided weekly to the participants as ready-to-eat items or as packed food portions together with detailed instructions for storage and re-heating or cooking (method, temperature, duration). Participants will be asked to eat to appetite throughout both dietary periods to maintain constant body weight and to complete a daily record indicating the number of portions eaten for each food item supplied, any foods not consumed, or any additional foods that were eaten.

Participants will be contacted twice a week by the dietitian who designed the dietary protocol to resolve any problems and to ensure dietary compliance.

Follow-Up Visits

Participants will be scheduled for their follow-up visits after completing each test diet for 2 weeks. All the procedures performed during baseline assessment including blood pressure, anthropometry, IVGTT, physical activity questionnaire, and glucose clamp will be repeated with the exception of the OGTT, as this will only be performed once at screening to identify undiagnosed diabetes.

Safety Considerations

During the screening, baseline, and follow-up procedures, any medical conditions or abnormalities detected will be promptly discussed with the participant by a qualified medical practitioner involved in the study. Where applicable, participants will be treated, referred, and/or advised to visit their general practitioner for follow-up. All participants will be advised of the results of

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their medical review and blood tests after completion of the study, and a medical practitioner from the study team will provide them with strategies to improve their diabetes and cardiovascular risk profile.

Ethics

This trial has received ethical approval from the Alfred Hospital Ethics Committee in Melbourne, Australia (Protocol ID: 36/06).

Outcome Measurements

The primary outcome in this trial is the difference (change) in insulin sensitivity between the 2 diets. Secondary outcomes include changes in insulin secretion, body weight, body mass index (BMI), waist, waist-to-hip ratio (WHR), resting systolic and diastolic blood pressure, lipid profile and markers of inflammation (ie, interleukin (IL)-1ß, IL-6, IL-8, and IL-10), tumour necrosis factor-α (TNFα), macrophage migration inhibitory factor (MIF), monocyte chemotactic protein-1 (MCP-1), C-reactive protein (CRP), nuclear factor-κB (NF-κB) activity, and circulating sRAGEs.

Data Collection and Analyses

Anthropometry

Body Mass Index (BMI) and Percent Body Fat

Body weight (kg) and height (cm) will be measured using a digital scale (BC-418MA, Tanita UK Ltd) and stable stadiometer (Seca 206), respectively, at baseline and following the intervention period during which participants will be lightly clothed and without shoes. BMI will be calculated as weight (kg)/height (m)^2. Body composition will be determined by bioelectrical impedance analysis (BC-418MA, Tanita UK Ltd).

Waist-To-Hip Ratio (WHR)

Central adiposity will be assessed using waist and hip circumferences, taken in duplicate by an experienced researcher using a constant-tension tape. Waist circumference will be measured at the midpoint between the upper iliac crest and the lowermost rib at the end of a normal expiration, while hip circumference will be taken around the widest part of the buttocks. The WHR will be determined as waist (cm)/hip (cm).

Metabolic Measures

All metabolic testing will be performed after a 12-hour overnight fast. Prior to metabolic testing, participants will be asked to abstain from strenuous exercise and caffeine for 3 days. The first metabolic testing day in females will be scheduled in the follicular phase of their menstrual cycle.

Oral Glucose Tolerance Test (OGTT)

Participants will ingest 75 g of glucose over 2 minutes. Blood samples will be drawn at 0 and 120 minutes to analyze plasma glucose levels and to determine diabetes status (WHO 1999 criteria).

Intravenous Glucose Tolerance Test (IVGTT)

Using IVGTT, acute insulin secretory response will be measured. First, baseline blood will be collected at -10 and 0 minutes, after which 50 ml of 50% glucose will be delivered intravenously over a 3-minute period. Blood will then be collected for measurement of insulin at the 3, 4, 5, 6, 8, 10, 15, 20, 25, and 30 minute time points. The early insulin secretory response will be calculated as the mean incremental plasma insulin level from the 3rd to the 5th minute after the glucose bolus.

Hyperinsulinemic Euglycemic Clamp

A euglycemic glucose clamp will be used to measure insulin sensitivity. After collecting baseline blood and plasma glucose levels at 0 minutes, the clamp will be initiated by an intravenous bolus injection of insulin (9 mU/kg). Insulin will then be constantly infused at a rate of 40 mU/m2/min for approximately 120 minute into an arm vein, whilst glucose is variably infused to maintain euglycemia. Plasma glucose values will be monitored every 5 minutes during the clamp while the variable infusion rate of glucose is adjusted to maintain blood glucose at a constant concentration of 5 mmol/L for the last 40 minutes of the clamp.

Plasma glucose concentrations will be measured by the glucose oxidase method (ELM 105 Radiometer). Plasma insulin levels will be measured by chemiluminescent microparticle immunoassay and plasma high sensitivity CRP will be determined by immunotubimetric assay (Abbott Archicentre ci162000).

Measurement of Advanced Glycation End Products (AGEs) and Their Receptors

The concentrations of AGE- (CML, CEL, and MG-H1) modified proteins in serum and free AGEs in urine will be quantified using UPLC MSMS as previously described [24]. AGE-modified proteins will also assayed [25] in urine (neat) using an indirect ELISA as previously described [26].

The pool of sRAGE (circulating RAGE from proteolytic cleavage and AGER gene transcription; RnD Systems) and endogenous secretory RAGE (esRAGE) (circulating RAGE from AGER1 gene transcription only) will be analyzed in plasma by ELISA according to the manufacturer's instructions.

Cardiovascular Measures

Blood Pressure

Resting systolic and diastolic blood pressure and pulse rate will be measured using an automated oscillometric measurement system (Omron) after a 30 minute rest. The mean blood pressure derived from 3 measurements will be recorded.

Lipid Profile

Lipid profile-related parameters to be measured include plasma total cholesterol, triglycerides, and low density lipoprotein (LDL) and high density lipoprotein (HDL) cholesterol using a standard commercial enzymatic assay (Beckman Coulter LX20PRO Analyzer and Synchron) and Systems Lipid and Multi Calibrators (Beckman Coulter Diagnostics).

Inflammatory Markers

Cytokines and Chemokines

Plasma inflammatory markers (IL-1ß, -6, -8 and -10, TNFα, MIF, and MCP-1) will be measured using a commercial automated chemiluminescent enzyme immuno assay (EIA) and

immulite analyzer (Diagnostic Products Corporation), while plasma CRP will be analyzed using highly sensitive near infrared particle immunoassay rate methodology and a Beckman Coulter Synchron LX system Chemistry Analyzer (Beckman Coulter Inc).

Nuclear Factor-κB (NF-κB) Activity

Nuclear extracts of white blood cells will be obtained and analyzed for the binding capacity of the p50/p65 subunit of NF-κB to an NF-κB oligonucleotide consensus sequence as per the manufacturer's instructions (Active Motif, CA, USA).

Self-Reported Measures

Nutrient Analyses

During the test diets, the daily records of all foods eaten will be collected weekly from study participants. Food intake will then be analyzed for nutrient content by a dietitian using an Australian Food Composition program. Based on these records, the dietary intake of CML, CEL, and MGH1 will be determined for each participant over each dietary period. The mean daily energy, macronutrient, and AGE intake of participants during the 2 test diets will then be compared.

International Physical Activity Questionnaire (IPAQ)

The validated IPAQ determines the type of everyday physical activity that people engage in [21]. We will use the short version of IPAQ as a timely, convenient method to determine whether study participants have made any change in their physical activity which could influence our study outcomes. The short IPAQ asks participants to reflect on the past 7 days and report time spent on vigorous activity (eg, aerobics), moderate activity (eg, carrying light loads), walking, and sitting [21].

Discussion

Principal Findings

To the best of our knowledge, there is no human clinical trial published investigating the effect of high and low AGE diets on insulin sensitivity and secretion in individuals without diabetes, employing gold standard measures of insulin sensitivity and secretion, and comprehensively investigating mechanisms including chronic low-grade inflammation.

Insulin resistance increases with obesity and is a key pathogenic process underpinning type 2 diabetes. Interventions that reduce insulin resistance such as lifestyle measures including diet and exercise resulting in weight loss, as well as pharmacological therapies are used to prevent and treat type 2 diabetes [27]. However, to date, these agents have failed to decrease the burden of this disease. Diabetes is a major cause of morbidity and mortality, primarily due to chronic complications including an increased risk of cardiovascular disease. It is vital that additional effective primary prevention strategies are established to reduce insulin resistance and prevent and manage type 2 diabetes [28]. The current trial should thus inform and advance this important field of research.

By demonstrating that intake of a low AGE diet improves insulin sensitivity and/or secretion, large scale interventions using low AGE diets could potentially become a mainstream strategy for

diabetes prevention in overweight and obese individuals. This strategy would offer a cost-effective and easily administered intervention that could have a considerable impact on health outcomes in Australia and worldwide since it can be achieved by simple changes in cooking methods by individuals and/or processing by the food industry. Such improvements will not only lower diabetes risk, but since AGEs are also known to play an essential role in the development of micro-vascular complications, a low AGE dietary intervention could reduce cardiovascular risk factors as well as chronic low grade inflammation [11]. Therefore, lowering AGEs could have beneficial effects on decreasing risk factors associated with a wide range of metabolic conditions. High-quality clinical trials such as this are, therefore, an important first step towards elucidating the effects of a low AGE diet in promoting health and well-being by improving insulin sensitivity, decreasing cardiovascular risk factors, and potentially decreasing the risk of type 2 diabetes and its associated micro and macro vascular co-morbidities.

There is a paucity of human data investigating the effect of AGEs on insulin resistance in humans. One previous study by Uribarri et al [11] examined the effect of dietary AGE restriction on glucose homeostasis in 18 diabetic and 18 healthy individuals. They showed that in patients with type 2 diabetes, but not in healthy individuals, insulin resistance (estimated by HOMA-IR) improved after 4 months of dietary AGE restriction. We have recently published another trial in overweight and obese people without diabetes that demonstrated an improvement of HOMA-IR with a low AGE dietary intervention when compared to a high AGE diet [12]. In both of these studies, the intake during the 2 diets was isocaloric but not macronutrient matched. Therefore, some of the changes observed could have been due to differences in macronutrient intake. In addition, these studies depended on HOMA-IR, which is calculated from fasting glucose and insulin levels and hence cannot differentiate between insulin sensitivity and secretion. No human trials with AGE dietary manipulation have been carried out to date measuring insulin secretion, but we and others have previously shown that a greater exposure to AGEs either at very high concentrations or for an extended duration may ultimately impair pancreatic beta cell function resulting in reduced insulin secretion, particularly of the first phase in cells and in animal models [13,15]. Such effects appear to be mediated by changes in the AGE receptor RAGE [13,14,16]. A few previous studies have suggested that cooking methods, which result in lower AGEs in the food, can alter glucose homeostasis, but these studies used either single meal challenges [29-31] or did not account for changes in body weight [32].

With regard to putative mechanisms involved, AGE modulation could impact on insulin sensitivity via effects on insulin signaling pathways [33,34], likely mediated by a chronic low-grade inflammation [35]. Consistent with this, in the study by Uribarri [11], a diet low in AGE content was associated with a decrease in circulating concentrations of inflammatory cytokines in patients with type 2 diabetes but not healthy individuals.

Recent reports have also demonstrated a possible role of another AGE receptor AGE-R1 in the development of insulin resistance

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in the type 2 diabetic population [11]. In the study by Uribarri, a diet low in AGE content was associated with an elevation in AGE-R1 expression on peripheral blood mononuclear cells (PBMC)s in patients with type 2 diabetes but not healthy individuals [11].

Methodological Considerations

The strengths of the proposed study protocol include the gold standard study design, randomization, and double-blinding of both participants and investigators to limit bias. Other major strengths include the cross-over design which controls for individual variation between participants, the assessment of confounders such as dietary macronutrient and energy content and physical activity, and the use of direct rather than indirect measures of insulin sensitivity and secretion such as the OGTT, IVGTT, and the gold standard euglycemic clamp. Determination of many blood components will also allow for the comprehensive exploration of potential mechanisms involved. We will also have a comprehensive analysis of the dietary AGEs which are consumed during the study period which will be matched with AGE levels in both the blood and urine.

Despite these strengths, there are also potential limitations. First, self-selection bias may be present given that recruitment is based on voluntary participation by interested subjects. These subjects may not represent the entire target population because they may be characteristically different to other volunteers (ie, potentially more health conscious). Secondly, we are only recruiting overweight or obese adults (BMI>25), who are otherwise healthy (not medicated and without diabetes etc), and therefore the results of the study will not be generalizable to other populations such as those within a healthy weight range or those with diagnosed diabetes or other medical conditions and co-morbidities. Third, our study will only measure risk factors such as blood pressure, fasting glucose, and insulin sensitivity and insulin secretion. Longitudinal follow-up studies would be necessary to ascertain if change in these risk factors translates into decreased incidence of type 2 diabetes.

Conclusions

Type 2 diabetes and its associated complications are associated with significant morbidity and mortality as well as healthcare costs. Insulin resistance, the key risk factor for type 2 diabetes, increases with increasing body weight. While existing research suggests that consumption of a low AGE diet may prevent insulin resistance and type 2 diabetes, well-designed randomized trials are lacking. If our clinical trial shows that low AGE diet can improve risk for diabetes, our study may have important public health implications and could lead to feasible and cost-effective strategies to prevent type 2 diabetes and its complications.

Authors' Contributions

Barbora de Courten and Josephine Forbes designed and wrote the study protocol, obtained funding for the trial's execution, and wrote the first draft of the manuscript. Professor Maximilian de Courten and Associate Professor Karen Walker contributed to the study design, obtaining of funding, and to writing and editing the manuscript. Professor Casper Schalkwijk established the dietary AGE databases and gold standard measures of AGEs in plasma and urine for use in the study. All authors read and approved the final manuscript.

Conflicts of Interest

None declared.

Multimedia Appendix 1

NHMRC assessment.

[PDF File (Adobe PDF File), 122KB - resprot_v4i3e93_app1.pdf]

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Abbreviations

AGE: advanced glycation end product
BMI: body mass index
BP: blood pressure
CEL: carboxyethyllysine
CML: carboxymethyllysine
CRP: C-reactive protein
CVD: cardiovascular disease
DXA: dual-energy x-ray absorptiometry scan
ELISA: enzyme-linked immunosorbent assay
HbA1c: hemoglobin A1C
HDL/ LDL: high-/low-density lipoprotein cholesterol
HOMA-IR: homeostasis model assessment for insulin resistance
IL: interleukin
INFγ: interferon-gamma
IPAQ: International Physical Activity Questionnaire
IU: international units
IVGTT: intravenous glucose tolerance test
MCP-1: monocyte chemotactic protein 1
MGH1: methylglyoxal-derived hydroimidizolone
MIF: macrophage migration inhibitory factor
NF-κB: nuclear factor-κB
NHMRC: National Health and Medical Research Council
OGTT: oral glucose tolerance test
sRAGE: soluble receptor for advanced glycation end products
TG: triglycerides
TNFα: tumour necrose factor-α
WHR: waist-to-hip ratio

Mapping a Decade of Physical Activity Interventions for Primary Prevention: A Protocol for a Scoping Review of Reviews

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Abstract

Background: Physical activity is a key behavioral component for the primary prevention of noncommunicable disease. The uptake of physical activity is influenced by individual and broader factors including social, economic, and environmental conditions.

Objective: The purpose of this paper is to describe a protocol for a scoping review of reviews (SRR) that aims to map a decade of research focused on physical activity interventions within the domain of primary prevention.

Methods: The 5 stages of our SRRs design were adapted from a seminal scoping review methodology. Our search strategy was developed for the following databases: SPORTDiscus, PubMed, Scopus, the Cochrane Library, the Cumulative Index to Nursing and Allied Health Literature, PsycINFO, and Educational Resources Information Centre. Two reviewers (LG and AK) independently screened eligible studies and compared results to determine the final study selection. One reviewer will conduct the data extraction (LG); a second reviewer (AK) will assess the results to ensure comprehensiveness and accuracy of the scoping review synthesis.

Results: The SRRs will provide a broad overview of the physical activity research literature specific to primary prevention, and will describe key features of physical activity interventions. Potential gaps in the physical activity action areas will be identified, and thus, the results will inform future research directions.

Conclusions: This paper describes an innovative approach for comprehensively mapping an important topic's research trends in the last decade.

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Introduction

Background

Physical activity provides health benefits that include stress reduction, improved functional ability, and a key means of energy expenditure that contributes to weight control [1]. Conversely, physical inactivity is the fourth leading risk factor contributing to noncommunicable diseases (eg, cardiovascular disease, diabetes, cancer, and chronic respiratory disease), accounting for an estimated 6% of deaths globally [1,2]. Despite the fact that physical activity is recognized as a key factor for the primary prevention of diseases [3], physical activity levels continue to decrease globally despite an extensive range of interventions. Several researchers attribute this phenomenon to the complexity of behavior change to support physical activity [4,5].

Physical Activity and Exercise

Broadly, physical activity is defined as any bodily movement produced by skeletal muscles, which requires energy expenditure [6]. Exercise remains a key subcategory of physical activity, which focuses on achieving aspects of physical fitness through planned, structured, repetitive, and purposeful movements [7]. Concepts such as health-enhancing physical activity, active living, leisure-time physical activity, active transportation, and household physical activities have also been added to physical activity promotion to encourage greater participation in a variety of settings [8,9]. The type of physical activity that may produce the greatest health-risk reduction has not yet been determined [10,11]. Evolving concepts of physical activity have expanded the scope of physical activity interventions, presenting new challenges for primary prevention intervention research and surveillance.

Enhancing physical activity is a complex behavior change that is influenced by multiple factors [5,11]. Over the past decade, population-level approaches have sought to address the broader factors that influence behavior including social, economic, and physical environments; personal health practices; individual capacity and coping skills; and health services [12,13]. In 2007, the World Health Organization (WHO) published a guide for population-based approaches to increase physical activity as part of a global strategy to improve health outcomes [14]. Several key action areas were identified for increasing physical activity including policy, education, promotion, and creating supportive social and physical environments. These may be combined to produce multistrategy interventions. It was also suggested that population-based interventions should be combined with tailored interventions targeting specific population groups, such as people at risk for developing noncommunicable diseases. Vulnerable or marginalized populations that experience greater risk for noncommunicable diseases also tend to have the lowest levels of physical activity [15,16].

The proliferation of physical activity literature over the last decade addresses many relevant aspects: different types and intensities of exercise, sport, and leisure-time physical activity and their effects on health; the influence of settings (barriers/facilitators) on physical activity behaviors; and policies

developed in response to the alarming global trend of decreasing physical activity levels. Given the recognition of physical activity as important for preventing chronic disease, and the vast amount and complexity of published literature on this topic, a broad overview that maps physical activity research literature specific to primary prevention is warranted.

Reviews conducted in health disciplines tend to be systematic reviews of particular interventions or outcomes, but despite the rigorous results they produce to address specific questions, these methods are less useful when the aim is to address complex practice issues or broad research questions [17,18]. Scoping reviews have become increasingly used in response to a growing demand for effective and timely summaries of the breadth of primary research around a particular topic [19,20]. Here, we describe a protocol for a scoping review of reviews (SRR) to summarize the decade of primary prevention-focused physical activity interventions since the release of the WHO's guidelines [14].

Methods

Scoping Review

A scoping review is an ideal methodology for mapping key concepts within a research area and for identifying main sources and types of evidence available when the research literature is vast or diverse, or both [21,22]. Scoping reviews are different from systematic reviews, which attempt to answer a specific research question by collating all empirical evidence that fits prespecified eligibility criteria [23]. Thus, in this SRR there will be no attempt to "weight" the evidence to answer a specific question. Rather, our goal is to map intervention trends and concepts, and to summarize these findings to identify potential gaps in research.

Our SRR approach is adapted from Arksey and O'Malley's scoping methodology that describes up to 6 stages of the scoping review process [21]. An integral aspect of this methodology is a rigorous and transparent approach in each stage of the study design. We will adopt such an approach using an iterative process during each stage of the review to allow us to modify methods and record the methodological differences in an SRR compared with a scoping review of primary literature.

Stage 1: Establishing the Research Questions

Similar to other review designs [21], the initial research questions shape the design of the SRR (Textbox 1). These questions were established using an iterative process that involved team discussions as we became more familiar with the literature. Several key research questions were derived from the WHO's suggestions for population-based approaches for increasing physical activity [14]. We used the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)-Equity 2012 Extension [24] to determine the equity-focused question and the operational definition. Because our SRR does not appraise the findings of the included reviews, we did not attempt to establish whether interventions are effective. Instead, we will indicate in a separate category those reviews that explicitly address factors contributing to

intervention effectiveness or efficacy in their research aim, which may provide direction for future research.

Textbox 1. Overarching research questions.

Which physical activity strategies are being addressed in the literature [14]?

- Individual-targeted interventions (eg, individual behavioral interventions)
- Education or promotion (national, regional, or local informational education or promotion)
- Supportive social environments (eg, counselors, mentors, role models)
- Supportive physical environments (relevant settings and opportunities that determine availability)
- Policy (government or organizational policy)
- Multicomponent interventions (ie, several health-related strategies in a single intervention)

Which individuals or groups are targeted in the physical activity literature [14]?

- Individuals (eg, children, youth, adults)
- Family
- Community
- Subpopulation (eg, age group)
- Sectors (eg, schools, workplaces, primary care providers)
- Society (ie, general population)

How is equity addressed in the physical activity review literature?

- Equity is explicitly stated in the research objective
- Includes equity categories based on Preferred Reporting Items for Systematic Reviews and Meta-Analyses-Equity 2012 Extension [24] such as gender, age, ethnicity

What factors are being researched that may influence physical activity uptake?

- Social and health determinants
- Correlates
- Mediators/Moderators
- Barriers

What are the trends in physical activity concepts, action areas, and population targets?

Which reviews explicitly examine intervention effectiveness or efficacy?

Stage 2: Identifying Relevant Studies

Our SRR aimed to be comprehensive in identifying relevant studies, yet we limited our scope to include only published review literature to manage the vast quantity of physical activity literature. Team discussions established the eligibility criteria in the preliminary planning of the SRR analysis (Textbox 2). Similar to other scoping review methods [21], these criteria may be refined in later stages of the SRR.

A comprehensive search was performed in the following electronic databases: SPORTDiscus, PubMed, Scopus, the Cochrane Library, Cumulative Index to Nursing and Allied Health Literature, and Educational Resources Information Centre. Boolean terms "AND" and "OR" were used to build the keyword searches in the databases. We developed our search around physical activity intervention concepts and keywords that are broad, yet relate specifically to physical activity interventions within the domain of primary prevention (Multimedia Appendix 1). Our team librarian (JR) led the refinement of our database search strategies during this stage. Each search result was documented and the references were imported into separate folders using RefWorks reference management software.

Textbox 2. Eligibility criteria for the scoping review of reviews.

- Inclusion criteria
  - Published in English
  - Human subjects
  - Date range January 2003 to June 2014
  - All age groups
  - Research that targets the general population where no illness/condition is identified.
  - Review methods specifically described a systematic review, meta-analysis, meta-synthesis, scoping review, rapid review, critical review, or described a systematic approach.
  - Research located in developed Westernized countries (Canada, United States, Europe, United Kingdom, Australia, and New Zealand).

- Exclusion criteria
  - Journal articles that are not rigorous reviews (ie, those not listed in the inclusion list), such as book reviews, opinion articles, commentaries, or editorial reviews.
  - Research targeting a population because of a diagnosed illness or disease or interventions targeting treatment of a specific disease, illness, or condition.
  - Research about direct health benefits from physical activity.
  - Research that focuses on research design (eg, methods, protocols, theories).

Stage 3: Study Selection

We used a 2-stage study-selection process. In the first stage, a single reviewer applied the defined inclusion criteria (ie, interventions targeting healthy populations in developed countries) to titles and abstracts. Reviews that were overtly ineligible were removed, such as physical activity interventions that treated a previously existing health condition. All potentially eligible studies were then distributed to 2 independent reviewers (LG and AK) on the team. Each reviewer applied the eligibility criteria (Textbox 2) and any eligibility discrepancies were discussed between reviewers until consensus was reached or brought to the larger team for further discussion. For example, there was a discrepancy regarding physical activity interventions that targeted obesity as a health condition versus obesity as a risk factor. The team refined the eligibility criteria to include reviews that targeted obesity if the outcomes measured change in physical activity levels along with obesity-related outcomes.

Stage 4: Charting the Data

The data-extraction tool was developed using an iterative team process. The preliminary data-extraction categories were derived from our overarching research questions (Textbox 1). As

suggested by Daudt et al [20], each team member piloted the data-extraction tool independently, and the results were discussed as a team. At this stage, we used abstracts rather than full text to extract data and complete the chart. We determined that abstracts were a suitable source for data extraction based on the results of the pilot-extraction exercises.

Our data-extraction categories (Table 1) were derived from Arksey and O'Malley's scoping review protocol [21], the WHO framework for increasing physical activity [14], and the PRISMA-Equity 2012 Extension [24]. Adjustments to the data-extraction tool were accomplished using team discussion and consensus. For example, we attempted to extract in-depth details about the effectiveness of intervention outcomes in the pilot phase of extraction. Following a team discussion, we determined we did not aim to establish whether interventions were effective. Rather, we wanted to map and narratively describe review questions that focused on intervention effectiveness or efficacy. Two reviewers (LG and AK) will independently extract the data and compare results. Discrepancies will be discussed between reviewers until consensus is reached or brought to the larger team for further discussion.

Table 1. Data-extraction tool.

Data	Details extracted
Article summary	Author
	Title
	Publication year
	Number of studies
	Date range
	Review type
Population	Age (eg, adults)
	Descriptors (eg, workplace)
Action areas	Policy
	Education/Promotion
	Supportive physical environments
	Supportive social environments
	Multicomponent interventions
Physical activity concept	For example, leisure-time physical activity
Intervention	Descriptors
	Objectives
	Measures
Review focus	Process
	Impact
	Outcomes
Equity	Explicitly stated? Yes/No
Equity-related categories	For example, ethnicity
Effectiveness/efficacy	Factors that contribute to intervention effectiveness or efficacy

Stage 5: Collating, Summarizing, and Reporting the Results

This physical activity SRR will provide an overview of the breadth of physical activity research to inform our primary prevention research agenda. We will use Arksey and O'Malley's methods of reporting and provide a descriptive analysis of the extent, nature, and distribution of the studies included in the review [21] as well as a narrative, thematic summary of the data collected. Our primary objective is to describe key categories such as target populations, dominant action areas, and intervention characteristics. We will discuss the types of questions posed in review research about intervention effectiveness and provide suggestions for future research. Potential gaps in the physical activity action areas will be identified based on our summary of the review literature.

Discussion

Preliminary Findings

Our study is a scoping review of published reviews that is not limited to systematic reviews. We chose a broader selection of review literature to comprehensively explore physical activity interventions aimed at primary prevention. Extracting data from a variety of reviews may prove difficult, because the included studies will have a wide range of methodological approaches, settings, study populations, and behaviors. However, our goal is to map trends rather than answer a specific question, which will provide novel insights with regard to future research needs to enhance current primary prevention policies and programs.

Limitation

A potential limitation of this study may be a lack of quality assessment of the included articles, yet this is typical of a scoping review [18,20]. The use of abstracts may restrict our ability to provide conclusive knowledge claims about findings in the research field. Arksey and O'Malley [21] point out that scoping reviews are often conducted to inform future research. Thus, if we find there are limitations in the data from the abstracts, we have the opportunity to develop research questions related to a more specific topic and further explore a subset of the reviews.

Conclusion

Physical activity is an important intervention for the primary prevention of noncommunicable diseases and the promotion of health. Research suggests interventions require a multidimensional approach that encompasses the broader social, economic, and environmental factors that influence behavior

[13,16]. Our protocol for SRRs is an innovative approach for synthesizing comprehensive intervention research that provides an overview of the extent, range, and nature of physical activity research within the last decade. We have described the 5 stages underpinning our SRR protocol and we anticipate some iterative revisions based on the nature of scoping reviews. We are confident that our multicomponent data-extraction tool will provide new direction for physical activity interventions within the domain of primary prevention.

Acknowledgments

Authors' Contributions

AK conceptualized the review approach and provided general guidance to the research team. AK and LG drafted the manuscript, followed by numerous iterations and substantial input and appraisal from all other authors. All authors have approved the final version of this manuscript.

Conflicts of Interest

None declared.

Multimedia Appendix 1

Search strategy for SPORTDiscus.

[PDF File (Adobe PDF File), 42KB - resprot_v4i3e91_app1.pdf]

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Abbreviations

PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses
SRR: scoping review of reviews
WHO: World Health Organization

<u>Protocol</u>

Efficacy and External Validity of Electronic and Mobile Phone-Based Interventions Promoting Vegetable Intake in Young Adults: A Systematic Review Protocol

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Abstract

Background: Despite social marketing campaigns and behavior change interventions, young adults remain among the lowest consumers of vegetables. The digital era offers potential new avenues for both social marketing and individually tailored programs, through texting, web, and mobile applications. The effectiveness and generalizability of such programs have not been well documented.

Objective: The aim of this systematic review is to evaluate the efficacy and external validity of social marketing, electronic, and mobile phone-based (mHealth) interventions aimed at increasing vegetable intake in young adults.

Methods: The Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) protocol will be used to conduct this systematic review. The search strategy will be executed across eleven electronic databases using combinations of the following search terms: "online intervention", "computer-assisted therapy", "internet", "website", "cell phones", "cyber", "telemedicine", "email", "social marketing", "social media", "mass media", "young adult", and "fruit and vegetables". The reference lists of included studies will also be searched for additional citations. Titles and abstracts will be screened against inclusion criteria and full texts of potentially eligible papers will be assessed by two independent reviewers. Data from eligible papers will be extracted. Quality and risk of bias will be assessed using the Effective Public Health Practice Project (EPHPP) Quality Assessment Tool for Quantitative Studies and The Cochrane Collaboration Risk of Bias assessment tool respectively. The external validity of the studies will be determined based on components such as reach, adoption, and representativeness of participants; intervention implementation and adaption; and program maintenance and institutionalization. Results will be reported quantitatively and qualitatively.

Results: Our research is in progress. A draft of the systematic review is currently being produced for publication by the end of 2015.

Conclusions: The review findings will assist the design and implementation of future eHealth and mHealth programs aimed at improving vegetable consumption in young adults.

Trial Registration: PROSPERO International Prospective Register of Systematic Reviews: CRD42015017763; http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42015017763#.VVKtqfmqqko (Archived by WebCite at http://www.webcitation.org/6YU2UYrTn).

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Introduction

The Forgotten Age Group

Despite national and global social marketing campaigns and behavior change interventions, the current population's intake of vegetables remains low [1]. Among Australian adults, young adults are least likely to meet the recommended five or more serves a day [2]. As they transition from parental supervision to independent living, young adults are establishing self-determined food habits that will have implications for their future health. It can take decades before diet-related diseases appear; however, a strong association has been established between fruit and vegetable consumption and a decreased risk of chronic diseases [3-11]. For this age group, promoting the well-established long-term health benefits of vegetable consumption, as is typically done in nationwide social marketing campaigns, is not a salient enough motivator for this population, who are typically unconcerned about their future health and engage in more high-risk behaviors [12-14]. This age group needs to be targeted separately in social marketing campaigns and behavior change interventions. Promoting the benefits they value, such as enhanced performance and physical ability, short-term health outcomes, and improved appearance may have greater impact.

Digitalization of Interventions

The rise of the digital era offers potential new avenues for both social marketing and individually tailored programs, through texting, web and mobile apps to deliver health messages and facilitate change. Research indicates that electronic (eHealth) and mobile phone (mHealth)-based strategies are a promising channel for the delivery of interventions aimed at promoting healthful behaviors [15-17]. Young adults are among the most frequent users of these wireless information sharing platforms [18], and the total number of people using social networks is increasing rapidly [19]. Harnessing this technology could allow for the widespread dissemination of interventions in a low cost, accessible, convenient, and age-appropriate manner.

Assessing Efficacy

When assessing the efficacy of interventions, the degree to which they effectively incorporate behavior change theories should be considered. A review of recent eHealth and mHealth interventions revealed that interventions which included more behavior change techniques had larger effects compared to those that used fewer techniques [20]. Furthermore, consideration of the accuracy of measurement of fruit and vegetable intake is crucial when evaluating the effectiveness of interventions. Fruits and vegetables have varying nutrient profiles and product attributes, and thus should be promoted separately. Additionally, the assessment of vegetable intake should be measured separately from fruit using validated tools.

Assessing External Validity

Assessment of the external validity of studies is as equally important as determining efficacy. The external validity of studies has implications on the translation of interventions to the broader young adult population. With the young adult population neglected from many population-wide fruit and vegetable campaigns, investigation of the potential upscaling of current interventions is necessary.

To our knowledge, there is no published review to date focusing on the efficacy and generalizability of social marketing and eHealth and mHealth interventions on vegetable intake in young adults. This review addresses this gap in the literature.

Thus the aims are to: (1) systematically examine the effectiveness of social marketing, electronic and/or mobile phone-based interventions in increasing fruit and vegetable intake in young adults; (2) assess the efficacy/validity of tools used to monitor changes in fruit and vegetable intake; and (3) review the adequacy of reporting of external validity components.

Methods

Defining Search Terms

The Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) protocol will be used to conduct this systematic review [21]. The search terms have been selected to be broad and will include combinations, truncations, and synonyms of "online intervention", "computer-assisted therapy", "Internet", "website", "cell phones", "cyber", "telemedicine", "email", "fruit and vegetables", "young adult", and "randomized controlled trials". A separate search will be conducted to identify studies reporting interventions using social marketing and mass media to increase fruit and vegetable intake in young adults. This search will encompass terms such as "young adult", "fruit and vegetables", "social marketing", "social media", and "mass media". The Medline thesaurus Medical Subject Headings (MESH) terms will be refined according to each database. Although we are primarily interested in the implications of interventions on vegetable intake, the search term was broadened to include "fruit" as studies commonly report on fruit and vegetables concurrently.

Search Strategy

The following electronic databases will be searched for papers published between January 1990 and March 2015: the Cochrane Library, Cochrane Library of Systematic Reviews, Cochrane Central Register of Controlled Trials, CINAHL, Medline, Embase, PubMed, PyschINFO, Scopus, Web of Science, and Science Direct. The start of 1990 was selected, as it corresponded with the period during which the use of email became widespread [22]. Reference lists and JMIR journals will be hand searched for additional citations. Studies determined to be relevant to the review will be included.

Eligibility Criteria

Overview

The eligibility criteria for studies have been selected based on participants, interventions, comparisons, outcomes, and study designs (PICOS). Only studies written in English and published after 1990 will be included.

Participants

The target age group for the included studies will be young adults aged 18-35 years inclusive. The participants should be

healthy, with no disease or illness which would impact the primary outcome or ability to modify fruit and vegetable intake. There will be no limitation based on gender, ethnicity or socioeconomic status. Interventions set outside of universities will also be included in the review.

Interventions

The type of interventions that will be considered in the initial search will be eHealth or mHealth-based interventions. These are studies that employ the use of mobile phone apps, texting, email, phone calls, and websites to deliver the intervention. The secondary search will not be limited to eHealth or mHealth interventions and will include social marketing and mass media interventions. These are defined as studies that employ the use of media advertising through television, radio, billboards, and/or social media platforms as well as other community-based activities such as group education and cooking classes to increase fruit and vegetable intake.

Comparisons

Comparisons will be made between baseline and follow up results within and between studies. The differences between intervention and control arms (no intervention or minimal contact) will also be explored.

Outcomes

The primary outcome that will be investigated is the change in fruit and vegetable intake between baseline and follow-up. This can be reported in serves, frequency or grams. Fruit will be included as an outcome to account for studies reporting fruit and vegetable intake concurrently.

Study Designs

The first search will be limited to randomized controlled trials (RCTs) or cluster-RCTs with an aim of increasing fruit and vegetable intake in young adults. The social marketing search will not be limited by study design.

Study Selection

Titles and abstracts of all retrieved studies will be exported to Endnote X6 citation management software (Thomson Reuters, Philadelphia, PA, USA). Duplicates will be deleted before titles and abstracts are reviewed to group papers into either of the following: (1) meeting selection criteria; (2) requiring further examination; or (3) excluded. Papers determined as potentially relevant to the review will be downloaded as full text and reviewed for eligibility by two evaluators (MMN, JC) and further categorized (Figure 1). Discrepancies in evaluators' results will be resolved by discussion and, when necessary, in consultation with a third reviewer (MAF). The reasons for exclusion of studies will be recorded in a PRISMA flowchart which will illustrate the search, screening, and selection results (Figure 1).

Figure 1. Preferred reporting items for systematic reviews and meta-analyses (PRISMA) flow diagram.

Identification

| Records identified through database search 1 *(e- and m-health interventions)* (n =) | Records identified through database search 2 *(social marketing and mass media)* (n =) |

Additional records identified through other sources Hand search (n=)

Additional records identified through other sources Hand search (n=)

Records after duplicates removed (n =)

Records after duplicates removed (n =)

Screening

Records screened by title and abstract (n =) Records excluded (n =)

Records screened by title and abstract (n =) Records excluded (n =)

Eligibility

Full-text articles assessed for eligibility (n =)

Full-text articles assessed for eligibility (n =)

Full-text articles excluded, with reasons(n =)

Full-text articles excluded, with reasons(n =)

Included

Studies included in qualitative synthesis (n =)

Data Collection

A data extraction table will be designed using principles of the PRISMA statement for reporting systematic review [21], and the Cochrane Collaboration's tool for assessing risk of bias [23]. Once piloted for use on included studies, the following data will be collected: study details (authors, year, country of publication, funding, and affiliations); participants (characteristics, setting, inclusion/exclusion criteria, attrition, and blinding); intervention and comparator details; duration; and outcome measure (change in fruit and vegetable intake).

Data Analysis

Reporting of Intervention Outcomes

An appropriate method of reporting the treatment effect will be determined based on the type of data extracted from included studies. It is anticipated that the mean differences in fruit and vegetable intake between baseline and follow up will be reported. These results will be tabulated to enable qualitative description of results and heterogeneity assessment for potential pooling of results using meta-analysis.

Risk of Bias Assessment

Using the Cochrane Collaboration's tool [23], risk of bias will be determined for each included study, taking into consideration

selection (random sequence generation and concealment of allocation methods), attrition (completeness of outcome data), detection (blinding of participants and personnel), and reporting (selective reporting of outcome measures). Two authors (MMN and JC) will independently evaluate each study for risk of bias and will code them as low-risk, high-risk or unclear risk. Any discrepancies will be settled through discussion.

Quality Assessment

The quality of each study will be determined by two independent parties using the Effective Public Health Practice Project (EPHPP) Quality Assessment Tool for Quantitative Studies [24]. The following components will be considered in order to assign a quality rating to each study: study design, selection bias, blinding, confounders, outcome collection methods, participant withdrawals, and dropouts. Studies will be given a rating of "weak", "moderate" or "strong" by two authors (MMN, JC), with conflicting ratings resolved through discussion with a third independent reviewer (MAF).

Rating External Validity

A table collating the reported external validity components of the included studies was designed based on the criteria for rating external validity developed by Green and colleagues [25]. The table explores components under three sections: (1) reach, adoption and representativeness of participants; (2) intervention

implementation and adaption; and (3) program maintenance and institutionalization (sustainability of program implementation). Qualitative and quantitative data relating to these external validity components will be extracted. Extracted data will be used to report the number and percentage of studies adhering to the external validity components. The adequacy and frequency of reporting of these components will be explored between studies.

Results

Our research is in progress. A draft of the systematic review is currently underway and will be submitted before the end of 2015.

Discussion

This review will present a summary of the efficacy and external validity of the published studies that have used eHealth and mHealth or social marketing strategies to engage young adults in improving their vegetable intake. The findings will provide a scope for the development of future interventions and social marketing campaigns targeted at this age group.

Authors' Contributions

MMN, JC and MAF developed the research question and MMN drafted the review protocol. All authors have read the final protocol and will contribute to screening, extraction, analysis, and writing of the review manuscript.

Conflicts of Interest

None declared.

Multimedia Appendix 1

MEDLINE Search Strategy.

[PDF File (Adobe PDF File), 14KB - resprot_v4i3e92_app1.pdf]

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Abbreviations

EPHPP: Effective Public Health Practice Project
MESH: Medline thesaurus Medical Subject Headings
PICOS: participants, interventions, comparisons, outcomes and study designs
PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analysis

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Protocol

Interleukin 2 Topical Cream for Treatment of Diabetic Foot Ulcer: Experiment Protocol

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Abstract

Background: It is estimated there are 2.9 million diabetic patients in the United Kingdom, and around 5%-7% of patients have diabetic ulcers. This number will continue to increase globally. Diabetic ulcers are a major economic burden on the healthcare system. More than £650 million is spent on foot ulcers or amputations each year, and up to 100 people a week have a limb amputated due to diabetes. In T1DM, the level of IL-2 is reduced, and hence, wound healing is in a prolonged inflammatory phase. It is not known if IL-2 topical cream can shorten the healing process in T1DM patients.

Objective: The objective of this study is to understand the pathophysiology in type 1 diabetes (T1DM) and investigate possible future treatment based on its clinical features. The hypothesis is that IL-2 cream can speed up wound healing in NOD mice and that this can be demonstrated in a ten-week study. An experiment protocol is designed in a mouse model for others to conduct the experiment. The discussion is purely based on diabetic conditions; lifestyle influences like smoking and drinking are not considered.

Methods: Skin incisions will be created on 20 nonobese diabetic (NOD) mice, and IL-2 topical cream will be applied in a 10-week study to prove the hypothesis. Mice will be randomly and equally divide into two groups with one being the control group.

Results: T1DM patients have a decreased number of T regulatory (Treg) cells and interleukin 2 (IL-2). These are the keys to the disease progression and delay in wound healing. Diabetic ulcer is a chronic wound and characterized by a prolonged inflammatory phase.

Conclusions: If the experiment is successful, T1DM patients will have an alternative, noninvasive treatment of foot ulcers. In theory, patients with other autoimmune diseases could also use IL-2 topical cream for treatment.

Introduction

Background

Clinical Problem

The incidence of one major cause of chronic wounds, the diabetic ulcer, is increasing globally. There are an estimated 2.9 million diabetic patients in the United Kingdom; around 5%-7% suffer from diabetic ulcers, and 67% have one or more risk factors. These numbers are expected to increase. Up to 85% of amputations are preceded by foot ulcers, and a recent World Health Organization report pointed out that a reduction in amputations could be achieved through success in reducing ulcer incidence [1]. According to a recent National Health

Service report, £650 million is spent on foot ulcers or amputations each year, and up to 100 people a week have a limb amputated due to diabetes [2]. This research proposal is aiming to help patients with type 1 diabetes in wound healing using immunology principles.

Immunology in Type 1 Diabetes

Type 1 diabetes (T1DM) is an autoimmune disease the cause of which remains unknown. In T1DM patients, β-cells in the pancreas are destroyed by autoimmune responses, resulting in a lack of insulin production. Scientists generally believe that it arises either by genetic or environmental factors, and those factors contribute three criteria for developing T1DM. First, β-cell-reactive T cells are being activated, and hence, a

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proinflammatory response is induced. Last and most importantly, the immune regulation of autoreactive responses fails [3].

Environmental Factors

The enterovirus is believed to be the most common viral infection causing T1DM. Other viruses like rotavirus, mumps, cytomegalovirus, and Epstein-Barr virus might be able to trigger autoimmune responses or associate with T1DM, as they have the ability to infect or lyse β-cells directly [4]. During infection, the number of pattern recognition receptors increases in the islets to facilitate the innate immune system's identification of microorganisms. The virus activates the production of interferon α (IFN-α) and IFN-β chemokines and overexpresses the major histocompatibility complex (MHC) I molecule; subsequently, the chemokines attract T cells to produce proinflammatory cytokines such as interleukin 1 β (IL-1β) and IFN-γ. As the infection process continues, antibodies and cytotoxic T lymphocytes disrupt β-cells and induce apoptosis. Killing is mediated via the interaction between Fas ligands on the CD4$^+$ T cell and Fas on the β-cell, and eventually the β-cell antigen (MHC II molecule) will be released.

The reason why the infection is chronic is that specific antibodies from persistent infections can target Coxsackievirus (one of the RNA enteroviruses) and adenovirus receptors and FcγRII and III to enhance the infection of monocytes and macrophages. Antibody-dependent enhancement of infected monocytes and macrophages could increase the spread of the virus to β-cells and continuously stimulate autoimmunity.

Initial viral infection in children is thought to be beneficial, as their bodies develop adaptive immunity. However, in T1DM patients, T regulatory (T$_{reg}$) cells are reduced due to an ineffective regulatory system. Hence, viruses keep replicating and persistently result in high concentrations.

Human Genetic Factors

Genetic factors have a big impact on the abnormal immune system in T1DM patients. They are blamed for about one-third of the susceptibility to T1DM, and over 20 different regions report such linkage [4]. Viral infection may trigger autoimmunity, but it is only part of the disease mechanism. Apart from activating the different kinds of immune cells, the body also synthesizes different enzymes in response to the invasion, and genes control this. Gene *IDDM10* has been picked as an example here.

The IL-2 receptor is expressed on immune cells in response to the stimulation of T-cell receptors (TCRs) during antigen binding. This could increase the binding of IL-2, which is vital in T-cell proliferation. The IL2α chain (CD25) is part of the IL-2 receptor and expresses during the predevelopment stage of the T and B lymphocytes. Chromosome 10 contains more than one susceptibility locus; they are called IDDM10. One of the regions is 10p15-p14, where the IL2α chain (CD25) is encoded. Mutation in this region would possibly lead to an IL-2 receptor α deficiency and hence affect the FOXP3 protein. Tag single-nucleotide polymorphisms were analysed, and it was discovered that the deficiency is likely due to linkage disequilibrium [5]. Interestingly, FOXP3 is strongly associated

with T1DM; however, its gene (on chromosome Xp11) has no genetic association in T1DM patients [6].

Immune Response in Type 1 Diabetes

Various T cells are activated when MHC I and II are expressed by a virus or β-cell. At the same time, exposure of proinflammatory cytokines on a β-cell drives the β-cell to upregulate IL-8 and chemokine (c-c motif) ligand 5 (CCL5), which draw target cells to migrate to the infection site by chemotaxis. In normal practice, CD4$^+$ T cells express IL-22, while islet cells express the IL-22 receptor to activate the signal transducer and activator of transcription (STAT) 3 [3]. STAT3 is important to compete with IL-2 and hence to upregulate protective gene transcription. The difference between a healthy individual and a diabetic patient is the introduction of IFN-α, which makes IL-22 switch STAT3 to STAT1. STAT1 is responsible for the expression of inducible nitric oxide synthetase.

T$_{reg}$ cells are the critical immune cells in T1DM immune modulation. These cells are important, as they monitor and kill autoreactive T cells to prevent pathological self-reactivity. In patients with T1DM, T$_{reg}$ cells no longer effectively control the islet autoreactive T cells and consequently, the body loses immune tolerance and continuously activates B cells and effector T cells. However, the nature of the dysfunction remains unclear [7].

FOXP3 is a transcriptional factor which acts as lineage specification factor of T$_{reg}$ cells. Its specific contribution in the differentiation and function of T$_{reg}$ cells remains uncertain. Several experiments have been done in animals and humans to test the effects of a defective FOXP3 or a deficiency in FOXP3. Evidence shows that FOXP3 is critical in maintaining self-tolerance by suppressing self-reactive T cells. One may expect that the faulty FOXP3 gene is crucial in contributing to T1DM. It is true that patients with FOXP3 deficiency will develop immunodysregulation polyendocrinopathy enteropathy X-linked syndrome (IPEX). More than 80% of IPEX patients acquire T1DM at very early onset [8]. Indeed, *IDDM10*, which encodes the IL2α chain (CD25), is the causative reason. CD25 is so important because it is the key cytokine for the fitness and function of FOXP3$^+$ T$_{reg}$ cells. In other words, CD25 maintains the stability of and upregulates FOXP3. It is believed that it involves a direct pathway linking IL-2 signalling to the expression of the FOXP3 gene through STAT proteins [9]. Studies [10] also show that IL-2 is vital for T$_{reg}$ cell survival. In T1DM patients levels of IL-2 are reduced, and one can deduce that this will affect FOXP3 effects on T$_{reg}$ cells. It is believed that the loss of expression of FOXP3 not only results in a loss of regulatory function but could also be associated with the conversion of T$_{reg}$ cells into potential effector T cells and with the secretion of IFN-γ and IL-17. These cytokines may further reduce the secretion of IL-2 and form a vicious circle. Another suggestion is that the effector could become resistant to suppression [7]. The elevated amount of T$_H$1 and T$_H$17 is the evidence of failure of immune suppression. The numbers increase throughout T1DM's development.

Cytotoxic T-lymphocyte–associated protein 4 (CTLA-4) is a protein receptor on the T-cell surface that downregulates possibly by recruiting phosphatase to the TCR. There is controversy about the main functions of CTLA-4; it could be involved in another essential part of the T_{reg} cell function but is perhaps not involved in the expression of FOXP3 [11]. Serum levels of sCTLA-4 (soluble form) are higher in patients with autoimmune thyroid diseases compared to healthy subjects. However, it is not clear whether this phenomenon is due to DNA mutations or to an indirect effect correlated to the affection status [12]. The reason for functional change in immune regulation caused by mutation is unknown. T-cell development is not affected in T1DM patients but the number and activities of T_{reg} cells appear unusual. Investigation shows that performance of suppression by T_{reg} cells is weaker in the higher ratio of effector T cells [13]. Different evidence demonstrates that T_{reg} cell functions are impaired in patients with T1DM. Perhaps this affects the wound-healing processes.

Immunology at the Cellular Level

Although the T1DM pathophysiology is different from T2DM, both types of diabetes share many clinical features (eg, insulin resistance, cardiovascular disorders). The mechanism is not fully discovered yet; a paper suggested insulin therapy might be a primary inducer. In a cultured hepatocytes model, significant insulin resistance was developed under prolonged exposure to insulin, and this is similar to the setting of insulin therapy [14]. Apart from insulin resistance, high triglyceride level is often measured in patients with persistent or inadequate insulin therapy. On the other hand, untreated T1DM patients may not face the problem of insulin resistance [15]; however, hyperglycemia could lead to ketoacidosis. Ketoacidosis eventually enhances the flux of free fatty acid (FFA) to the liver and promotes hypertriglyceridemia [16]. In addition, in obese subjects with T1DM, insulin resistance can accelerate progression of T1DM complications [14].

It is believed that there are inflammatory events around adipose tissue and immune responses to elevated blood glucose. Those events can be observed in all tissues that process energy homeostasis (eg, fat, muscle, liver, and blood vessels) [17]. Eventually, once these factors are transported to the pancreas by the blood, islet autoimmunity might occur [18]. FFA interacts with toll-like receptors (TLRs) and facilitates the following immune activities. First, FFAs induce the formation of lipid rafts in cell membranes, which favor the TLRs' signalling. Production of reactive oxygen species (ROS) is involved in the activation of inflammatory pathways via TLR. Hence, ROS may lead to the induction of stress kinases. ROS could also initiate the IL-1 system through the formation of NLRP3 inflammasomes. Meanwhile, production of IL-1β could be facilitated through FFA metabolites or via TLR2 or 4. FFA can directly activate these receptors, as they are sensitive to lipids [19].

Adipose tissues per se can induce immune responses. Although the mechanism that initiates the inflammation is unknown, inflammation is associated with an accumulation of immune cells in obese patients. It is deduced that hypertrophy is responsible, as cellular contents might leak into cellular spaces

and promote an inflammatory response or induce adipocyte death [17]. Earlier research [20] concluded that obesity is associated with an increased accumulation of T cells and macrophages in adipose tissue, and CCL5 is an adipokine that is upregulated in adipose tissue through obesity in humans. However, it is not clear what antigen attracts T cells. Although more T cells are presented in comparison to a leaner state, the ratio between T_{reg} cells and $CD4^+$ T cells dramatically decreases with increasing levels of obesity [21]. The impact of T cells in adipose tissue on neighboring cells is likely through soluble mediators. Fat-resident regulatory and conventional T cells can synthesize various cytokines, which have a direct impact on the synthesis of inflammatory mediators and glucose uptake by adipocytes. T_{reg} cells are not just involved in immune response; they could also increase the circulation of blood glucose.

Increased tumor necrosis factor α (TNF-α) has been detected in the adipose tissue of obese mice and is recognized as one of the immune characteristics [17]. This has also been observed in the serum samples of diabetic patients using the enzyme-linked immunosorbent assay [22]. In vitro, TNF-α induces changes in the expression of a number of transcripts that encode inflammatory mediators, including IL-6, CCL5, serum amyloid 3, intracellular adhesion molecule 1 and matrix metallopeptidase (MMP) 3. These cytokines are described as a network that stimulates the production of acute-phase proteins. IL-6 is the main stimulator, while IL-1 and TNF-α are the central mediators of inflammatory reactions [22]. Hypoxia, often seen in hypertrophy, could also raise immune response. Hypoxia can recruit macrophages and induce the expression of numerous proangiogenic and proinflammatory genes inside macrophages. This may be closely associated with infection and the wound-healing process, as the recruitment of macrophages is the key in those events.

Meanwhile, hyperglycemia provokes a similar immune response and activates different cytokines, transcriptional factors, and ROS in the islets. Glucose can stimulate nonenzymatic glycation and generate advanced glycation end products (AGEs), one of the factors in the stimulation of the pattern recognition receptor, RAGE. Once RAGE is activated, the production of nuclear factor-κB (NF-κB), ERK1, ERK2 (MAPK) and ROS will be induced [17]. All these products are fundamental for the next step in immune response—the production of IL-1β and other cytokines. The other important reason to maintain low or normal concentrations of ROS is because β-cells have limited antioxidative enzymes and consequently are susceptible to oxidative stress [19]. Production of mature IL-1β highly depends on caspase 1, as it involves a rate limiting step in IL-1β processing [23]. Caspase 1 plays its role by activating an inflammasome, and eventually the caspase 1 inflammasome secretes mature IL-1β. Apart from ROS, islet amyloid polypeptide (IAPP) contributes to the induction of IL-1β by triggering NLRP3 inflammasome. In addition, stimulation from TLR2, TLR4 and RAGE could lead to NF-κB activation and could produce various cytokines and chemokines, including IL-1β.

Thus far, few activation mechanisms of IL-1β have been mentioned; these are induction via TLR, IAPP, and ROS. In

addition to induction, IL-1β could be upregulated under high glucose concentration, as more Fas is likely to be expressed on β-cells, and Fas could induce such secretion.

IL-1 acts as a sensor of metabolic stress and activates immune response in β-cells, insulin-sensitive tissue, and blood vessels [17]. In low concentrations of IL-1β, it can promote β-cell function and survival. However, if IL-1β is continuously activated, a broad range of CC-chemokine ligand will keep being produced, for example, CCL2, CCL3, and CCL8. These are formed via NF-κB activation in epithelial, endothelial, and immunocompetent cells [23]. Those chemokines are known to have a role in monocyte recruitment. At the same time, IL-1β stimulates the IL-1 receptor (IL-1R) on fat cells and later, FFA is liberated. As more and more FFAs are present in the blood, they form a vicious circle of inflammation. IL-1 has been found to have profound effects on the function of β-cells, inducing them to undergo apoptosis via ERK [24]. In brief, IL-1β indirectly recruits macrophages to adipose tissue and islets and amplifies islet inflammation [18]. IL-1 receptor antagonists (IL-1RAs) are greatly expressed in prediabetes; however, the expression decreases along the pathogenesis. This results in an imbalance between the agonist IL-1β and IL-1RA. This indicates that the inflammation might be greatly enhanced due to the susceptibility of β-cells to IL-1β [19].

Diabetes and Complications: Nephropathy, Atherogenesis, and Neuropathy

Diabetic Nephropathy

Diabetic nephropathy is a typical complication in both types of diabetes. It is a progressive and chronic kidney disease (CKD) in the glomerulus and is characterized by hyperfiltration [25]. Microalbuminuria is gradually developed due to the extracellular matrix accumulation in basement membranes and mesangium [26]. CKD does not merely affect the kidney but also impacts the vascular system, immune system, and skin and growth factors [27]. The precise cause of diabetic nephropathy is undiscovered, but scientists suggest that hyperglycemia, activation of cytokines, and inflammation are possible causes [28].

An experimental wound model has been applied in mice and studied with different analyses. It included study of the kidney glomerular tuft area, histology and immunofluorescence, tissue gnostics quantification, and polymerase chain reaction [27]. Although the study was based on CKD, its result helped to widen our understanding. The results verified that CKD wounds had statistically tremendous disruption of normal reepithelialization kinetics and granulation tissue deposition rates. Consequently, the epithelial gap was relatively larger, and the formation of granulation tissue was decreased. In terms of cellular proliferation and angiogenesis, these activities were notably decreased in the early stages of wound healing. At the same time, the inflammatory state was maintained and increased for 14 days. Surprisingly, this research showed that there was no correlation between IL-1β, TNF-α, and wound healing [27]. This might reflect the idea that IL-1β and TNF-α are important in the progression of diabetes but not in wounds.

The physical conditions of wounds have also been reviewed. Dryness, rashes, microangiopathy, and even calciphylaxis were considered to correlate with the severity and duration of the CKD state [27]. Dryness is often associated with infection; however, no wound infections were observed in this experimental setting, and indications were that the wounds were systemically based. Although bacterial infection is not the cause of CKD, infections tend to be observed in patients with CKD as well as those with diabetes-related foot infections. In 653 samples from 379 patients, 23% of wounds were detected with methicillin-resistant *Staphylococcus aureus*; it is believed that the infection is responsible for increased morbidity and mortality [29]. Infections often compromise wound-healing progress.

Atherosclerosis

Atherogenesis is considered a threat to healing by contributing prolonged inflammation and inadequate blood and oxygen supply to tissue. Although it alone does not cause ulceration, it can be serious enough to cause amputation of affected limbs [30]. Its characteristics include abnormalities in endothelial cells and in the function of vascular smooth muscle cells and platelets. These abnormalities could induce endothelial dysfunction, an early, integral component of atherosclerosis. The following section studies the connection between diabetes and atherosclerosis. Based on current understanding, inflammation is the key that drives atherosclerosis, and diabetic conditions may in turn promote vascular inflammation.

Nitric oxide (NO) has an imperative role in protecting blood vessels by regulating vasodilation, as well as mediating molecular signals and thus preventing leukocyte and platelet interaction. However, in diabetic patients, hyperglycemia, FFA, and insulin resistance are believed to be the major cause of reduced level of NO. Hyperglycemia and FFA can increase the generation of ROS and hence ROS inactivates NO by disturbing the phosphatidylinositol 3 kinase pathway via the activation of protein kinase C. Meanwhile, FFA could further weaken endothelial function by reducing endothelium-dependent vasodilation. When the liver deals with excess FFA, it enriches production of very-low-density lipoprotein. Plaque is easily formed in diabetic patients because plasma coagulation factors and lesion-based coagulants are elevated, whereas thrombomodulin and protein C decline. A reduced level of NO and endothelial dysfunction favor the migration of vascular smooth muscle cells into nascent atherosclerotic lesions.

Although the individual role of C-reactive protein (CRP) in atherogenesis is still under investigation, it could contribute to atherogenesis together with LDL. It is reported that the CRP level is elevated during inflammation and under hyperlipidemic conditions, and it presents throughout all stages and colocalizes in activated complements in humans [31]. CRP is potentially able to activate macrophages, endothelial cells, and vascular smooth muscle cells, hence promoting inflammation. In addition, CRP could also increase MMP synthesis, as proven by fluorescence microscopy of the endothelial layer. MMPs have been considered the central pathway linking inflammation and plaque instability or rupture [32].

Diabetic Neuropathy

Diabetic neuropathy is the most common diabetic complication in both T1DM and T2DM, with 45%-60% of ulcerations believed to be purely neuropathic [1]. It is considered a disorder and contributes by polyol pathway, microvascular injury, and AGEs. Diabetic neuropathy is further classified as peripheral, autonomic, proximal, and focal neuropathy. The following discussion focuses on diabetic peripheral neuropathy (DPN), as it is the most common among all types and is closely linked to the wound-healing processes. The predominant pathological characteristics of DPN are loss of axon, demyelination [30], capillary basement membrane thickening, endothelial cell hyperplasia, and neuronal ischemia and infarction [33]. Large myelinated fibers are generally lost due to toxic and metabolic disorders, yet small unmyelinated fiber losses are also recorded in peripheral nerves. The second characteristic, demyelination, would result in sensitive changes and a decrease in conduction velocity. Notably, this could affect all types of nerves in the central and peripheral nervous systems. Peripheral nerves are surrounded by large numbers of blood vessels to ensure a good blood supply. However, atherogenesis limits blood flow, as the presence of plaque reduces the blood vessel lumen. Insufficient blood flow results in a reduction of nerve conduction velocity as well as circulation of nerve growth factor.

Damaged nerves to intrinsic foot muscles lead to an inequity between flexion and extension of the affected foot. Skin breakdown and ulceration are progressively shown, since foot deformities cause abnormal bony prominences and build pressure points. In addition, neuropathy reduces the functionality of sweat and oil glands. As a result, the foot loses the natural ability to moisturize the skin and hence becomes dry. Often, dry skin increases susceptibility to microorganisms and subsequently to the developing of infection. Patients with severe peripheral neuropathy may also suffer from neuropathic edema in the lower legs. This is possibly related to vasomotor changes and arteriovenous shunting [34]. It is generally believed that the loss of sensation is the biggest problem caused by neuropathy. Patients are often unable to feel pain from the affected site, and thus wounds gradually get worse without being noticed [35].

Wound Healing Process

Origins of Ulcers

Diabetic neuropathic ulcers are most likely to be seen on a patient's palm and the soles of the feet. In general, a diabetic foot ulcer is more predominant. Ulcers do not happen spontaneously; they can begin with minor skin infections or cuts. Wound healing is a complex process involving blood clotting, inflammation, proliferation, tissue remodelling, and eventually wound closure; the phases overlap each other. Diabetic wounds are chronic wounds in which the wounds are trapped in the inflammation phase and do not heal within three months [36].

Inflammatory Phase

Wound healing is a complicated process and involves the nervous and immune systems. The first stage, the inflammatory phase, begins with a passive leakage of circulating leukocytes from damaged blood vessels towards the wound site. T cells and Langerhans cells secrete cytokines and chemokines in response to the injury [37]. Various cell types secrete growth factors, which have a role in recruiting neutrophils and macrophages from nearby uninjured blood vessels. The transforming of growth factor β 1 and vascular endothelial growth factor expression are generally interrupted due to reduced IL-1RA. As mentioned earlier, the level of IL-1RA is reduced in diabetic patients. Reduction could induce prolonged NF-κB translocation, and subsequently lead to suspended wound healing [36]. Cytokines, chemokines, and growth factors all together are the important mediators, and activate intracellular signalling to drive cell proliferation, migration, and differentiation.

Like other chronic wounds, a diabetic ulcer is characterized by the imbalance of proinflammatory and anti-inflammatory factors. This feature possibly arises due to macrophage dysfunction. In diabetic mice, macrophages isolated from a wound showed momentous impairment in efferocytosis; in other words, cell debris was not cleared up effectively, resulting in an accumulation of apoptotic cells. Fas ligands drove the apoptotic cell burden to enhance proinflammatory but weaken anti-inflammatory cytokine response [38]. Although disruption of the blood supply and hypoxia can increase the presence of macrophages at a wound site, it may not benefit healing when the impairment in efferocytosis is considered as well as the delayed migration [39].

Proliferative Phase

There are three important events in the proliferative phase: angiogenesis, formation of granulation tissue and the extracellular matrix (ECM), and reepithelialization. Angiogenesis is the most critical of these events and is the key process of successful wound healing. New blood vessels are essential to deliver nutrients and oxygen to support the growth of cells and tissue and the formation of a wound matrix [37].

Cellular hypoxia, a major issue in chronic wounds, is one of the consequences when angiogenesis is blocked or retarded. It is thought that angiogenesis could be affected by diabetic neuropathy to some degree. Various cells need oxygen to survive and function. For example, fibroblasts and epithelial cells require oxygen to migrate, and collagen fibril crosslinking requires oxygen to carry out hydroxylation. Infection is likely to occur with insufficient oxygen, as the bactericidal potency of leukocyte oxidative phosphorylation is changed.

Granulation and Reepithelialization

Formation of new granulation tissue and reepithelialization are the mechanisms to restore the function of the skin and bring about permanent closure of the wound gap. Granulation tissue is formed in the dermis, performed by fibroblasts, whereas reepithelialization is carried out in the epidermis by keratinocytes. Both mechanisms correlate with each other closely to bring about the outcome.

Reepithelialization begins with the migration of keratinocytes. Upon arrival at the injured site, keratinocytes modify or dissolve cell-cell and cell-matrix adhesions by releasing collagenases (MMP1) and different types of MMPs. These changes facilitate

the formation of a laminin V and collagen IV-rich basement membrane through provisional matrix substrates. Debris and blood clots are also dissolved during this progression to benefit the migration of other cells. Keratinocytes themselves produce growth factors and basement membrane proteins to accelerate reepithelialization [37]. ECM is not just a supportive three-dimensional structure; it also encourages cell proliferation, survival, function, migration, and differentiation. Cell-matrix interaction can indicate the process of ECM remodelling in wound healing [40].

Normal fibroblasts come from different parts of the body and migrate to the wound site. The primary source is the surrounding healthy dermis, while bone marrow progenitor cells and circulated fibrocytes are alternative sources. These cells migrate and join together in response to stress fibers and various growth factors promoting the migration. Fibroblasts use the fibrin crosslinking fibers, formed in the later period of the inflammatory phase, to migrate across the wound, and eventually they adhere to fibronectin. Fibroblasts synthesize, bind, and align collagen fiber into the wound bed in the contraction step [37]. Contraction is the other key step in granulation and is performed by myofibroblasts. Myofibroblasts are differentiated from fibroblasts and are similar to smooth muscle cells in terms of structural and biochemical properties. They express microfilaments and α-smooth muscle actin to connect various wound edges by attaching to desmosomes [41]. Insulin-like growth factor 1 (IGF-1), which is produced by epidermal T cells, is the growth factor that stimulates this process. Experiments on rats have demonstrated that an increase in IGF-1 could enhance the expression of myofibroblasts and tissue repair capacity [41]. Research results showed that a low IGF-1 level is associated with both types of diabetes and, generally, with adults under 65 [42]. Other research on human acute and chronic wounds both in vivo and in vitro also reported there was lower IGF-1 production in chronic wounds under flow cytometry analysis [43]. Scientists proposed that T cells in chronic wounds are less alert to activation and bypass TCR stimulation, likely due to much less IL-2 production by the T cell [43].

There are a few difficulties to consider in the proliferative phase. First, MMPs are excessively synthesized in diabetic patients; the high level of activity could cause unnecessary collagen loss. A high level of MMP1 is vital in wound healing; however, too much MMP8 and 9 could be dangerous. A longitudinal study was conducted on T2DM patients with foot ulcers investigating the impact of MMP levels on recovery. The study recorded levels of MMPs and tissue inhibitors of metalloproteinases around the wound edge and concluded that reduced MMPs do not contribute to good healing [43]. The second issue is glycation of collagen under elevated blood glucose levels. Collagen and elastin could easily carry out irreversible crosslinking with AGEs via nonenzymatic glycation [40]. Evidence proves that both mechanical and biochemical roles are impaired after glycation. The same study pointed out that cell-induced material contraction is also inhibited under observation in immunostaining [44]. In addition, the formation of collagen is retarded in an insufficient oxygen environment.

Hypothesis and Aims

Impaired function and a decrease in numbers of T_{reg} cells have been discussed in detail above. In T1DM, the level of IL-2 is reduced, and hence, wound healing is in a prolonged inflammatory phase. If optimum IL-2 dosage is given to patients, perhaps it can increase the T_{reg} cell survival rate and response; this likely can be achieved through immunotherapy. Immunotherapy is often used on cancer patients, and research on treating patients with T1DM is ongoing. In 2013, experimental results showed that a low IL-2 dose could increase the number of T_{reg} cells; however, a high dosage might induce β-cell impairment in humans. IL-2 was given by injection in the experiment, and some T1DM patients had serious injection site reactions [45]. Similar results have also been observed in mice. In the nonobese diabetic (NOD) mouse model, mice were given a low dose of IL-2 (25,000 IU per day) for five days, and IL-2 appeared to act specifically on T_{reg} cells in inflamed nonlymphoid tissue. Although the effect was more remarkable in tissue with ongoing autoimmunity such as the pancreas, results also showed that IL-2 can upregulate CD25 expression and suppress IFN-γ in skin. Moreover, no harmful effects were detected in other cells, which means that the risk of generalized immune suppression is low. These two experiments demonstrated that IL-2 could be a safe therapeutic choice for treating inflammation. In terms of the IL-2 effects on wounds, experiments have been done on Adriamycin-treated [46] and Lewis [47] mice and have demonstrated positive effects of IL-2 on wound healing. These experimental results imply that there is hope for IL-2 treatment in healing. The effect of IL-2 on diabetic wounds has not been investigated on animal models or humans. It is predicted IL-2 treatment would only work in T1DM, as there is no reduction of IL-2 in T2DM.

The hypothesis is that IL-2 cream can speed up wound healing in NOD mice and that this can be demonstrated in a ten-week study. Inspired by the success of insulin cream, it is decided that IL-2 will be given in cream form at a low dosage. A human IL-2 gene could be modified by genetic technology and will subsequently be inserted into *Escherichia coli* for synthesis. The first aim is to study the effect of IL-2 cream on the wound-healing process to prove the hypothesis. The second aim is to test the cream's pharmacokinetics and determine the effective dosage (with no serious side effects).

Methods

Intervention

A ten-week-old male NOD mouse's hair will be removed before the surgery. During the surgery, the mouse will be anesthetized by open-mask method and circular dorsal skin incisions at least 1 cm in diameter will be created on the left- and right-hand sides in parallel (see Figure 1). The left side will be cut through the epidermis and above the dermis, and the right side will be cut through the dermis but not reaching to muscle.

An aseptic technique will be used to prevent bacterial infection. After surgery, a thin protective dressing will immediately be placed on the wound site. Throughout the experiment, all mice will be fed the same standard mouse diet and water and will

live in a pathogen-free and temperature-controlled animal facility with a 12-hour light and dark cycle until sacrificed. Mice will be euthanized 24 hours after the last treatment.

Twenty male mice will be randomly and equally divided into two groups. In one group, a thin layer (0.1 g) of IL-2 cream will be applied on each wound every 24 hours; the other group will be the control group and will receive typical wound care. The cream will first be applied 24 hours after the surgery. Both

groups will have typical wound care, which includes changing dressings and cleaning the wounds daily with saline water.

As in a previous study, recombinant human IL-2 will be given in a 25,000 IU dosage per day [48] for the first seven days, with future doses being adjusted after evaluation. Active ingredients of the topical cream include 250,000 IU/g recombinant human IL-2, liquid paraffin 6% w/w and white soft paraffin 15% w/w; inactive ingredients are purified water and glycerol.

Figure 1. NOD mouse surgery position.
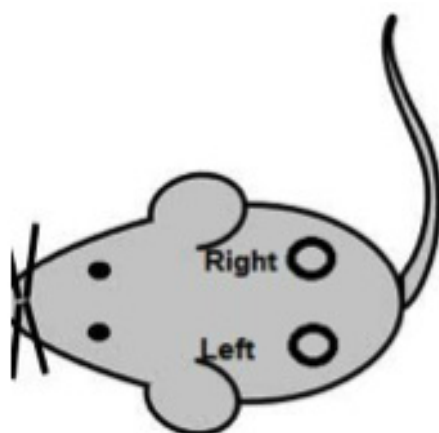
Data Collection

Both groups will have the following measurements unless otherwise specified. Two blood samples, a total of 0.3 mL, will be taken from the tail vein before surgery and every 24 hours after daily care. One of the samples will be used to check the level of insulin (pmol/L) in the serum and the white blood cells (K/uL) and the differential of white blood cells, based on 100 cells counted in plasma. Cytokines in serum will specifically be detected by cytokine array for quantitative measurement and will be observed for changes in the amount. T_{reg} cells will be isolated by magnetic cell separation and analysed by fluorescence-activated cell sorting, chosen for studying the surface expression of $CD4^+$ and $CD25^+$ of the T_{reg} cells [48]. A wound biopsy will be performed every week, starting from day 0, for histologic analysis. The epithelial gap and granulation tissue will be measured after hematoxylin and eosin (H&E) staining under a digital microscope. The percentage of epithelial gap closure and granulation tissue area will be quantified and calculated using a computer image analysis system and pixel density. The epithelial gap is defined as the distance between the edges of keratinocyte migration across the wound [27]. Maximal wound breaking strength will be measured by tensiometer in g/mm^2 after the mice are sacrificed [49].

Body weight will be measured daily in grams by an electronic balance. A pharmacokinetic test will be conducted by high-pressure liquid chromatography to measure the concentration of IL-2 in plasma in IU/mL [50].

Statistical Analysis and Expected Results

A 2-tailed unpaired Student t test with a 95% confidence interval will be calculated to demonstrate the effect of IL-2 cream in

both shallow and deep wounds as well as the difference between the two groups.

The number of immune cells and cytokine trends is expected to be similar to that in normal wound-healing progress. The IL-2 level should reach its peak after 24 hours of administration, while the pharmacokinetics are unknown and should be investigated. It is hoped that the insulin level will increase as well. H&E staining should show a shorter epithelial gap and granulation tissue, and the total epithelial closure of the wound should be bigger in contrast to the control group.

Ethical Issues

To limit the suffering from the incisions as much as possible, the mice will be given anesthesia before surgery, and the surgeries will be completed within 15 minutes. A mortality risk exists, as this is an invasive operation, but the risk should be low because the surgery does not involve injury to vital organs. Moreover, proper wound care will be given to minimize wound deterioration and infection. All mice in this experiment will receive humane care throughout the study and euthanasia at the end of the study.

IL-2 has been proven effective in cancer patients and has become one of the current treatments. One can see that there is a therapeutic value in conducting a similar experiment. The experiment is unlikely to be replaced by computer models or conducted on humans at this stage, so mouse models are chosen. Dosages will be given in a safety range based on similar experiments and may be adjusted after weekly evaluation of health and progress.

As this is a pilot experiment and no previous data exists, only small numbers of mice are used. The sample size should be big enough to show the differences and prove the hypothesis. Male mice are studied to prevent unnoticed pregnancy in female mice.

Results

This project is currently on hold as funding has not been secured yet.

Discussion

Lifestyle changes or surgical intervention could significantly improve ulcers in T2DM patients. However, clinical procedures might not be as effective on T1DM patients. Considering the success of imiquimod cream for treating melanoma and the latest results of IL-2 therapy in diabetic patients, it is realistic to develop topical immunotherapy. So far, no related experiment has been done on animal models or humans. If this experiment is successful, T1DM patients will have an alternative, noninvasive treatment. Since the use of topical cream doesn't require much education, it will be suitable for both young and elderly patients and will enhance compliance. In addition, the risk of infection and serious skin reaction could be reduced in comparison to intravenous treatment. It is assumed that this treatment can be safely used without contraindications with oral medicine. Last, it can protect skin from dryness as other creams do and can maintain a moist environment for the wound. In theory, patients with other autoimmune diseases could also use IL-2 topical cream for treatment.

Conflicts of Interest

None declared.

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Abbreviations

AGE: advanced glycation end product

CCL: chemokine (c-c motif) ligand

CKD: chronic kidney disease

CRP: C-reactive protein

CTLA-4: cytotoxic T-lymphocyte–associated protein 4

DPN: diabetic peripheral neuropathy

ECM: extracellular matrix

FFA: free fatty acid

H&E stain: hematoxylin and eosin stain

IAPP: islet amyloid polypeptide

IFN: interferon

IL: interleukin

IGF: insulin-like growth factor

IPEX: immunodysregulation polyendrocrinopathy enteropathy X-linked syndrome

MHC: major histocompatibility complex

MMP: matrix metallopeptidase

NO: nitric oxide

NOD: nonobese diabetic

RAGE: receptor for advanced glycation endproduct

ROS: reactive oxygen species

STAT: signal transducer and activator of transcription

T1DM: type 1 diabetes

TCR: T-cell receptor

TLR: toll-like receptor

TNF: tumor necrosis factor

Treg cells: T regulatory cell

Protocol

Achieving Consensus in the Development of an Online Intervention Designed to Effectively Support Midwives in Work-Related Psychological Distress: Protocol for a Delphi Study

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Abstract

Background: The development of an online intervention designed to effectively support midwives in work-related psychological distress will be challenging due to the ethical, practical, and therapeutic issues surrounding its design. Related literature suggests that midwives may require an anonymous, confidential, and therapeutic platform that facilitates amnesty and nonpunitive approaches to remedy ill health. However, it is unclear which requirements may be most salient to midwifery populations.

Objective: The objective of this paper is to describe the design of a Delphi study, intended to achieve expert consensus on the needs of midwives in work-related psychological distress who may be supported via an online intervention. This protocol may also serve as a research framework for similar studies to be modeled upon.

Methods: A heterogeneous sample of at least thirty experts on psychological well-being and distress associated with midwifery work will be recruited. Their opinions regarding the development of an online intervention designed to support midwives in work-related psychological distress will be collected through 2 rounds of questioning, via the Delphi Technique. When 60% (≥18, assuming the minimum is 30) of panelists score within 2 adjacent points on a 7-point scale, consensus will be acknowledged. This Delphi study protocol will invite both qualitative and quantitative outcomes.

Results: This study is currently in development. It is financially supported by a full-time scholarship at the Centre for Technology Enabled Health Research at Coventry University (Coventry, UK). The implementation of this Delphi study is anticipated to occur during the autumn of 2015.

Conclusions: The results of this study will direct the development of an online intervention designed to support midwives in work-related psychological distress, summarize expert driven consensus, and direct future research.

Introduction

Background

The mental health and well-being of health care professionals has gathered significant attention due to its direct correlation with quality patient care [1]. Midwives may be at an increased risk of developing psychological distress due to the traumatic work environments they endure [2]. These environments report incidents of workplace bullying, emotionally demanding clinical case loads, and a pressure to work despite feeling unwell enough to do so [1,2]. Interventions designed to support midwives in work-related psychological distress are required if the global shortage of midwives and the poor effects that midwives' psychological distress has on patient care are to be remedied. It is unclear who may be responsible for the well-being of health care staff in the United Kingdom, yet it is clear that there is a paucity of support for midwives in distress [3].

Midwives generally find it challenging to disclose personal experiences of psychological distress [4,5]. In addition, health care professionals who experience the distressing effects of functioning within traumatic work environments may not recognize mental ill health in themselves [6,7].

To enable midwives to seek help with the consequences of work-related psychological distress, a platform of amnesty, confidentiality, and anonymity may be required before any benefits may accrue [8,9].

Can Online Interventions Be the Answer?

An online intervention may be one solution that midwives may turn to in work-related psychological distress, as a preferred option of support [10]. To develop an online intervention that fits the needs of midwives, their employers, and professional bodies, it will be important to first define what characteristics an online intervention should have.

This paper outlines a protocol for a Delphi study designed to achieve expert consensus about what midwives in work-related psychological distress may need to be supported via an online intervention and peer support platform. The expert consensus will be used to inform the development and content of an online intervention for midwives in work-related psychological distress.

Methods

The Delphi Study Design

The Delphi Technique has been used extensively within health, social science, and intervention research [11-13]. It involves rounds of discussion whereby experts are invited to disclose their opinions on particular topics for which there is a paucity of knowledge. It is assumed that the opinions of many outweigh those of the individual, and thus, any consensus generated may be considered to be a valid expert opinion [14,15]. Because there is an incomplete state of knowledge about what midwives in work-related psychological distress may require when accessing an online intervention designed to effectively support them, a Delphi study was considered to be a suitable research tool to augment unanimity in opinion [16]. The distinct characteristics of the Delphi technique are (1) anonymity, (2) iteration, (3) controlled feedback, and (4) statistical "group response" [17].

Achieving consensus is the primary aim of the Delphi study, yet the measurement of consensus varies greatly [18]. There is no firm consensus as to what may be considered a consensus within a Delphi study. Within this Delphi study, a primary

criterion is that at least 60% (≥18, assuming the minimum is 30) of Delphi panel members must indicate a preference within 2 adjacent response points on a 7-point Likert scale for consensus to be reached.

Rigid Delphi study designs have been criticized for their inability to allow their experts to elaborate on their opinions [12]. Therefore, this Delphi design will be a modified one [15,19]. Free text response options will accompany each statement put to panel members [20] to provide experts with the opportunity to elaborate on their opinions.

The research team who will conduct this Delphi study includes 6 academics with professional backgrounds in midwifery, general medicine, psychology, and academic research.

Participants

There are no clear guidelines in relation to what panel size is most appropriate for a Delphi study design [20]. A minimum of 30 experts will be recruited to this Delphi panel. Heterogeneity within the expert panel will play an essential part in ensuring study quality [16]. Therefore, panel members will be selected from different fields relating to midwifery care, health care, psychological distress, professional practice, and academia. They will be identified through a stakeholder analysis (see Multimedia Appendix 1). These experts will be midwives, researchers, lecturers, health care professionals, students, patient groups, and maternity-based organizations. Inclusion criteria are shown in Figure 1.

Once experts have been identified, they will be directed toward information about the aim and content of the Delphi study. A formal invitation will also be given (see Multimedia Appendix 2 and [21-31]). Potential participants will be invited to consent to participate as the online Delphi study begins (see Multimedia Appendix 3). Potential and recruited panel members will also be asked to refer other suitable individuals. This layer of recruitment aims to eliminate any bias from the research teams' recruitment selection. Solicitation of nominations of appropriate field experts is typically recommended as best practice in the Delphi study design [32].

Informed consent will be obtained from all participants as the first round of questioning begins online, and will include the consensual agreement to publish anonymized data and nonidentifiable data results (see Multimedia Appendix 3). Participants will be directed to appropriate support services both online and offline due to the sensitive nature of the subject matter. Participants will also receive copies of any publications that may result from the study and a summary of outcomes.

Figure 1. Participant inclusion criteria.

Expert Panel Inclusion Criteria

Either: A listed author in at least one publication relevant to
-Midwifery
-Psychology
-Psychological trauma
-Psychiatry
-Health care services
And/or: Practical knowledge in
-Midwifery
-Midwifery education
-Research
-Therapies
-Health services
-Patient experience
-Staff experience

Participant Recruitment

Overview

Experts will be invited to participate by the research team. They will be invited via email and social media contact with a formal invitation to become a part of the panel (see Multimedia Appendix 2). Figure 2 shows the flowchart for participant recruitment.

It is anticipated that some experts may withdraw from the study during its course [33]. Therefore, social media will also be used to recruit participants to compensate for potential dropouts. A minimum of 30 panel members will be recruited to this study, although the team recognizes that there is no consensus regarding what the optimal number of participants for a Delphi study may be [14,34]. Should less than 50 experts be recruited before the Delphi study commences, an additional 50 people will be invited to participate to compensate for potential dropout rates and to avoid a failure to achieve adequate panel numbers.

Figure 2. Flowchart for participant recruitment.

Expert panel members identified through networking and social media

Expert panel members identified through relevant literature

Expert meets Inclusion Criteria and is invited to participate

Experts who agree to participate are asked to recommend others who fit the criteria

Definitive Expert Panel Agreed
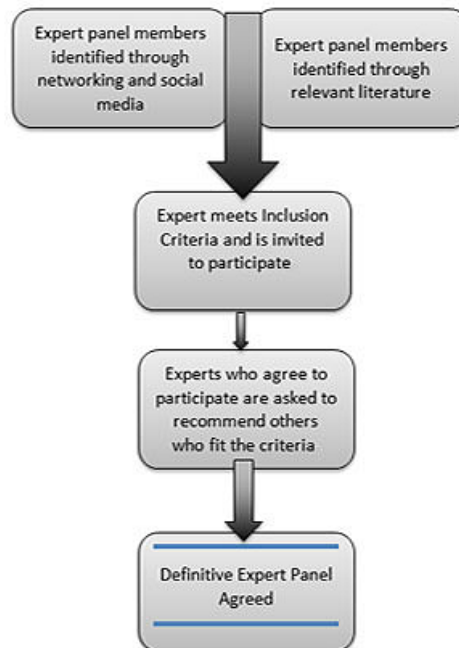
Social Networking Recruitment

The research team will consult their social, academic, and occupational networks to identify potential experts who meet the inclusion criteria. Suitable candidates will receive an email inviting them to participate in the Delphi study.

Twitter will also be used for research recruitment due to its high-quality health care, research, and academic communities. Twitter is evidenced to be a highly effective tool for health care research recruitment [35]. Stakeholder groups identified in the

stakeholder analysis will then be asked to promote the study to their online followers. A link to a blog page with inclusion criteria, further information, support resources, and an online survey will be provided to facilitate online recruitment [36]. Willing and suitable participants can then express their interest in partaking in the study by contacting the research team directly.

Recruitment Through the Academic Literature

Experts within the field of midwifery, psychology, psychiatry, and health care will be identified through literature searching. The research team will identify key papers of relevance, the authors of which will then be invited to participate. They will be invited via email and social media contact with a formal invitation to become a part of the panel (see Multimedia Appendix 2).

Procedure

Overview

This Delphi study will employ the principles of anonymity, repetitions at each stage of questioning, and feedback between rounds of descriptive statistics regarding the group's response and summaries of free text responses about each item in the item panel [37]. The Delphi study technique was chosen as it prevents dominant individuals from controlling the process of group discussion [16]. This is particularly salient in hierarchal environments, such as the health care system, where many participants are anticipated to originate. The anonymity the Delphi study facilitates can also allow for unashamed freedom of speech, which in turn, leads to a more accurate opinion giving [38].

Experts will only be sent further correspondence should they indicate an initial interest to participate in the study. In the absence of any response to the initial invitation sent by the research team, it will be assumed that the recipient has no interest in participating in the study, and will therefore receive no further correspondence.

Experts who continue to participate within the study but do not respond to the first Delphi round will be sent 2 reminders via email or social media contact. To withdraw from the study, experts must directly contact the research team and explicitly state their withdrawal. Unless this action is confirmed, all experts will receive reminders and survey links for each round. Two weeks will be allocated for Delphi experts to respond to each round of questioning [39]. In total, there will be a 5-week interval between the initiation of the first round and the start of the second round of questioning.

Reminders will be sent to participants 1 week before each round begins in order to maximize their participation. A link to the survey will then be given to all participants.

Questions

Questions have been designed to explore consensus about the design, construction, purpose, and content of an online intervention to support midwives in work-related psychological distress (see Multimedia Appendix 4). These questions were developed in response to a review of the literature. This is an acceptable and a common modification of the Delphi process [39]. Literature reviewing remained broad in scope and included a combination of the search terms "burnout," "psychological distress," "midwives," "midwifery,""midwife," "online intervention," "self-help groups," "CBT," "mindfulness," "stress," "depression," "anxiety," "peer support," "mental health literacy," "second victim," "PTSD," "post-traumatic stress," "workplace bullying," and "NHS." In reading and re-reading

the retrieved literature, a theoretical basis was developed for what may or may not be useful in the development of an online intervention designed to support midwives in work-related psychological distress. These theories are put forward for testing before the expert panel.

There will be 3 themes of questioning and 2 response options available. The 3 themes will be intervention design and practical inclusions, inclusions of therapeutic support, and ethical inclusions. The 2 response options available will be a 7-Point Likert scale and open text responses.

Delphi Survey Design

Bristol Online Survey [40] will be used to administer the Delphi study. Round 1 will consist of a structured questionnaire. Respondents will be asked to indicate their priority rating for a series of items via Likert scale responses. They will also have the option to disclose why they chose to mark each item with lower or higher priority within an open text field. Respondents will also be invited to provide additional comments through the provision of a free text response. Finally, panelists will have the opportunity to suggest new questions to be put forward during the second round of questioning.

Round 2 will consist of a second questionnaire that is based on the information provided in the first round. The primary aim of this round will be to offer the panel the opportunity to reconsider their responses from Round 1 for those items for which consensus was not achieved in Round 1. This opportunity will be offered in light of feedback about the groups' responses in Round 1. New questions may also be added to this second round in response to suggestions put forward by the panel during the first round. Respondents will be asked to review these new questions and indicate their priority rating. Respondents will be invited to provide comments through the provision of a free text response option for each item in the second questionnaire. They will also again be given the opportunity to disclose why they have chosen to mark each item with lower or higher priority within an open text field.

Analysis

Because there are no conclusive guidelines for establishing consensus in Delphi literature [41], taking account of the average accord and the 7-point scale, consensus will be reached if 60% ($\geq$18, assuming the minimum is 30) of respondents are within 2 adjacent response points on the 7-point scale (eg, if 60%, $\geq$18 assuming the minimum is 30, of participants select 2 and 3 in response to a specific item). Items which do not achieve consensus in Round 1 will be re-presented in Round 2.

The mean, minimum, and maximum scores for each item will also be calculated and reported to panel members as feedback after each round.

Any free text responses provided by participants to specific items will be analyzed with thematic analysis [42]. Themes may be reframed, reviewed, and revised throughout this thematic analysis, as coherent patterns are formed. This thematic analysis of qualitative open responses will be presented in a table format and feedback will be provided to panel members after each round.

Results

This study is currently in development. It is financially supported by a full-time scholarship at the Centre for Technology Enabled Health Research at Coventry University (Coventry, UK). Ethical approval for this study has been granted by Coventry University Ethics Department. The implementation of this Delphi study is anticipated to occur during the autumn of 2015. Project reference id P35069.

Discussion

Preliminary Agenda

The aim of this Delphi study is to reach consensus on the salient themes and elements to be included within an online intervention to support midwives in work-related psychological distress. The results of this research will be used to inform the development of an online intervention designed to support midwives in psychological distress.

A key weakness of the Delphi technique is that it lacks a theoretical framework [14]. The advantage of using a Delphi study technique within this research will be that ideas, definitions, and experiences of a variety of experts can be synthesized to inform development of the intervention. Panel members will be drawn from a variety of backgrounds, and as such will be able to contribute a variety of evidence and multidisciplinary perspectives.

Biases may occur in Delphi studies that could also distort the consensus. Desirability bias from both the experts and the research team could impede the achievement of a "true" consensus [43]. There is also the risk of ambiguity and conditional statements given within the questionnaire [44]. In this case, panel members may be interpreting the questions and statements differently. This may also lead to a polarization in results. A 7-point judgment scale is used to avoid elements of ambiguity; however, this may not protect results against some polarity [45]. To mitigate these risks, the questionnaire has been reviewed and piloted among peers.

Conclusions

This paper describes the design of a Delphi study. This will be the first Delphi study to explore the online support needs of midwives in work-related psychological distress.

Conflicts of Interest

None declared.

Multimedia Appendix 1

Stakeholder analysis.

[PDF File (Adobe PDF File), 97KB - resprot_v4i3e107_app1.pdf]

Multimedia Appendix 2

Formal invitation presented to potential participants.

[PDF File (Adobe PDF File), 102KB - resprot_v4i3e107_app2.pdf]

Multimedia Appendix 3

Informed consent form.

[PDF File (Adobe PDF File), 92KB - resprot_v4i3e107_app3.pdf]

Multimedia Appendix 4

Delphi study questionnaire.

[PDF File (Adobe PDF File), 200KB - resprot_v4i3e107_app4.pdf]

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Protocol

Measuring Life Events and Their Association With Clinical Disorder: A Protocol for Development of an Online Approach

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Abstract

Background: Severe life events are acknowledged as important etiological factors in the development of clinical disorders, including major depression. Interview methods capable of assessing context and meaning of events have demonstrated superior validity compared with checklist questionnaire methods and arguments for interview approaches have resurfaced because choosing the appropriate assessment tool provides clarity of information about gene-environment interactions in depression. Such approaches also have greater potential for understanding and treating clinical cases or for use in interventions.

Objective: (1) To argue that life events need sophisticated measurement not satisfactorily captured in checklist approaches. (2) To review life-events measures and key findings related to disorder, exemplifying depression. (3) To describe an ongoing study with a new online measure and to assess its psychometric properties and the association of life events in relation to disorder and educational outcomes.

Methods: The Computerised Life Events Assessment Record (CLEAR) is under development as a tool for online assessment of adult life events. Based on the Life Events and Difficulties Schedule interview, CLEAR seeks to assess life events to self and close others, link these to other events and difficulties, and utilize calendar-based timing, to improve upon checklist approaches.

Results: The CLEAR study is in the preliminary stages and its results are expected to be made available by the end of 2015.

Conclusions: There is currently no sophisticated technological application of social risk factor assessment, such as life events and difficulties. CLEAR is designed to gather reliable and valid life-event data while combating the limitations of interviews (eg, time consuming and costly) and life-event checklists (eg, inability to accurately measure severity and independence of life events). The advantages of using such innovative methodology for research, clinical practice, and interventions are discussed.

Introduction

Overview

Links between life events and clinical disorders have a long history, given the fact that stressful life events are an important predictor of the onset and course of various disorders across the life span, including depression, eating disorders, and psychosis [1-5]. In addition, long-term stressors (difficulties) play an important role in the onset and maintenance of disorder, notably depression, but these are often overlooked [6,7].

Empirical investigation of life events and disorder started with checklist self-report approaches in the 1960s [8], but the field was invigorated by the introduction of investigator-based interviews from the 1970s onward by Brown and Harris [9], with the Life Events and Difficulties Schedule (LEDS) Interview [9], and by Paykel [10] and Dohrenwend et al [11]. This paper is mainly concerned with the LEDS approach, although some points will equally apply to other interview measures as well. The LEDS focused on contextually assessed life events: first to incorporate the likely meaning of the event for an individual rather than using a generic scoring system, and second to avoid bias in reporting due to depressed mood and making sense of an illness episode retrospectively [12]. Although such approaches added to the complexity while improving the validity of life-event measurement, they invoked high costs in researcher and participant time as well as in researcher training. This has led to the use of checklist approaches in recent years [13], especially in the search for gene-environment interactions (GxE) in depression, because these studies require large sample sizes.

This paper outlines the ineffective measurement of life events in many contemporary research studies. It also presents a new online computerized approach—Computerised Life Events Assessment Record (CLEAR)—designed to optimize interview advantages while incurring low cost and being time effective. The ongoing development and future testing of CLEAR will be outlined with a focus on clinical health. It is expected that this new online method will offer an enhanced but readily available life-event measure with important implications for studying disorders.

The development of CLEAR has implications for genetic studies of depression as well as for more effective clinical application. For instance, some individuals are more likely to experience severe life events, because of psychosocial vulnerability (eg, difficulty in relationships resulting in more relationship events) [14]; likewise, based on similarities observed in twins [15,16], it appears that some individuals select themselves into high-risk situations due to genetic or familial factors [17,18]. Here the measurement of life events has proved critical, with genetic studies producing inconsistent findings for GxE in depression [19]. Thus, while several large studies have found a significant relationship between GxE for the serotonin transporter polymorphism (*5-HTTLPR* genotype) and life events in depression [20,21], others have failed to do so [22,23]. Uher and McGuffin [24] pointed out that the failures to replicate GxE results are more common in studies using checklist life-event questionnaires rather than interviews. Certainly, studies that have elicited stressful life events using more involved methodologies (eg, life-history calendar or interview) have tended to find significant interactions between life events and the *5-HTT* gene [25,26]. Thus, the current research demand for more sophisticated measures of life events lies in the genetic field, which would also aid any study requiring large sample sizes, clinical assessment, and treatment interventions.

Life-Event Interviews and Questionnaires

Among the different in-person semistructured interviews, probably the most widely used is the LEDS [9,27]. This approach encourages narrative accounts of events that can elicit the full social context, their timing, and sequence in relation to disorder onset. LEDS encapsulates a large range of events to the self and close others. It deals with the likely meaning of events by collecting contextually relevant information (both biographical and current circumstances) and rates according to precedent examples, stripped of subjective response.

This interview is considered the "gold standard" for measuring life stress and is superior to checklist approaches. The disadvantage comes from the time and labor involved [28] in analyzing the numerous constructs rated and the algorithms required (eg, for "severe event" definitions). For example, the LEDS interview takes 1-2 hours, but up to 16 hours to complete with full ratings and checking [29]. This incurs high costs and places a burden on the interviewer, making it an unattractive alternative to checklists for most studies [30]. Thus, there is a need for an approach that has the reliability and validity benefits of such comprehensive face-to-face interviews while being more economical.

Key Features of Life Events and Measurement Issues

Events and Change

The early investigation of life events by checklist (eg, Holmes and Rahe questionnaire [8]) characterized "a life change unit" as the main element with generic scoring of stressfulness routinely applied to events. Thus, "death of a spouse" was given the highest stress weighting (100), and minor violations of the law given the lowest (11). This approach makes 2 assumptions, which we challenge: first that life events require routine practical change and second that the stressfulness valence can be decided generically. In terms of change, we agree that the more extensive and permanent the negative life change, the more likely it is to invoke a stress response. Thus, permanent negative changes (eg, death of a spouse) get the highest ratings in this self-report, with routine and conditional change being rated the lowest (eg, begin or end school or college). However, this scheme has a pedestrian view of change as an observable shift in routine. In real life, however, degree of change is often not known at the commencement of an event (eg, partner leaves home after a row), or the change is definite but has not yet occurred (eg, forecast of redundancy), or news of the event occurs after the change has happened (eg, death of a relative abroad). Some of the most damaging events present no immediate practical change (eg, betrayal in a close relationship) but require substantial cognitive reappraisal. It is also important to ask, "Change to whom?" Events to close others, particularly those experienced jointly with the self can also have highly stressful impacts (eg, partner's severe illness requiring the respondent's caring

responsibility). These are not usually included in self-report approaches. The LEDS covers events in 12 different domains, with up to 10 subdivisions in each, as well as routinely covering events to self and to a range of predetermined close others [27]. Thus, the array of events included is vastly higher and arguably captures a more realistic range of stressful experiences.

Context and Severity

The other aspect involves the estimated severity of the event in terms of a likely stressful and negative emotional response in most people. In checklist approaches, this is generically ascribed. Yet, apart from the worst ones (eg, death of a spouse), almost all are dependent on context for their likely severity. For example, marriage and pregnancy are not inherently stressful unless the context is negative (eg, unplanned pregnancy, unstable partnership, health risks, or financial and housing difficulties), where a much higher stress score is allocated. A more recent checklist identified those events most often scored as severe life events in interview measures [13] and included events to close others, but the scoring of events is still generic rather than context dependent. Yet a study by Dohrenwend and colleagues [31] found that the lack of context contained within questionnaire measurement hid response heterogeneity. There was high variation in what respondents classified under each event and they often elicited trivial events [29]. Therefore, questionnaire categories can mask important differences in responding. Life-events checklists ultimately provide a total score based on the number of items endorsed, sometimes with a weighting applied. They do not assess the severity of each event experienced, with a view to one event being able to predict disorder. In interview measures such as the LEDS, context is determined by careful questioning about circumstances leading to and surrounding the event, with salient aspects included into the event context for judging severity. All of these contextual factors are objectively classified, not dependent on the emotional response of the individual.

Meaning of Events: Loss, Danger, and Humiliation

Interview measures have found that the likely meaning of an experience plays a central etiological role in the development of depression, with life events tied to changes involving loss (of relationship, role, cherished idea, or sense of self), danger (threat of a future loss, conflicts in core social roles, threats to plans you have made), or punishing environments (entrapment, humiliation) being the most predictive of disorder [1,7]. Equally, an individual's plans and concerns need to be considered; an event may derail long-term plans or undermine a role involving behavioral commitment (eg, caring mother, diligent student, dedicated worker). One prospective LEDS study found that a "severe event" in a life domain of previously determined high commitment more than doubled the risk of a depressive episode when compared with others in areas of lower commitment [6]. A further study showed that specific attributes make events more predictive of disorder: humiliation and entrapment [7]. "Humiliation" is an event involving a put down, devaluation, or rejection, and "entrapment" confirms imprisonment in an ongoing, highly punishing situation involving a chronic stressor or difficulty [7]. Entrapment events additionally predict comorbid depression and anxiety [7,32], as well as relapse of

depression [33] and operate cross-culturally [34]. Therefore, a full determination of an event's capacity to provoke a depression requires careful exploration and scoring of the salient experience including recent plans and behavioral commitment [7,35]. Questionnaire approaches tend to lack this depth and clarity, and therefore, underestimate the presence of stressors by overly summarizing the range of events possible without attention to such attributes.

Timing and Chronicity of Stressors

The timing of events is critical to determining their etiological role in depression onset. Events that occur after onset can only have a maintenance role at best. Therefore, precise timing of events is required. In addition, other important stressors are chronic, with severity levels that can vary over time. These are termed "difficulties" and comprise problematic situations, which last 4 weeks or more, and can go on for years. These can occur in as many domains as events, and can be antecedent or consequent to the event. An important analysis of such linkages showed that an event preceded by a severe difficulty (hence "matched") for at least 6 months and in the same domain greatly increased the risk of depression onset [6]. In this case, the potential for entrapment or an erosion of hope can add to the burden of the ongoing problem (eg, a partner's demand for a divorce in the context of a conflictual marriage; or a failed attempt at rehousing in the ongoing problem of serious overcrowding). Using these criteria, women with a severe event "matching" a difficulty had a threefold greater chance of developing depression [6]. Questionnaire measurement cannot reflect such links and is imprecise regarding the timing of the event in relation to onset of disorder. Severe events of etiological importance occur within 6 months of onset and often within half of that time [35]. In addition, the effects of life events gradually decay over time, with the strongest effect in the month immediately following the life event with some variation by event type [2,36]. Without knowing the timing of events, any precision is lost, which restricts the causal attribution of life events to disorder [37] and the investigation of specific stressors for different disorder outcomes [38].

Independence From Individual's Own Actions

Life-event interviews also categorize "independence" of the event. This is the extent to which the event is likely to be separate from the actions, planning, or control of the individual, that is, it occurs externally to the individual. Independence allows researchers and clinicians to estimate whether the event is a cause or consequence of disorder. For example, losing a job because the employer has gone bankrupt would be judged totally independent outside of personal control; personal health events are "nearly totally" independent, interactions with close others only "possibly independent," and intentional acts as "nonindependent" [9]. Events that are a part of the depression itself or its treatment (suicide attempt or psychiatric hospital admission) are rated as "least independent" and termed "illness related." Genetically sensitive twin studies of depression and life events have described genetic influences for nonindependent events, but not for independent events [39]. Both relate to depression.

Given this context, the inadequacy of checklist life-event questionnaires for etiological study of depression is apparent. Although quick and easy to administer, requiring few resources, they are subject to serious methodological limitations compromising the quality of the data gathered.

Need for a New Approach

Digital health interventions are increasingly seen as a way to assess, treat, and prevent psychological disorder and deliver mental health provision. Such Web-based assessments and services have the ability to overcome geographical barriers, lower delivery costs, and reduce workforce demands [40]; in addition, the systems are convenient, assessments can be answered anonymously, and personalized feedback can be provided [41]. They can also provide avenues of research into processes related to mental health and well-being [42]. While digital health is a rapidly expanding area of research and practice, there is no sophisticated technological application of social risk factor assessments (such as life events and difficulties) that can benefit from many of the same advantages. There are, however, online measures with precoded algorithmic scoring used successfully within research for psychiatric diagnoses in children and adolescents (eg, Development and Well-Being Assessment, [43]) and adults (eg, OPCRIT, [44]) and for highlighting individuals at risk of physical illness such as Parkinson's disease (eg, PREDICT-PD, [45]). Such tools have also aided assessment with vulnerable children [46]. Thus, it seems likely that complex social risk factors could be measured in the same way.

The current project in progress aims to address the need for improved and accessible life stress measurement by developing an online data capture tool (CLEAR) and testing its psychometric properties and its association with disorder and educational outcomes. Currently, the project is in its early stages and CLEAR is still under development. In the following sections, we outline the basic architecture of the CLEAR system and the study to test it once complete.

Methods

Participants

CLEAR is a new complex measurement tool, and therefore, its feasibility and usability will be assessed by life-event expert and nonexpert volunteers (n=20) across a range of ages. These groups will act as a panel to test out CLEAR before it is finalized. Panelists will rate either their own experience, or case study examples from archived interview data, to determine both user friendliness and whether the full context of the event can be adequately captured. Their feedback will inform improvements to the system.

The project will utilize 3 different samples to develop and test CLEAR. A midlife sample (average age 52) will be recruited from the Depression Case Control (DeCC) study, involving a pool of 2299 respondents from London, Cardiff, and Birmingham, originally studied for gene-stress interaction and depression [47]. Those with prior recurrent depression will be assessed by clinical interviews (n=125) and unaffected controls (n=125) will be reapproached for the study. Half of the depressed cases will be selected based on having previously reported a lifetime common illness (asthma, hypertension, osteoarthritis, and thyroid problems), as will 25% of the controls (31/125) consistent with original prevalence rates. Furthermore, 125 1st-year undergraduates (average age 19) will be included for studying educational outcomes. This will test whether CLEAR can capture life events during different life stages. In addition, it will add to the limited evidence base regarding whether life events are related to student performance [48,49]. This is an important area to understand as students show higher rates of depression [50], and younger adults, in general, experience a higher rate of life events [51]. Developing a greater understanding of their experience can help with providing improved support at this critical life stage, which may have a lasting impact on future opportunities.

Procedure and Analysis

Participants will be approached by letter or email, which will explain the study and enclose an information sheet and consent form. Those who are interested in the study will be sent the CLEAR URL and log-on details, which will allow them to access and complete CLEAR from any Internet-enabled computer or tablet. The validity of CLEAR will be assessed by interviewing 30 participants from each of the samples (10 undergraduates, 10 recurrent depression cases, and 10 unaffected controls) using the in-person LEDS interview and CLEAR in counterbalanced order. The time taken for each participant to complete CLEAR will depend to some extent on how many life events have occurred over the 12-month period. However, the average in-person LEDS takes approximately an hour to complete, and therefore, it is assumed this will be the average time taken to finish CLEAR.

The data generated will be rated blind/reviewed by separate researchers and compared using Cohen kappa and intraclass correlation coefficients (ICCs) for level of agreement between the 2 methods. The total number of life events captured, the domain category, severity rating, and the timing of events will be compared to give an indication of how well CLEAR mimics the in-person method for full reporting and recall. Any further modifications will be made to CLEAR if required.

Test-retest reliability of CLEAR will be undertaken using an additional 20 undergraduates, 20 depression cases, and 20 controls from each of the samples, measured an optimal 3-4 weeks apart for stability in reporting (using Cohen kappa and ICC). CLEAR will be tested on the remaining participants (n=285) and the rates and types of life events and difficulties reported in the 3 samples will be compared and analyzed in relation to sex, social class, and age using chi-square statistics. The association between life events and past/recent depressive disorder and physical illness (DeCC sample), and academic performance (undergraduate sample) will be tested using logistic regression to look at the contribution of life events and indicators of social disadvantage to health and educational outcomes. Once both reliability and validity of CLEAR have been determined, the program will be available for more general use.

Security is a key concern of CLEAR; the CLEAR servers are built from CentOS Linux 5.4, which is a secure variant of Linux, has no services or ports installed, and includes only what is

strictly necessary for CLEAR. In addition, a firewall is installed to further restrict access to the server. All data are entered into CLEAR under a unique log-on, and therefore, no names or contact details are entered on to the CLEAR system. The data are stored on a secure MySQL database that is updated whenever a participant enters information through the CLEAR interface. The log-ons will be stored in a password-protected file with the participant's study ID numbers. A separate password-protected file will contain the ID numbers and any identifying respondent information (eg, contact details). Therefore, for this study there is the ability to recontact participants if needed.

Results

The CLEAR study is in the preliminary stages and its results are expected to be made available by the end of 2015.

Discussion

CLEAR Instrument

Respondents complete CLEAR by providing demographic information; information about close others; and life events and difficulties over the past year in 12 domains (education, work, reproduction, housing, money, crime, health, romantic, other relationships, children, death, and miscellaneous). The assessment also includes a fixed battery of measures, a depression questionnaire (General Health Questionnaire, GHQ, [52]), and an interpersonal vulnerability questionnaire (Vulnerable Attachment Style Questionnaire, VASQ [53]). However, for projects tailored to other research questions, the integrated calendar system can be used to record events over a greater observation period, and paper or electronic questionnaires can be used in addition to CLEAR. The information is provided through a mixture of checklists for closed answers, text boxes for open-ended answers, and logic-driven checklist menus. CLEAR also contains a feedback system that allows for a personalized calendar, menus, and references to specified close others.

The logic-driven menus guide the respondent based on their prior answers. For example, if a respondent chooses the "education" category, this presents them with a menu of options (eg, selection interview, examination results) and depending on response, a following different set of options is provided (eg, application rejected/accepted versus passed/failed exam). Once respondents have completed these, they describe and score various aspects of the event including the event context, independence, and their feelings about the event. For each event, respondents are asked if this relates to any other event or difficulty and a menu (which continually updates) is presented with all previously entered events and difficulties. Thus, they are also able to link events and difficulties. This creates a dynamic feedback system in which more links between events and difficulties can be added as CLEAR is completed. Throughout this process, there are detailed instructions (including video) and domain-specific examples to inform the respondent. Important aspects, such as level of threat/unpleasantness, are given labels benchmarking the target level to encourage appropriate ratings.

CLEAR is scored using a precoded algorithm to produce a rating of "severe" life event as well as "D-matching" events and other indices. For analysis of the in-person LEDS interview, a derived variable of "severe life event" is one, which is rated (1) "marked" or "moderate" on long-term contextual threat/unpleasantness (ie, objective assessment, present at 10 days after the start); (2) "self" or "joint" focused; and (3) is not "illness related" (ie, part of the disorder investigated such as treatment/hospitalization or symptom related such as suicide attempt). The same algorithm for combining these 3 scales in producing a binary severe life-event variable will be precoded in the CLEAR online version from the data entered and made available for the report produced, or downloading to SPSS (SPSS Inc., Chicago, IL, USA) for further analysis. For "matching difficulty events," a stated link to rated difficulties of "very marked," "marked," or "high moderate" severity is required, in the same domain (eg, work or marital), and of 6 months duration prior to the event. This will similarly be precoded consistent with the regular interview analysis of data.

Information can be pooled from various sources to assign the likely negative meaning of the event for the respondent based on demographics in combination with objective ratings of the event circumstances. The logic-driven menus provide detail about the basic event type and circumstances that may apply (eg, for moving house a submenu is provided where an individual can choose an option "forced to move" and from the following menu tick options that may apply such as "large cost of moving" and "neighborhood less desirable"), and the self-report data provide demographic information including current circumstances (eg, employment status, number of dependents) and historical data (eg, education and employment history). The system also requires self-assessed threat/unpleasantness ratings of events and difficulties. Together, these will be used to produce an overall objective severity rating. In addition, the written descriptions provide further surrounding detail that can be reviewed by researchers to check for reliability. Furthermore, using both the open-ended text-box answers and scores can help researcher review each case in depth, which also allows for quality control checking and enabling extended qualitative analysis if needed, or in a minority of cases recontacting respondents.

The logic-driven menus guide individuals toward the type of events likely to be stressful, from more general to more specific event types. There is evidence to suggest that inclusion of detailed instructions of different event types in each category gives better test-retest reliability with less "fall off" of event reporting over time, and greater agreement between respondent and co-informant [54,55]. Therefore, adopting this approach may help maximize reliability and prevent recall fall off, which will be assessed through a comparison of CLEAR and the in-person LEDS interviews.

Each stem menu of events leads down a path until the options are no longer relevant. However, at each stage, the respondent is given the option of rating "something else/other." In this way, stressful events that do not fit into proscribed categories or criteria can also be included. This ensures that the specification of events does not make the definition of events too narrow [56].

Difficulties with recall can be a problem for both interview and checklist methodology, even over a 12-month period [24]. Comparisons of longitudinal and cross-sectional studies demonstrate that more events are reported longitudinally than retrospectively [57]. However, using Web-based systems to conduct prospective longitudinal assessments may be a lower resource-intensive method of obtaining detailed descriptions of psychopathology processes over time [58]. In addition, when CLEAR is used retrospectively, recall may be aided as respondents can edit their responses and can complete it over a few sittings and see their own calendar of events before finalizing sequences. Studies have found that respondents who initially fail to report serious events, when given more time to think after initial prompting trigger greater recall or appraisal of the event [59].

Recall is also helped through a personalized calendar that is updated as life events and anchoring anniversaries or social occasions (eg, holidays, birthdays) are added to the system. The timing of important psychopathology-related timings (eg, peak depression) can be added to the calendar. Events are often linked to other events in autobiographical memory; therefore, the use of calendars can lead to better quality (ie, more complete and accurate) retrospective reports of events, even after several years [58,59]. When used in conjunction with self-report methods it improves completeness of the data and dating accuracy [60]. In addition, the use of multiple, self-generated, and personal landmarks further enhances memory [61].

The CLEAR system aims to be as personalized as possible. In general, simple approaches such as addressing individuals by their name can sufficiently personalize a message to heighten attention to the information provided [62]. CLEAR will use the data input, to reflect information back to respondents in a meaningful way. This will include personalization of menu options, such as forenames of close others used to populate the answer options to particular questions (eg, *who was involved in the event*?) or only being presented with certain questions (eg, *what is your partner's job?*) if they have answered yes to a previous question (eg, *do you have a partner?*). In addition, normative feedback will be presented to summarize and personalize risk and resilience factors based on the information collected. For example, respondents will be given a pre-prepared brief report, which is tailored to their scores on the GHQ and VASQ, as well as a simple calendar of their events when completed. It is hoped that this will increase motivation and enhance the effectiveness of the system at conveying information and improving respondent's appropriate response.

Lastly, the online system can be completed in private. Compared with interviews, self-administered measures can elicit more events that may be sensitive, embarrassing, or have the potential to bring about negative consequences [30,63]. One study investigating the impact of social anxiety on well-being found that an online survey was able to obtain in-depth qualitative information about delicate or stigmatizing difficulties [64], and adds to a growing literature suggesting that anonymity of the Internet facilitates open discussion of problems, which may be hard to talk about face-to-face [41].

The CLEAR system will also be programmed to provide basic reports for clinicians/health professionals on individuals in health settings with appropriate permissions. Health professionals can be provided with unique log-ons to CLEAR to access the data-generated reports from the database. The reports will provide a summary of each life event (severity score, date, classification from the menus, and written context from the respondent), a calendar denoting sequence and timing, and the scores from the GHQ and VASQ with appropriate description of resulting classification. The data from CLEAR can also be downloaded into SPSS files or specific data can be downloaded based on applied filters (eg, all events in the housing category). The data are a mixture of quantitative variables (eg, event category, threat, age, relationship to person close to them) and qualitative variables (eg, event written description and emotional reaction). The provision of such automated reports, once tested for their informative and useable characteristics, will be a major benefit of the measure to ongoing practice.

Advantages for Clinicians and Researchers

The first observations concerning life events occurred in the early 20th century in the clinical field when understanding the experience of depressed patients [65], with Meyer the first to create life charts to document events linked to disorder [66]. Thus, clinical approaches as a basis for treatment were an original driver for investigating life events and depression, and a need still exists in modern approaches such as cognitive behavioral therapy [67] where understanding individual appraisal and response to events is critical to effect cognitive and behavioral change. Having easy access to sophisticated measures of life events are therefore of potential help to clinicians and could be used in combination with tailored digital health interventions; for example, cognitive behavioral therapy packages formulated to be used in response to severe life events occurring within an individual's life.

Severe life events are relatively common, but only a minority of individuals exposed develop depression. Therefore, the role of personal vulnerability is important. Studies including both low self-esteem and negative interpersonal relationships (ie, conflict with partner or child or lack of close support) as vulnerability indices showed interaction effects with stressful life events in the development of depression [68,69]. Certainly, women selected for these vulnerabilities in a prospective study showed 50% risk of new clinical depression onset [68,69]. While the focus of CLEAR is on the provoking agents for depression, additional questionnaires of vulnerability can be included to generate a fuller picture of the individual, with a future prospect of further developing these online.

Conclusions

This paper argues that life events are complex phenomena not currently served by the most commonly used measurement approach, that is, checklists. This is potentially damaging research investigating the etiology of depression: problematic measurement must surely lead to problematic results. It is hoped that CLEAR's technological advances will produce a useful compromise between life-event checklists and interview approaches, overcoming some of the limitations of

questionnaires while reducing the burden inherent in face-to-face interviews. CLEAR should have the capacity to capture life-event details and context, different attributes of the event, timing of the event, and linkages between events and difficulties. Although it will not provide exhaustive coverage of all possible events, it is presumed that the majority of events will be captured and that most respondents will be able to rate the bulk of their events accurately given the guidance provided through the menus, examples, and appropriate benchmarking. Thus, this new method of measuring life events may be able to gather high-quality data, hopefully with reliability and validity comparable to the gold-standard interview approach, overcoming the problems inherent in relying on checklist approaches in etiological research.

It is also hoped that the CLEAR approach to assessing life events and difficulties will aid those in clinical practice. The provision of recent life charts of events labeled in terms of their likely stressful nature and with attributes relating to loss, danger, humiliation, and entrapment will allow clinicians to consider the level of stressor experienced in seeking to estimate patient appraisal and coping capacity.

Conflicts of Interest

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       vulnerability. Psychol Med 1998 Jan;28(1):39-50. [Medline: 9483682]

Abbreviations

CLEAR: Computerised Life Events Assessment Record
DeCC: Depression Case Control
GHQ: General Health Questionnaire
GxE: gene-environment interactions
ICC: intraclass correlation coefficients
LEDS: Life Events and Difficulties Schedule
VASQ: Vulnerable Attachment Style Questionnaire

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Protocol

Depression Awareness and Self-Management Through the Internet: Protocol for an Internationally Standardized Approach

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Abstract

Background: Depression incurs significant morbidity and confers increased risk of suicide. Many individuals experiencing depression remain untreated due to systemic and personal barriers to care. Guided Internet-based psychotherapeutic programs represent a promising means of overcoming such barriers and increasing the capacity for self-management of depression. However, existing programs tend to be available only in English and can be expensive to access. Furthermore, despite evidence of the effectiveness of a number of Internet-based programs, there is limited evidence regarding both the acceptability of such programs and feasibility of their use, for users and health care professionals.

Objective: This paper will present the protocol for the development, implementation, and evaluation of the iFightDepression tool, an Internet-based self-management tool. This is a cost-free, multilingual, guided, self-management program for mild to moderate depression cases.

Methods: The Preventing Depression and Improving Awareness through Networking in the European Union consortium undertook a comprehensive systematic review of the available evidence regarding computerized cognitive behavior therapy in addition to a consensus process involving mental health experts and service users to inform the development of the iFightDepression tool. The tool was implemented and evaluated for acceptability and feasibility of its use in a pilot phase in 5 European regions, with recruitment of users occurring through general practitioners and health care professionals who participated in a standardized training program.

Results: Targeting mild to moderate depression, the iFightDepression tool is based on cognitive behavioral therapy and addresses behavioral activation (monitoring and planning daily activities), cognitive restructuring (identifying and challenging unhelpful thoughts), sleep regulation, mood monitoring, and healthy lifestyle habits. There is also a tailored version of the tool for young people, incorporating less formal language and additional age-appropriate modules on relationships and social anxiety. The tool is accompanied by a 3-hour training intervention for health care professionals.

Conclusions: It is intended that the iFightDepression tool and associated training for health care professionals will represent a valuable resource for the management of depression that will complement existing resources for health care professionals. It is also intended that the iFightDepression tool and training will represent an additional resource within a multifaceted approach to improving the care of depression and preventing suicidal behavior in Europe.

Introduction

Overview

Depression and suicidal behavior, including both suicide and nonfatal self-harm, are 2 important and largely overlapping public health problems in Europe [1]. European countries are overrepresented among the highest national rates of suicide in the world [2,3], and unipolar depressive disorders are the third cause of disability-adjusted life years in Europe [2]. People suffering from major depression are 21 times more likely to die by suicide than nondepressed individuals [4]. Depressive disorders are present in approximately half of completed suicides [1,5], and this proportion is even higher if the presence of subclinical depressive symptoms is considered [6,7].

Research Context of iFightDepression: Depression and the Current Situation of Care

Given the connection between depression and suicide, it is not surprising that improving the care of people with depression is considered an effective suicide prevention approach [8]. Several successful European studies provide support for this approach. The pioneering Gotland study [9,10], the Nuremberg Alliance against Depression [11,12], and further studies evaluating multilevel community-based interventions, such as the implementation of a local Alliance against Depression in Hungary [13], have demonstrated that interventions to improve the recognition and treatment of depression can effectively reduce the incidence of suicidal acts. The European Alliance Against Depression (EAAD) [14] and the European Commission-funded "Optimising Suicide Prevention Programs and their Implementation in Europe (OSPI-Europe)" project [15] have explored the potential of such community-based interventions to improve awareness of depression and to prevent suicidal behavior across several European countries. These interventions operate on multiple levels within the community, including the following: (1) cooperation with primary care services, focusing on trainings for general practitioners (GPs) to improve professional recognition of depression, including education about lethal medication and information regarding the detection, assessment, and diagnosis of depression; (2) public relation activities involving education of the broad public with a multifaceted depression awareness campaign; (3) cooperation with community facilitators and stakeholders, including training workshops focusing on recognition of depression, facilitation of access to appropriate care, and cooperation to restrict access to lethal means; and (4) facilitation of care and support for patients, high-risk groups, and their relatives, with the provision of information regarding helplines and emergency contacts and the initiation of, and support for, self-help groups [16].

Such multilevel interventions have demonstrated effectiveness with regard to the reduction of stigma toward depression, improvement of both lay and professional knowledge and awareness of depression, and increased motivation of individuals to seek help for depression as a result of broad general public health campaigns and increased professional recognition of depression. However, despite this promising evidence, the need to improve the care for individuals who are motivated to seek help for their depression has become evident [17,18]. Specifically, as the number of depressed individuals motivated to seek help increases, the demand on available resources and support services increases as well. As a result, individuals may encounter structural barriers such as limited availability of specialized care in rural areas, or lengthy waiting times for psychotherapeutic treatment [19]. Thus, once a person decides to access help for depression, or professional education increases awareness and detection of depression in clinical practice, there may be limited effective assistance available.

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The importance of improving the care for individuals with depression is also demonstrated in light of diagnostic and therapeutic deficits at the primary care level. Patients with depression who seek help often present to general practice with mainly somatic complaints [20,21]. If depression occurs in individuals living in difficult life circumstances (eg, those experiencing somatic comorbidities and unemployment), it is often seen as a secondary phenomenon, a reaction to life circumstances, and not as an independent severe disorder that should be treated according to appropriate guidelines. In addition, recent studies have demonstrated that depression is underdetected and inadequately screened within primary care [22,23]. These are a number of reasons why only approximately 50% of depressed patients are correctly diagnosed at the primary care level [24,25].

Even if a diagnosis is made, very often specific psychotherapy is not available, nor is pharmacotherapy prescribed. When pharmacotherapy is initiated, there are sometimes challenges with drug dosage and time span [26,27]. Finally, even if pharmacological or psychological treatment is offered, there may be considerable compliance problems [28,29]. Moreover, many national health services in Europe are increasingly ill placed to provide specialized interventions for depression in light of the current economic recession: governmental cost-saving measures adopted in several countries have included the reduction of budgets for mental health services with subsequent effects on service availability [30]. Given the decreasing availability of effective treatment services for depression, it is apparent that additional resources are urgently needed to offer support to both patients and health care professionals for the management of depression.

Depression and Self-Management Using the Internet

Because of the current constraints within national health services and the resultant limitations on delivering best practices of mental health care delivery within primary care [31], much of the responsibility for the initial care of mild to moderate depression lies with primary care providers. In such settings, there is a need for treatment complementarity: primary care providers and patients should be provided with *a range* of evidence-based and effective options for the management of depression. Antidepressants are effective and are widely used to treat depression, but patients may be reluctant to use antidepressant medication. Clinical guidelines regarding the management of depression now recommend a "stepped-care" approach to depression, whereby lower intensity psychosocial interventions may be used to treat lower levels of depression [32]. This is important, given that even mild or minor forms of depression negatively affect quality of life [33], and are associated with functional impairments [34], increased mortality, and risk of transition to severe depression and suicidal behavior [35]. Lower intensity psychosocial interventions often incorporate the concept of self-management, an approach that can complement treatment combinations for mild and moderate depression by empowering patients while reducing demands on health care services [36].

Self-management is an important aspect in the management of long-term illnesses. It refers to "interventions, trainings, and skills by which patients with a chronic condition, disability, or disease can effectively learn how to take care of themselves and effectively deal with difficult situations" [37]. Originally applied to chronic somatic diseases with success [38-40], it is increasingly being applied to mental health [41]. The Internet has provided new avenues for self-management as it enables cost-effective access to self-management resources at the patient's own convenience and in a location of their choice. Computerized cognitive behavioral therapy (cCBT) is one type of a lower intensity intervention recommended for the treatment of mild to moderate depression in several clinical guidelines [32,42], which incorporates the principles of self-management.

The Preventing Depression and Improving Awareness Through Networking in the European Union Project

The Preventing Depression and Improving Awareness through Networking in the European Union (PREDI-NU) is an international European Union-funded project that involves expert clinicians and researchers in the fields of depression and suicide prevention from 11 European countries, in addition to an international expert advisory panel. The project was funded from September 2011 to September 2014 and builds upon the aforementioned research by the EAAD and OSPI-Europe. Specifically, the PREDI-NU project intends to fill gaps in the availability of evidence-based self-management resources for mild to moderate depression through information and communications technology. In light of this, it encompasses the following 3 main aims:

1. The development of a multilingual European depression awareness and information website [43], to raise awareness of depression and suicidal behavior, to improve knowledge and attitudes regarding depression and suicidal behavior, and to promote help seeking and mental health.

2. The development of an evidence-based, multilingual self-management program for mild to moderate depression to be implemented and "guided" by primary care practitioners or mental health professionals who attend standardized professional training.

3. Implementation of the self-management program in 5 European regions, in addition to evaluation of the acceptability of the program and feasibility of its use, to inform future implementation of the program after project running time.

The purpose of this paper is to describe the study protocol regarding the development, implementation, and evaluation of the self-management program.

Methods

Development of the Self-Management Program

A systematic review informed by the realist approach [44] explored the evidence for cCBT. This was conducted during the 1st year of the PREDI-NU project to inform development of the self-management program. The systematic review aimed to specifically examine (1) what interventions work, for whom, and in what circumstances, and (2) to identify best practice recommendations for implementation of self-help ehealth technologies. This review consisted of a rigorous systematic

literature search resulting in 52 papers, of which 22 were meta-reviews or systematic reviews, 5 were guidelines, and the rest were feasibility studies or studies informing the development, implementation, or use of cCBT. For the purposes of this protocol paper, results from the review will be referred to generally, and extensive results will be published in a separate future study.

The review indicated that numerous cCBT programs for depression have been developed, and that positive randomized controlled trial evidence exists for several packages, namely, Beating the Blues [45], MoodGYM [46,47], and Colour Your Life [48]. However, there is no clear evidence of any one program being more effective than another; additionally, there is little knowledge to guide the development or implementation of such interventions. Furthermore, despite evidence of their effectiveness, there is limited evidence on the acceptability (to both patients and professionals) and feasibility of the use of Internet-based self-management interventions for the management of depression, which may limit their uptake in primary care practice [49] and is likely to be a contributing factor to the high rates of attrition and noncompletion of such programs. Moreover, many established programs are available only in English and only with payment of a fee to the user or for the general practice. Although the review indicated that guided Web-based interventions are more effective in reducing depression than unguided programs [32,50-52], there is no clear evidence regarding the optimal level or format of delivery of guidance, and little consistent evidence to support implementation of cCBT overall.

This systematic review was supplemented by scoping existing cCBT websites internationally and identifying key features for inclusion within the self-management program to be developed. To ensure that procedures and materials meet international standards of evidence-based practice, a rigorous consensus process informed development of the program, involving a panel of international experts on cCBT and a scientific advisory board of international experts with extensive experience of Web-based interventions for depression and related mental health issues. Representatives from patient and family organizations also provided input into this consensus process.

Design and Contents of the Self-Management Program

Using the aforementioned, evidence-based, and best-practice approach, the PREDI-NU consortium developed the iFightDepression tool, a guided Internet-based self-management program for individuals experiencing mild to moderate depression, with versions for both adults aged 25 years and older and young people between 15 and 24 years of age. The iFightDepression tool is derived from a cognitive behavioral therapy approach and primarily focuses on the associations between thoughts, feelings, and behavior. A screenshot of the home page of the iFightDepression tool is shown in Figure 1.

In addition to introductory and emergency contact material, the iFightDepression tool comprises 6 core modules relating to behavioral activation, sleep and mood monitoring, and cognitive restructuring: "Thinking, Feeling, and Doing"; "Sleep and Depression"; "Planning and Doing Things That You Enjoy";

"Getting Things Done"; "Identifying Negative Thoughts"; and "Changing Negative Thoughts". Individuals are encouraged to complete the modules in the structured order in which they appear in the tool; this is to encourage individuals to initiate behavior activation, to examine the relationship between their sleep, moods, and activities, and to integrate positive activities into their daily schedules before the modules relating to cognitive restructuring are undertaken, as these may be more challenging. It has also been suggested that individuals complete the modules at a rate of no more than 1 module/week, with an estimation of 30-40 minutes for the completion of each module. However, while these instructions are recommended, users can determine their personal pace and order of modules if they wish, as suggested by patient representatives involved in the development of the tool. Each module incorporates associated tasks and corresponding worksheets to consolidate learning and promote self-monitoring. In addition to encouraging users to plan and reflect on activities, moods, and thoughts, the tasks and worksheets help users to observe the associations between what they think, what they do, and how they feel.

The "Sleep and Depression" module is innovative and is based on the recently published vigilance regulation model of affective disorders [53]. It supports patients to examine the relationship between the duration of their sleep/time in bed and mood, and to identify personal optimal sleep times. Research suggests that there is a subgroup of patients who feel more tired, exhausted, and depressed after longer-than-usual sleep/time in bed, and that they show improvement after shortening of sleep/time in bed [53]. The effects of partial or total therapeutic sleep deprivation on depression are striking and well established [53]. However, in contrast to chronic sleep restriction, therapeutic sleep deprivation cannot easily be implemented in routine care or self-management approaches. The iFightDepression tool encourages patients to explore the association between their sleep patterns and their mood and to adjust their personal sleeping habits accordingly.

In addition to the 6 core modules, there are optional modules (2 tailored specifically for young people and 1 for both young people and adults) that address related psychosocial issues, namely, relationships, social anxiety, and healthy lifestyle habits.

The iFightDepression tool also encourages individuals to monitor their mood using an embedded, electronic version of the Patient Health Questionnaire-9 (PHQ-9) [54], a short questionnaire that measures the presence/absence of depressive symptoms in the 2 weeks prior to completing the questionnaire, in addition to the frequency of these symptoms. Individuals' scores on the PHQ-9 are automatically plotted on a graph, which allows individuals to visually and clearly track their mood over time. The PHQ-9 was also included within the tool as a safety measure—should an individual's depressive symptoms worsen (as evidenced by 3 consecutive scores reflecting a specific result of "severe depression," and/or a positive response to the 9th item within the questionnaire—"thoughts that you would be better off dead or of hurting yourself in some way"), a feedback window automatically appears that encourages the user to contact their GP, health care professional, or emergency services.

Figure 1. Home page of the iFightDepression tool.
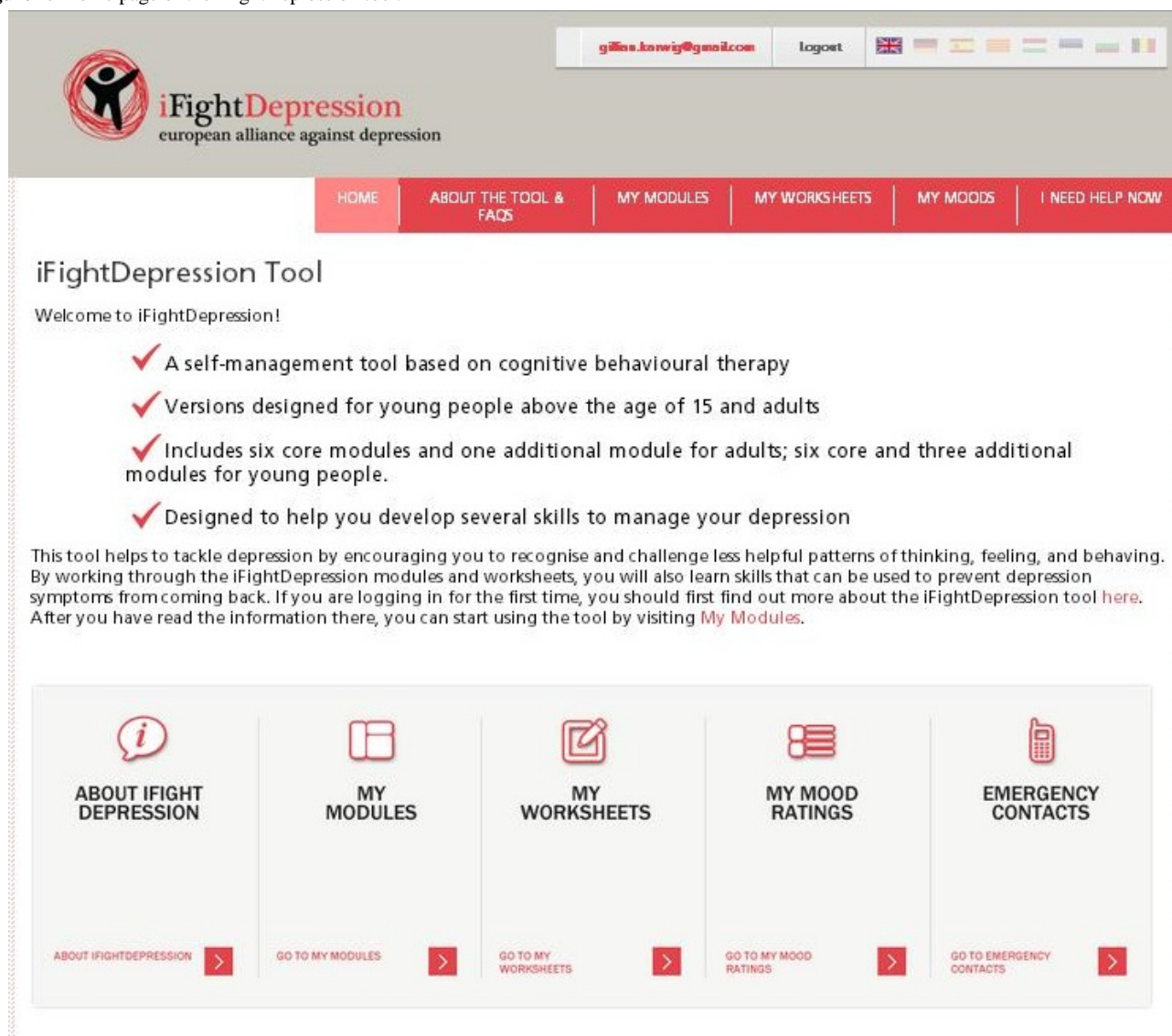
Implementation of the iFightDepression Tool

Specific Protocol Regarding Implementation of the Tool

The iFightDepression tool was implemented through GPs and health care professionals who completed a standardized 3-hour training workshop regarding implementation and guidance of the tool. Specifically, the tool was targeted toward professionals working in the area of mental health who are experienced in the assessment and diagnosis of depression; for example, GPs, family physicians, psychologists, psychiatrists, community mental health nurses, mental health social workers, and clinical nurse specialists. Trained health care professionals were instructed to initially assess patients presenting with depression for eligibility to use the tool (ie, a diagnosis of mild to moderate depression); it was recommended to professionals to use the PHQ-9 or the WHO-Five Well-Being Index in addition to their clinical judgment to ensure that the iFightDepression tool represented an appropriate resource for a patient, given his/her current level of depression. Professionals subsequently provide guidance as the individual commences use of and progresses through the tool.

The iFightDepression tool is intended to complement the available approaches for clinicians regarding the management and treatment of depression, as an adjunct to a patient's usual care. However, the iFightDepression tool is also intended to be used as a single resource for an individual when deemed appropriate; for example, to bridge waiting times for patient access to face-to-face psychotherapy.

Implementation Phases of PREDI-NU

Two phases of implementation occurred during PREDI-NU, with a pilot phase undertaken at the beginning of the 2nd year of PREDI-NU in 5 European regions, followed by a first-phase evaluation to inform enhancement of the iFightDepression tool for continued implementation in these regions. Specifically, following the pilot phase, feedback about the acceptability of the tool and feasibility of its use from patients, health care professionals, and a group of healthy Internet users, in addition to recommendations and input from the scientific advisory board of international experts, was used to enhance all materials relevant to the intervention, including the tool itself and materials for the professional training workshop. The 3rd and final year of the project involved the implementation of the

optimized tool, aiming at sustainable implementation through the development of materials for Train-the-Trainer workshops to qualify senior health professionals to deliver the standardized 3-hour professional training workshops to peers, colleagues, and additional interested professionals.

Before the pilot phase of implementation, local advisory panels were formed in each of the intervention regions, allowing the regions to explore and balance adaptation to local resources and constraints and facilitate access to health care professionals. Shared decision making was undertaken across regions regarding adaptation to procedures of implementation to ensure what could be described as an "empowerment implementation" approach [55].

Professional Guidance

"Guidance" was incorporated into the protocol for implementation of the iFightDepression tool as a key element, whereby individuals both maintain contact with and receive support from a trained GP or health care professional throughout their use of the tool. Guidance was included for the following reasons:

1. The systematic review of previous cCBT interventions demonstrated that guided Internet-based interventions are more effective than nonguided interventions.

2. It is expected that the incorporation of guidance may minimize potential attrition of individuals using the iFightDepression tool, as the review indicated that some level of human contact may improve completion rates of online self-help interventions by increasing motivation.

3. Furthermore, the inclusion of guidance represents an additional safety net as individuals whose depressive symptoms worsen throughout their use of the tool will be encouraged to contact and inform their GP or mental health professional: both during interaction with their health care professional and by way of the informative "feedback" window that is displayed within the tool if patients demonstrate more severe depressive symptoms or suicidal and self-harm ideation after completing the PHQ-9.

The systematic review also indicated that no clear evidence exists regarding the optimal level or format of delivery of guidance. A standardized set of guidelines was thus established regarding guidance of the iFightDepression tool. It comprised the following:

1. Guidance would amount to at least 45 minutes over the course of an individual's use of the iFightDepression tool, and that guidance would be mainly motivational in nature.

2. The nature of the guidance can be flexible and may differ between professional groups (GPs, psychotherapists, other mental health professionals) as they are working within different settings and time constraints. The exact means of implementation may also depend on the personal preference and working style of the professional.

3. There should be at least two face-to-face sessions in addition to the initial personal appointment where the tool is recommended to patients: halfway through a patient's use of

the tool and upon completion of the tool. These face-to-face sessions may be incorporated within standard follow-up appointments provided by the health care professional as part of treatment as usual. This level of guidance is in line with previous studies and national guidelines for the primary care of depression [32].

4. Additional guidance can be provided by telephone; however, it may also be provided in other ways, such as by email or text.

Professional Training

To ensure a standardized approach to implementation of the self-management program, both regionally and internationally, a specific mandatory training workshop was developed for all health care professionals interested in implementing the iFightDepression tool and in guiding patients. The training workshop is 3 hours in length and focuses on the symptomatology and treatment of depression, the concepts of self-management and cCBT, the contents of the iFightDepression tool, and the specific protocols for implementing and guiding the tool in routine practice in addition to assessing individuals for eligibility to use the tool. The development and inclusion of such standardized professional training sessions is innovative as the systematic review informing PREDI-NU indicated that the majority of existing guided cCBT studies do not specify whether the professionals providing guidance and support were specifically trained to use the interventions with clients in a standardized manner. Furthermore, it facilitates the potential for the increased detection and recognition of depression, particularly within primary care services.

Evaluation Aims

PREDI-NU primarily focused on assessing the acceptability of the iFightDepression tool and the feasibility of its use for patients, primary care practitioners, and health care professionals. A comprehensive evaluation strategy including quantitative and qualitative analyses of process and outcome measures was integrated throughout all phases of the project. In line with the aim of describing the protocol of the development, implementation, and evaluation of the iFightDepression tool, procedures and instruments of evaluation will be listed briefly below, while a separate future report on the results of the evaluation process will be published after further data have been obtained and analyzed.

Process evaluation comprised focus groups to explore the views, experiences, and recommendations of the professionals guiding the tool, patients using the tool, and healthy Internet users, to obtain more detailed information regarding the acceptability of the tool and the feasibility of its use. Data from the focus groups were transcribed and categorized according to a specific template developed by the PREDI-NU Consortium regarding the iFightDepression tool itself, procedures of implementation and guidance of the tool, recruitment and assessment of patients, and experiences of the professional training.

Outcome evaluation measures included a range of questionnaires developed to assess the specific characteristics of each patient. Baseline measurement of patient characteristics comprised checklists to be completed by both patients and professionals.

The professional's checklist recorded the patient's mental health history, current treatment, and clinical evaluation. The latter partly drew on the Clinical Global Impression-Severity of Illness measure, which allows for a clinical impression about the current mental health status of the patient to be obtained [56]. The patient's checklist recorded the patient's mental health history, their current situation, and attitudes toward and expectations of Web-based self-management. It was also mandatory for patients to complete the PHQ-9 at baseline, 6 weeks, and 3 months after first log-in. The postintervention assessment at 3 months comprised additional items addressing their experience of the iFightDepression tool. The PHQ-9 was available at all times to patients to regularly assess and monitor their mood at a self-chosen frequency (eg, daily or weekly).

Evaluation measures also included a questionnaire for professionals after training. This questionnaire assessed the adequacy, feasibility, and acceptability of the training program and expectations about working with the iFightDepression tool, including procedures of recruitment and guidance. It is intended that the implementation and evaluation of the tool via professionals will allow for linkage of patients' data to the clinical appraisal of their GP or health care professional. It is expected that the incorporation of quantitative and qualitative data will ensure a more complete picture of the acceptability and feasibility of the tool.

Finally, the intensity of the intervention was derived from recording the number of users of the tool, number of information materials distributed, number of trainings provided, number of professionals attending training, and number of patients invited to participate in the study.

Results

Targeting mild to moderate depression, the iFightDepression tool is based on cognitive behavioral therapy and addresses behavioral activation (monitoring and planning daily activities), sleep regulation, problem solving, cognitive restructuring (identifying and challenging unhelpful thoughts), mood monitoring, and healthy lifestyle habits. There is also a tailored version of the tool for young people, incorporating less formal language and additional age-appropriate modules on relationships and social anxiety. The tool is accompanied by a 3-hour training intervention for health care professionals, who are guiding the patients while using the tool.

Discussion

Effectiveness of Online Interventions

Evidence exists demonstrating the effectiveness of a number of online interventions for depression that are based on the principles of cognitive behavioral therapy. However, only a small number are supported by robust research evidence. Little evidence exists regarding the acceptability of these interventions or the feasibility of their use, for either individuals experiencing depression or health care professionals managing depression in clinical practice. While a comprehensive review of the literature has demonstrated that "guided" online interventions are more effective than nonguided interventions, there is little evidence regarding the optimal length, content, and type of the guidance.

In this paper, we have described the protocol for the development, implementation, and evaluation of a new Internet-based guided self-management program—the iFightDepression tool.

Implementation of the Ifightdepression Tool

The iFightDepression tool can be considered innovative for a number of reasons. It is free of charge for both professionals and patients to use and implemented through health care professionals with defined standards of referral and guidance. It is multilingual, and is currently available in 9 languages—English, German, Spanish, Catalonian, Dutch, Hungarian, Estonian, Italian, and Bulgarian. In addition, it includes youth-focused modules and a specific module addressing the relationship between sleep patterns and mood. Implementation of the tool was undertaken in a standardized manner, with the development of a specific training workshop for professionals. Finally, the iFightDepression tool was enhanced based on results from an evaluation process that focused on assessing the acceptability of the tool and feasibility of its use, both with patients and health care professionals. The iFightDepression tool therefore represents an evidence-informed and standardized online intervention for individuals with mild to moderate depression that can be implemented throughout Europe in a uniform manner. It is intended that the iFightDepression tool will empower patients by virtue of its focus on increasing the capacity of individuals to self-manage their symptoms of depression with guidance from their health care professional. It is also intended to afford health care professionals a free evidence-based resource for effectively managing depression within their practice in a feasible manner [27], either as an adjunct to treatment as usual or as a single resource where appropriate. As a feasible and evidence-based addition to existing treatment options, the iFightDepression tool and associated professional training represent a promising resource in addressing the growing divide between the number of individuals in Europe who are in need of care as a result of their depression [57], current structural constraints of health systems [58], and the decreasing availability of resources for improving the care of depression. There is the potential for the iFightDepression tool to be used within a stepped-care approach and included in the range of treatment interventions in primary care and mental health services for mild to moderate depression [59]. It is intended that iFightDepression, as a resource that specifically addresses mild to moderate depression, will assist in preventing individuals from developing a more severe form of depression and subsequent suicidal behavior. An additional potential use of the tool could involve that of relapse prevention, as a resource for patients who have recovered from severe depression but who still fall within the mild to moderate range of depression. Furthermore, the iFightDepression tool may be of particular interest and benefit for depressed individuals who may not be able to access face-to-face interventions, such as those with hearing deficits or those who may not be able to travel due to severe chronic physical illnesses.

As the approach was adopted throughout the PREDI-NU project across a number of European regions, it is evident that the iFightDepression materials can easily be transferred to different national and international contexts. Throughout PREDI-NU,

several institutions from the project consortium that had not originally planned to implement the iFightDepression tool within their regions have either commenced or planned to commence implementation of the tool, including those in Bulgaria and Belgium. Consequently, there is a clear potential for wider implementation of the tool in other countries and regions.

The funding for the PREDI-NU project ended in August 2014, and the iFightDepression resources are administered via the EAAD, allowing for sustainable use of the iFightDepression tool and the project outcomes. These will be integrated within the materials and procedures of implementation of the 4-level community-based intervention of the EAAD [60] as an addition to the multifaceted approach for improving the care of people with depression and preventing suicidal behavior. In addition, an online version of the standardized training program will be developed and further research will be conducted to evaluate the effectiveness and efficacy of the iFightDepression tool. Thus, there is a clear indication of iFightDepression to complement the range of available resources for mild to moderate depression within primary care and mental health services in Europe.

Acknowledgments

Conflicts of Interest

None declared.

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Abbreviations

cCBT: Computerized Cognitive Behavioral Therapy
EAAD: European Alliance Against Depression
GPs: general practitioners
OSPI-Europe: Optimising Suicide Prevention Programs and their Implementation in Europe
PHQ-9: Patient Health Questionnaire-9
PREDI-NU: Preventing Depression and Improving Awareness through Networking in the EU

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Protocol

Using Video Games to Enhance Motivation States in Online Education: Protocol for a Team-Based Digital Game

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Abstract

Background: Video and computer games for education have been of interest to researchers for several decades. Over the last half decade, researchers in the health sector have also begun exploring the value of this medium. However, there are still many gaps in the literature regarding the effective use of video and computer games in medical education, particularly in relation to how learners interact with the platform, and how the games can be used to enhance collaboration.

Objective: The objective of the study is to evaluate a team-based digital game as an educational tool for engaging learners and supporting knowledge consolidation in postgraduate medical education.

Methods: A mixed methodology will be used in order to establish efficacy and level of motivation provided by a team-based digital game. Second-year medical students will be recruited as participants to complete 3 matches of the game at spaced intervals, in 2 evenly distributed teams. Prior to playing the game, participants will complete an Internet survey to establish baseline data. After playing the game, participants will voluntarily complete a semistructured interview to establish motivation and player engagement. Additionally, metrics collected from the game platform will be analyzed to determine efficacy.

Results: The research is in the preliminary stages, but thus far a total of 54 participants have been recruited into the study. Additionally, a content development group has been convened to develop appropriate content for the platform.

Conclusions: Video and computer games have been demonstrated to have value for educational purposes. Significantly less research has addressed how the medium can be effectively utilized in the health sector. Preliminary data from this study would suggest there is an interest in games for learning in the medical student body. As such, it is beneficial to undertake further research into how these games teach and engage learners in order to evaluate their role in tertiary and postgraduate medical education in the future.

Introduction

Video and Computer Games for Educational Purposes

Over the last three decades, researchers have begun investigating how video and computer games can be utilized for nonrecreational activities such as rehabilitation, memory retention, and education [1]. The growing research interest into serious applications for digital games coincides with the rise of the "digital age," from the mid to late 1980s onward, during which time video and computer games have evolved from

existing predominantly in the domain of hobbyists into a widespread activity in contemporary society [2].

Within the field of digital game studies, a considerable amount of research has been conducted into the use of games in education [3,4]. This research has often focused on demonstrating whether games can be used for educational purposes for primary and secondary learners, with considerably less research into their use for tertiary and postgraduate education. The literature is sparser in relation to the application of digital games for continuing professional development and lifelong learning.

Current research suggests that digital games can be used effectively for educational purposes, but whether they can be tailored to teaching specific learning objectives, and the type of games best suited to doing so, remains unanswered. However, the 2014 Horizon Report [5] identified game-based learning as an area that is likely to have a major impact on learning in the next 2 years. The finding of this report is indicative of the growing interest in using digital game technology more effectively in education.

Using Digital Games for Education Effectively

As research in this area moves forward, it is important to begin exploring what is unique about the educational experience provided by digital games compared to other educational approaches, and when and how they can be effectively utilized within a curriculum. This gap has been identified in the literature and there is a suggestion that to address it in the future, researchers need to explore the nature of the game play experience and how the player and platform interact, rather than focusing on one or the other [6].

In the area of medical education, digital games have been applied in certain formats for several decades [7]. The health sector, alongside the fields of aviation and military training, was one of the first fields to adopt a specific type of digital game for education training simulators, which began being used in health in the mid-1990s [8]. More recent research has explored the use of digital games as tools for patient education in areas such as childhood diabetes management [9]. Researchers have also demonstrated that digital games can have a positive effect for training health professionals, with a considerable interest in the medium as a tool for reducing the learning curve for surgeons [10].

There is also some suggestion in the literature that digital game-based learning may compliment the problem-based learning approach currently utilized in medical education [4]. This finding suggests there may be a role for digital games to play in postgraduate medical education in some areas. Digital games may also prove a useful tool for engaging learners in subjects that prove time intensive or contain unique concepts, terminology, or are difficult to recall. Anatomy and histology education is one such subject, with the literature indicating that retaining knowledge is considered a significant challenge for learners of the subject [11]. Additionally, anatomy content can be difficult to internalize and contain terminology learners find hard to retain [12]. Although few digital games have been utilized to teach anatomy, a nondigital card game was used to

help reinforce content from lectures for optometry students learning anatomy [13]. Additionally, a study evaluated the use of a board game in a cohort of medical and dental students, and successfully demonstrated improved attitudes and perceptions toward their learning of anatomy, as well as anatomy test scores of study participants [14].

This protocol describes a study into the use of a team-based strategy game for medical education, with a particular emphasis on tertiary and postgraduate level training. The study aims to explore the player-platform and player-player interaction of an online, team-based, digital game, with the aim of identifying how digital games can be used as effective educational tools for maximum knowledge coverage. A secondary goal of the study is to evaluate the role of digital games as revision aids for adult learners and to help them assess the limits and strengths of their existing knowledge.

The use of digital games to teach adult learners is an important area for study, as the demographic has largely been overlooked in the literature thus far. In the context of adult education, there are several aspects of video and computer games that may prove valuable, but are as yet unexplored. A core element that has been researched in the field of games studies, but not significantly in educational game studies, is how players interact when playing collaborative video and computer games, a mode which has become popular in the last decade, and its impact on player engagement [15]. Educational researchers have yet to thoroughly explore these collaborative game interactions in the context of educational engagement, or in the context of existing research conducted into collaboration in education [16], but such research suggests that the collaborative and competitive elements of video games may be a core engagement element.

Methods

Primary and Secondary Study Outcomes

This research study uses a mixed methodology to explore the way player-player and player-platform interaction occurs in the context of educational digital games. The primary outcome of the study is to evaluate how a digital game supports player engagement, particularly its value for encouraging cooperative review of player knowledge in a specific content domain. The secondary outcome is to evaluate the impact of the game platform as a tool for adult learners to individually assess their knowledge strengths and deficits, to target revision accordingly. Additionally, the research team aims to obtain preliminary data on how digital games might be integrated into unit of study curriculums in the future.

Game Platform of "They Know"

The game platform "They Know" is a team-based strategy game that was designed for use in a range of educational curriculums. In the context of this study, the platform will be used to develop a game for the study of anatomy and histology for medical students. The game platform distributes anatomy knowledge across a game map, using interconnected nodes that represent key learning categories. Players are divided into 2 teams and allocated to a home base at opposite sides of the map. The aim of the game is to work cooperatively with teammates in order

to take control of an opposing team's home base by crossing the map. In order to cross the map, players must answer multiple choice questions at each node they pass, related to its specific learning category.

The primary population group involved in this research will be second-year medical students studying anatomy at the University of Sydney, Australia. A minimum sample size of 8 participants is required in order to complete the game session. Participation in the study is entirely voluntary (Figure 1).

In order to develop the anatomy game for the platform, an expert development group will be convened. This group will consist of subject matter experts in the area of anatomy, who are also familiar with a curriculum of relevance to the study population. The expert development group will also include educational designers who will be involved in the design of the game map and the coordination of game play sessions.

In order to obtain baseline data, participants will be asked to complete a brief Internet survey after they have consented to be involved in the study, but before they access the educational digital game. This survey will provide basic demographic information, along with data on the level of experience study participants have had with either commercial or educational video games and other online educational activities previously. Additionally, the survey will ask players to provide information on how they currently revise anatomy content, with a specific focus on collaborative approaches.

Participants will then be asked to participate in a game session. Each game session will consist of three 1-hour matches of the game, at spaced intervals. These spaced intervals will be a minimum of 2 days apart, a spacing that has been chosen to provide participants with an opportunity to do relevant revision between matches or have intermatch discussions with their teammates if they desire. Metrics collected by the game platform across the session will also be collected and analyzed to measure the impact of the game on player knowledge. Game metrics collected will include information regarding how quickly participants answered questions and how accurately.

During the game matches, players will be observed by a study coordinator and will be filmed so that the research team can review how players interact with their teammates. Filmed sessions will be analyzed retrospectively in a structured manner in order to observe incidence of player cooperation, as well as to evaluate whether this interaction was social (general chit-chat), strategic (discussion about how to navigate the map, or specific game mechanics), or educational (discussion about a players knowledge, or requests for assistance answering questions).

At the end of each match, participants will be asked to complete a Likert ranking of the match. This ranking will ask participants to rate 5 domains on a scale of 1-6: challenge, competitiveness, engagement, enjoyment, and replay likelihood. The postmatch ratings will be used to evaluate how participant engagement and enjoyment varied across the whole session.

After the conclusion of the session, participants will be asked to undertake semistructured interviews to explore their experiences with the game. The semistructured interviews will provide an opportunity to begin distinguishing how players interacted with the educational content in a unique manner as a result of using the game format. Semistructured interviews will include discussion of how cooperative game play impacted on the learning experience, as well as the value of the technology as a tool for shaping revision and review of a set curriculum. The research team will also be working with the study participants to explore the ways in which their knowledge has been structured as a result of playing the educational video game.

By conducting this study, the research team hopes to make contributions to the current understanding of video games and their use for educational purposes. In particular, it is hoped that undertaking this study will develop a more comprehensive understanding of the use of video games for educating adult learners, a group currently not significantly researched in the field of game studies. Finally, this study is researching the use of a genre of games that has never been utilized in medical education, and has only had minimal research interest in the broader educational research.

Permission to conduct this study was received from the University of Sydney's Human Research and Ethics Committee.

Figure 1. Game play diagram.

Game Play Visualisation

Homebase

Each team starts at their homebase and moves across the map to that of their opponent.

Nodes

Nodes contain multiple choice questions for specific learning areas or text chapters. To 'win' a node players must defeat the node by demonstrating comprehensive understanding of node content.

Team A

Team B

The Map

The map scaffolds the educational content for players in a way that should ensure the full breadth of course content is learnt. To win the game players must move from their homebase to that of the opposing team. They have the best chance of winning the game by working as a team to cover every node on the map.

Results

This protocol describes a research study in its preliminary stages. However, several research outcomes have been achieved. First, after consultation with the medical faculty, a specific content area, first- and second-year anatomy and histology, has been chosen as the focus of the game. Additionally, an expert content development group has been convened to begin development of content for the digital game platform suitable for second-year medical anatomy students. This content group consisted of 6 subject matter experts and educational designers.

Additionally, development of the game platform has been finalized and tested by small groups of experienced commercial game players. These early tests have been used to ensure the stability of the game platform prior to being utilized by the medical students, as well as to determine expected match times for playing each game map.

Finally, second-year medical students have been recruited to participate in the study. A total of 54 second-year medical students expressed their interest in participating in the study. These individuals will be contacted to participate in small group sessions of the digital game containing the anatomy content. It is anticipated that with 54 participants it will be possible to run up to 6 sessions with 8 participants per session.

Discussion

Preliminary Findings

The literature on the use of educational digital games has repeatedly shown them to have a positive effect on learners [3]. In the context of medical education, there has been significant research interest in the use of digital games in clinical training, such as for surgical skills training [17]. There has also been a small amount of research into the use of digital games for continuing education, including one study into their usability for resuscitation skills retraining [18]. Far less research has been undertaken around applying digital games in the tertiary and postgraduate context, though there is some literature to suggest there is interest from students toward the use of digital games to enhance health education [19]. Although this protocol can only describe preliminary outcomes of the research study, recruitment data for the study would suggest there is some level of interest from students within the study population toward the use of a digital game to teach anatomy. This preliminary finding appears to support the existing research in this area, and has the potential to add data to an area of research that is underexplored.

At the postgraduate level, there are numerous units of study that are considered challenging for learners, but integral components of medical education. Anatomy is a good example of this phenomenon, as it is a necessary foundational subject for this student group, but learners often find it complex and difficult

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to learn [12]. In order to continue to offer high-quality educational experiences to learners, it is important for educators to explore tools that may enhance the educational impact of curriculums. The team-based strategy game described in this research protocol may prove a valuable tool for imparting such information, due to mechanics that make games highly engaging and the networked structure of the game map used in this genre of game, which is anticipated to align well with an anatomic curriculum.

Developing methodologies that can effectively capture how a learner interacts with a technological medium and not just the end result of that interaction is a challenge for researchers of many disciplines. In medical education digital game research, randomized controlled trials are the dominant methodology used, which are a very effective means of demonstrating a knowledge change [20]. However, they are less valuable for capturing what about the medium is unique and effective. This protocol has explored a mixed methodological approach, which may be of benefit to other health researchers interested in evaluating digital games for use on a large scale, such as in a postgraduate unit of study curriculum. The use of structured observation provided a powerful tool for developing understanding of player-player and player-platform interaction. Paired with semistructured interviews, this approach should provide a holistic perspective of how digital games can be uniquely utilized for knowledge retention and consolidation.

In all areas of digital games studies, there is a shortage of research investigating how the medium teaches effectively, particularly how various game mechanics work [21]. It is important that a better understanding of this technology's strengths and weaknesses is developed in order to effectively utilize it in the context of medical education.

Conclusions

Digital games are a common recreational medium in contemporary society. They have also been shown to be effective for serious applications, such as education or memory retention. In medical education, they have great potential to engage with adult learners, but there is minimal research exploring how to effectively use them for this purpose. Further research in this area would be of benefit to both learners and educators alike.

Acknowledgments

Conflicts of Interest

None declared.

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Original Paper

Street Food Environment in Maputo (STOOD Map): a Cross-Sectional Study in Mozambique

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Abstract

Background: Street food represents a cultural, social, and economic phenomenon that is typical of urbanized areas, directly linked with a more sedentary lifestyle and providing a very accessible and inexpensive source of nutrition. Food advertising may contribute to shaping consumers' preferences and has the potential to drive the supply of specific foods.

Objective: The purpose of this study is to characterize the street food offerings available to the urban population of Maputo, the capital city of Mozambique, and the billboard food advertising in the same setting.

Methods: People selling ready-to-eat foods, beverages, or snacks from venues such as carts, trucks, stands, and a variety of improvised informal setups (eg, shopping carts, trunks of cars, sides of vans, blankets on the sidewalk, etc) will be identified in the district of KaMpfumu. We will gather information about the actual food being sold through direct observation and interviews to vendors, and from the billboard advertising in the same areas. A second phase of the research entails collecting food samples to be analyzed in a specialized laboratory. The street food environment will be characterized, overall and according to socioeconomic and physical characteristics of the neighborhood, using descriptive statistics and spatial analysis. The study protocol was approved by the National Committee for Bioethics for Health in Mozambique.

Results: Data collection, including the identification of street food vending sites and billboard advertising, started on October 20, 2014, and lasted for 1 month. The collection of food samples took place in December 2014, and the bromatological analyses are expected to be concluded in August 2015.

Conclusions: The district of KaMpfumu is the wealthiest and most urbanized in Maputo, and it is the area with the highest concentration and variety of street food vendors. The expected results may yield important information to assess the nutritional environment and the characteristics of the foods to which a great majority of the urban population living or working in Maputo are exposed. Furthermore, this study protocol provides a framework for a stepwise standardized characterization of the street food environment, comprising 3 steps with increasing complexity and demand for human and technical resources: Step 1 consists

of the evaluation of food advertising in the streets; Step 2 includes the identification of street food vendors and the characterization of the products available; and Step 3 requires the collection of food samples for bromatological analyses. This structured approach to the assessment of the street food environment may enable within-country and international comparisons as well as monitoring of temporal trends.

Introduction

Most of the dietary changes that frequently arise from urbanization and globalization involve decreases in the consumption of foods rich in fiber such as legumes, fruits, vegetables, or whole grains and a more frequent intake of processed foods that are more likely to be energy dense and rich in sugar and salt [1]. The nutrition transition is associated with a higher frequency of noncommunicable diseases (NCDs), which are the main cause of mortality worldwide. It is estimated that by 2030, NCDs will become the most common cause of death in the African continent, surpassing the combined burden of communicable and nutritional diseases and maternal and perinatal deaths [2].

Specifically in Mozambique, a steep increase in urbanization is being observed (percentage of urban population: 21% in 1990, 31% in 2010, 36% estimated by 2050 [3]) and Western lifestyle behaviors, such as the use of processed food products (eg, sugar sweetened beverages, chicken powdered stocks), now coexist with traditional practices, as illustrated by the consumption of traditional dishes and alcoholic beverages [4,5]. Although communicable diseases are the most important contributors to the morbidity and mortality burden, NCDs are becoming more frequent and are estimated to have accounted for one-fifth of all deaths in 2010 [6].

According to the Food and Agriculture Organization of the United Nations, the term "street food" refers to a wide range of "ready-to-eat foods and beverages sold and sometimes prepared in public places, notably streets" [7]. Worldwide, 2.5 billion people eat street food every day [8], which represents a cultural, social, and economic phenomenon that is closely linked with urbanization.

Time dedicated to cooking at home has dramatically decreased among urban dwellers [9,10] and street food usually provides a very accessible and inexpensive source of energy and nutrients. A cross-sectional survey conducted in South Africa, using a nationally representative sample, found that 11% of the population consumes street food at least twice weekly [11]. Several studies have shown that street foods contribute a substantial proportion of the recommended daily allowance of energy and protein for adolescents attending school [12] and urban market women in Nigeria [13]. Moreover, these foods were shown to be fundamental for the daily diet of low-income male urban workers in Hyderabad [14], urban construction workers in Nairobi [15], and street traders in Calcutta [16].

Global influences via advertising and increased availability of imported products contribute to changes in the types of goods consumed [17,18]. A survey conducted in 2005 showed that advertising of fast food, soft drinks, and alcoholic beverages represented a relevant share of the total billboard advertising in the city of Maputo, suggesting the need for assessing the influence of advertising on food availability and dietary habits.

In countries under epidemiological transition, the characterization and monitoring of trends in the street food environment, and specifically the nutritional profile of street food, is particularly important in the context of the efforts for prevention of NCDs. Nevertheless, at present, there is little research on the street food environment in Mozambique. The purpose of this study is to characterize the street food offerings available to the urban population of Maputo and the billboard food advertising in the same setting. The specific aims are: (1) to characterize and map the spatial distribution of street food vendors and food advertising in the city of Maputo; (2) to describe the nutritional composition of the food sold in the streets; and (3) to classify the foods being sold according to the extent and purpose of their processing, such as unprocessed/minimally processed foods, processed ingredients, and ultra-processed food products.

Methods

Overview

This project will comprise a survey for identification and mapping of street food vendors, sampling of street foods and assessment of the billboard food advertising, in Maputo, Mozambique.

The protocol was approved by the National Committee for Bioethics for Health in Mozambique (Comité Nacional de Bioética para a Saúde, Ref. 223/CNBS/14).

Street Food Vendors

Inclusion and Exclusion Criteria

People selling ready-to-eat food, beverages, or snacks from any venue other than a permanent storefront business or established farmers market are potentially eligible for the study. We will select carts, trucks, stands, and a variety of improvised informal setups (eg, shopping carts, trunks of cars, sides of vans, blankets on the sidewalk, people with coolers on the side of the road, etc), as well as "in-transit" street food vendors.

The exclusion criteria are the following: (1) food establishments with 4 permanent walls; (2) permanent storefront business; (3) street vendors selling exclusively nonfood products or raw foods not ready-to-eat; (4) street vendors operating in closed public spaces (ie, markets) or organized entities (ie, farmers markets,

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food fairs); and (5) food stalls and carts that are part of permanent stores or licensed establishments.

Recruitment Plan and Study Design

The administrative repartition of the city of Maputo is made up of 7 districts: KaMpfumu, Nlhamankulu, KaMaxaquene, KaMavota, KaMubukwana, KaTembe, and KaNyaka. The current study will be limited to the district of KaMpfumu, which is the wealthiest and most urbanized [19] among the municipal districts and is considered to represent the area with the highest concentration and variety of street food vendors.

KaMpfumu is composed of 11 neighborhoods: Bairro Central A, B, and C; Alto Maé A and B; Malhangalene A and B; Polana Cimento A and B; Coop; and Sommerschield. Field researchers will canvass specific portions of these neighborhoods and assess the presence of street food vendors in all publicly accessible roads.

Our sampling procedure starts with the identification of all the public transport stops present in the KaMpfumu district (n=134). Among them, we will randomly select 30 stops—of which, only 20 stops will be actively explored; the rest will be made available if the desired number of vendors to be interviewed is not met using the initial group. For each stop we will draw a 500-meter buffer to identify the study area. We will exclude those portions of buffers that fall outside the administrative borders of the district and, in order to avoid sampling the same area more than once, we will treat the overlapping of 2 or more buffers as 1 whole. The actual study area will be delimited using natural borders (ie, sea, mountains) and main avenues/streets.

The public transport stops distribution, which includes *chapas* (private vans) and public buses, was assessed in 2012 as part of a bigger project of formulation of a "Comprehensive Urban Transport Master Plan for Greater Maputo" undertaken by the government of Mozambique with the assistance of the government of Japan [20]. The rest of the maps have been produced by the Maputo Municipal Council (Conselho Municipal Cidade de Maputo) through the interpretation and digitalization (scale 1:5,000) of a 2012 aerial map with high resolution (2m) [19].

Data Collection

Field researchers will operate in pairs, canvassing the neighborhoods in search of street food vendors. Each pair will walk through each publicly accessible street in the selected area and, when a vendor is identified, investigators will mark the position on the map and approach the vendor. A similar methodology has already been field-tested in a previous research on street food vendors in the Bronx borough of New York City [21]. The interviews will be carried out daily, during working days, from 9:00 am to 4:00 pm.

Street food vendors will be asked if they agree to collaborate in the data collection and to participate in a short 10- to 15-minute interview. In the case of a positive response, the researchers will carry out the questionnaire immediately or at a later time more convenient for the vendor.

In addition to assessing the business' operating hours and location, researchers will gather information about the actual food being sold. They will observe and take note of the type of food products available, the size of portions, the price, and the types of food packages. The vendors will be specifically asked about the date and place of preparation, storage and packaging characteristics, and provenance of water being sold.

To prevent vendors from being interviewed twice, the questionnaire starts with a control question asking if the vendor has already been interviewed. Furthermore, after the completion of each interview, each vendor is given a sticker with the logo and Web site of the research project and is asked to put it on the box or cart used to sell products to signal to other interviewers that the vendor has already participated in the study.

Whenever the seller does not agree to participate in the data collection, or when the approach is not feasible—particularly with mobile vendors who are "in-transit"—researchers will still record the geographical position and any other relevant information that can be gathered about their activity, based on the observation of their vending site and of the products available.

For those ready-to-eat foods that are not industrially processed—which means they are either cooked and sold on the street or home-cooked and then sold on the street—a standardized recipe will be used as reference to estimate their nutritional composition. Previous nutritional studies will provide specific information for the Mozambican context [5].

The criteria defined by Monteiro et al [22] will be used to classify foods according to the extent and purpose of their processing into 3 groups: (1) unprocessed/minimally processed foods, (2) processed ingredients, and (3) ultra-processed food products.

Once a map of street vendors is completed, the second phase of the research entails collecting food samples to be analyzed for nutritional composition in a specialized laboratory. Only the most common home-cooked foods will be considered—sold whenever possible in at least 4 different vending sites—up to a maximum of approximately 25 different dishes.

A sample of each food, corresponding to 1 unit or the usual dose, will be bought from 4 different, randomly selected sites among the street vendors previously interviewed. Samples will be properly stored (cold chain) until the bromatological analyses are conducted.

Before analysis, samples will be defrosted, total weight compared to detect moisture losses during storage and shipping, and immediately analyzed for moisture. All determination will be performed at least in duplicate. The following analyses will be conducted:

1. Moisture analysis will be performed by oven drying at 103°C until constant weight [23];
2. Total fat and protein contents will be determined by the Soxhlet and the Kjeldahl procedures, respectively, while total carbohydrates plus fiber will be estimated by the difference [23];
3. Cholesterol and fatty acid analyses will be evaluated on the same lipidic extract, after acid hydrolysis, and using normal phase high performance liquid chromatography for

cholesterol and gas chromatography for the fatty acid ethyl esters, as validated by Cruz et al [24]. The distinction between *cis* and *trans* fatty acids will be included. For fried dishes, total polar compounds in the extracted lipids will be quantified by size exclusion high performance chromatography [25] in order to detect the degree of oil heat abuse;

4. Sodium and potassium content analysis (total Na+ and K+) will be quantified by flame photometry, using the method of Vieira et al [26]. Salt content will also be assessed using a mobile technology (B-721 LAQUAtwin Compact Salt Meter, Horbia, Tokyo, Japan) based on the ion electrode method [27].

Results will be expressed on a fresh mass basis, both per 100 g and per dose, based on the mass sold as individual dose by each individual vendor.

In the selection of the foods to be analyzed, priority will be given to those that are most commonly available and that are more representative of the typical home-cooked foods sold in the streets.

The food sampling was defined in such a way as to account for the expected diversity and variability of home-cooked foods among street vendors. However, no statistical analysis requiring a specific sample size was defined in advance, as this is essentially an exploratory analysis whose main purpose is to complement the data already available on the composition of home-cooked foods sold in the street.

Data Analysis and Sample Size

The study area will be divided into 15-block areas (Figure 1). For each area we expect to interview approximately 30 street vendors, up to a total of approximately 450 vendors.

The street food environment will be characterized—overall and according to socioeconomic and physical characteristics of the neighborhood [19]—using descriptive statistics and spatial analysis. Precision estimates will be computed taking into account the design effect due to cluster sampling.

Assuming a design effect up to 1.1, a sample size of approximately 450 will yield 95% confidence intervals up to 10% wide for observed proportions ranging between approximately 30% and 70%, and 95% confidence intervals for means with a width of approximately 20% of the observed standard deviation.

Training of the interviewers and use of standardized procedures for data collection is expected to contribute to a low proportion of missing data, and no imputation is being planned.

Figure 1. Study areas in the district of KaMpfumu, Maputo. Source: Ministry of Land and Urban Planning.
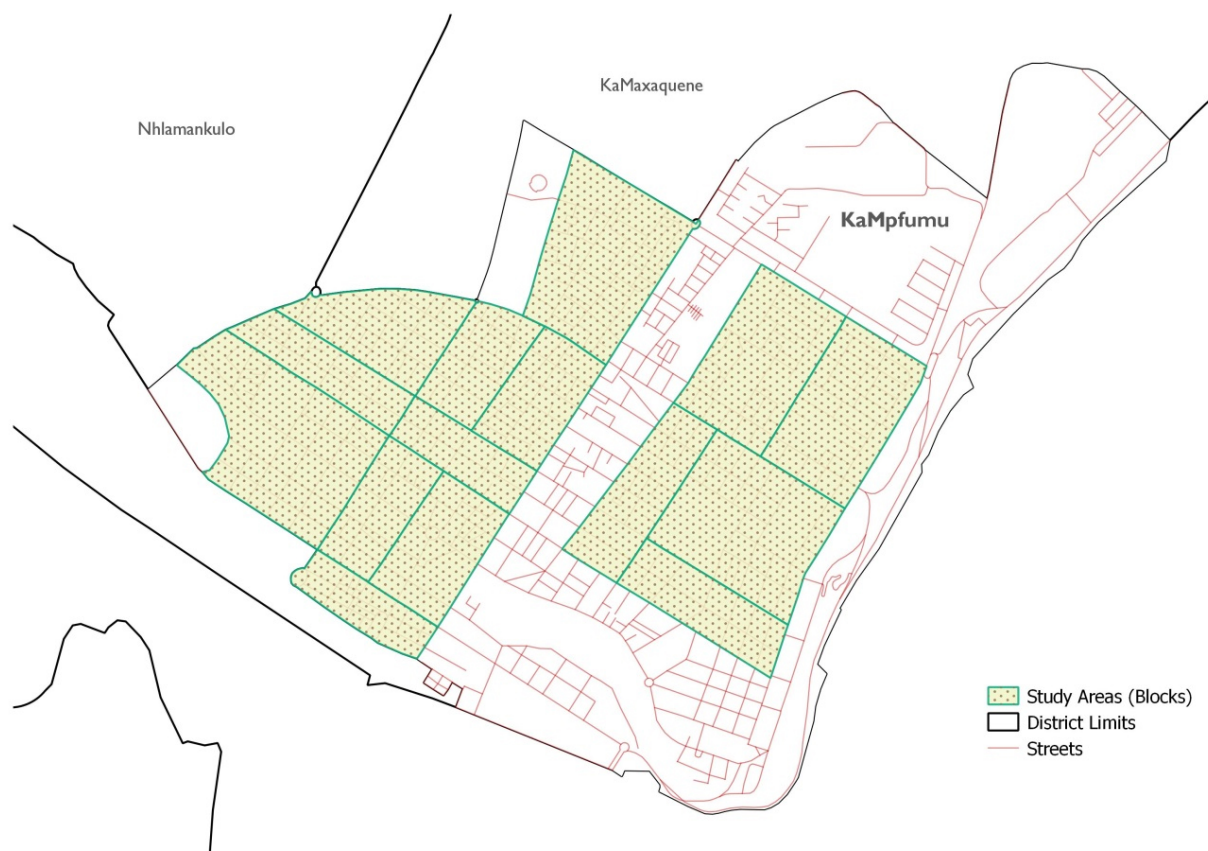
Ethical Considerations

The risks associated with participation in this study are minimal, they do not constitute a threat to confidentiality and are not expected to harm or disrupt the vendors' businesses.

Subjects may experience discomfort and nervousness to participate because of concerns related to investigations from regulatory authority, and this could be the main reason for refusal in participating. To minimize the risk that researchers could be perceived as agents of regulatory authorities, we will utilize residents of the neighborhoods to collect data. Moreover, we will make use of younger students who would unlikely be perceived as a threat.

To reduce the risk of interfering with vendors' businesses, when necessary, we will make attempts at interviewing them at different times of the day (ie, outside of rush hours) as long as this does not conflict with the research objectives. The questionnaire that will be used for field data collection is estimated to require around 10-15 minutes to complete, and most of the information will be gathered by simply observing the vending site without the need of constantly interacting with the vendor.

No data referring to human subjects will be collected, as the unit of the analysis is not the person selling but the vending site. The only information that will be collected refers to the products being sold and the characteristics of the vending site. Particularly, most of this type of information could be easily obtained just by observing the vending site and asking those same questions about price or provenance, for example, that clients normally ask when purchasing a good/service.

A waiver to the requirements for informed consent is reputed as necessary, given the particular conditions of the present study: no human data or any personally identifiable information is being recorded; the research involves no more than minimal risk to the participants; the waiver will not adversely affect the rights and welfare of the participants; the research could not be practicably carried out without the waiver; and participants will be informed about the research objectives and will be able to opt out of the study at any time.

Billboard Advertising

Inclusion and Exclusion Criteria

Fixed billboards with outdoor static advertising are eligible for the study, regardless of their size. We will select all permanent billboards located in any of the streets canvassed by field researchers when aiming to identify street food vendors.

The exclusion criteria are the following: (1) mobile advertising (eg, on vans or selling carts); (2) advertising screens; (3) sponsored equipment (eg, sun-umbrella, coolers, chairs); and (4) promotional printed material (eg, flyers, menus).

Study Design and Data Analysis

Field researchers will record the location and take photographs of all the billboards observed while canvassing the different neighborhoods of the KaMpfumu district of Maputo. The billboards will then be described regarding their size, format,

and content, including the use of marketing techniques with special appeal to children and adolescents (eg, cartoon characters, animation, celebrities, sports personalities) [28] and the food items advertised (eg, alcoholic beverages, including all types of beverages containing alcohol; soft drinks; fast food, including both pre-cooked and ready-to-eat meals; and non-fast food, including all types of food items not considered in the other groups).

Data analysis will comprise the description of the location of the billboards and their physical characteristics and content. The analyses will take into account, for example, the proximity of billboards to schools and youth recreational sites, as well as the assessment of their target audience through content analysis. No minimum sample size was defined since the primary objective of this section is mostly descriptive and thus its informative value is not exclusively dependent on the number of billboards.

Results

Data collection, including the identification of street food vending sites and billboard advertising, as well as their characterization by questionnaire or observation, started on October 20, 2014, and lasted for 1 month. The collection of food samples took place in December 2014, and the corresponding bromatological analyses are expected to be concluded in August 2015.

Discussion

The knowledge and insights gained from this study will potentially advance research efforts surrounding nutrition in the urban context and ultimately may lead to better prevention of diet-related NCDs (eg, obesity, cardiovascular diseases, malnutrition) and more suitable interventions (eg, food regulations and dietary guidelines). The expected results will provide important information on the nutritional environment and the characteristics of the foods to which a great majority of the urban population of Maputo is exposed, though generalization to other urban settings in Mozambique may not be possible.

However, this study protocol provides a framework for a stepwise standardized characterization of the street food environment, comprising 3 steps with increasing complexity and demand for human and technical resources: Step 1 consists of the evaluation of food advertising in the streets; Step 2 includes the identification of street food vendors and the characterization of the products available; and Step 3 requires the collection of food samples for bromatological analyses. This structured approach to the assessment of the street food environment may enable within-country and international comparisons as well as monitoring of temporal trends.

The project is presented to the general population in a Web site [29], where the main results will also be presented, in addition to the submission for publication in international peer-reviewed journals and scientific meetings. A report will be prepared for presentation of the main results to the local authorities.

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Acknowledgments

Conflicts of Interest

None declared.

Multimedia Appendix 1

Comments from funding agency's reviewer #1.

[PDF File (Adobe PDF File), 7KB - resprot_v4i3e98_app1.pdf]

Multimedia Appendix 2

Comments from funding agency's reviewer #2.

[PDF File (Adobe PDF File), 8KB - resprot_v4i3e98_app2.pdf]

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Abbreviations

NCD: noncommunicable disease

Original Paper

The Prevalence of Online Health Information Seeking Among Patients in Scotland: A Cross-Sectional Exploratory Study

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Abstract

Background: Online health information seeking is an activity that needs to be explored in Scotland. While there are a growing number of studies that adopt a qualitative approach to this issue and attempt to understand the behaviors associated with online health information seeking, previous studies focusing on quantifying the prevalence and pattern of online health seeking in the United Kingdom have been based on Internet users in general.

Objective: This exploratory study sought to describe the prevalence of online health information seeking in a rural area of Scotland based on primary data from a patient population.

Methods: A survey design was employed utilizing self-completed questionnaires, based on the Pew Internet and American Life Project; questionnaires were distributed among adult patients in 10 primary care centers in a rural community in Scotland.

Results: A convenience sample of 571 (0.10% of the total population in Grampian, N=581,198) patients completed the questionnaire. A total of 68.4% (379/554) of patients had previously used the Internet to acquire health information. A total of 25.4% (136/536) of patients consulted the Internet for health information regarding their current appointment on the day surveyed; 34.6% (47/136) of these patients were influenced to attend their appointment as a result of that online health information. A total of 43.2% (207/479) of patients stated the health information helped improve their health and 67.1% (290/432) indicated that they had learned something new. A total of 34.0% (146/430) of patients talked to a health professional about the information they had found and 90.0% (376/418) reported that the information was useful. In total, 70.4% (145/206) of patients were concerned about obtaining health information online from reliable sources. A total of 67.1% (139/207) of patients were concerned that a health site may sell their personal information, yet only 6.7% (36/535) checked the privacy policy of the site visited. However, 27.9% (55/197) of patients were not concerned about their employer finding out what health sites they visited, whereas 37.5% (78/208) were concerned that others would find out.

Conclusions: The results suggest that online health information-seeking behavior influences offline health-related behavior among the population surveyed. Patient attitudes to online health information seeking were focused on issues relating to trust, reliability, privacy, and confidentiality. This study provides support for the growing phenomenon of an empowered, computer-literate, health information consumer, and the impact of this phenomenon must be considered in the context of the patient-health professional dynamic. The unpredictable nature of human thought and action in relation to this field of study requires an ongoing program of ethnographic research, both physical and virtual, within a Health Web Science framework. This study has provided a baseline of the prevalence of online health information seeking in the Grampian region of Scotland.

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Introduction

Overview

The Scottish Government recently published a National Framework [1] to encourage digital participation at a local level in the hope that the Scottish people would have the opportunity to benefit from the wide range of information, goods, and services to which the Internet provides access. The Scottish Government are particularly focused on improving digital participation among those groups who historically have been less likely to access the Internet, such as the elderly and low-income households [2]. Paradoxically, these groups stand to benefit most from reduced-price goods and other lifestyle benefits, which the Internet can provide. Internet use at home has been steadily increasing in Scotland. From 2007 to 2013 the percentage of adults accessing the Internet for personal use has risen 17.1 points (62.7% in 2007 to 79.8% in 2013) [2]. This compares with a 15-point increase of Internet use among adults in the United States for the same period (71% in 2007 to 86% in 2013) [3]. Internet use in the home is increasing and, therefore, a range of online activities are potentially impacting people's lives. Information relating to health and well-being is one area in which the Internet is becoming increasingly important.

Scotland has a health service that is free at the point of need. As the population increases, the health of the nation continues to be an area of concern for the Scottish Government and the National Health Service (NHS) in Scotland. Internet use has enabled patients to access search engines, online symptom checkers, and health information sites to contribute to positive health outcomes for themselves or a loved one. This digitally literate population are described as "health seekers" [4]. Humans have information needs, which lead to certain behaviors in order to meet these needs [5]. Information seeking is both a conscious and unconscious process, which encompasses how information is sought, found, used, and also avoided [5]. Seeking information can fill gaps in knowledge and, therefore, decreases anxiety, which in itself can influence and improve health outcomes [6].

Online health seekers differ from offline health seekers by age, income, and education [7]. Those accessing health information online are affluent, well-educated adults [8]. These differences contribute to what is known as the digital divide [9-11]. In 2011, the US government launched a 38 million dollar scheme aimed at narrowing the digital divide, recognizing that health information online is contributing positively to health outcomes and that those who are medically disadvantaged need support in accessing the Internet [12].

Health information sought online by patients is not intended to replace physician care, but rather, to support it [13]. Health professionals also seek information online to help with a diagnosis and provide reassurance [13]. Health seekers are often looking for information about a loved one's care, which suggests a caregiver role [13]. Reasons for health seeking include the following: doing what is prescribed (professional logic), using personal judgement to inform decisions (consumer logic), and gathering information and experience from others (community logic) [13]. Through analysis of the patterns of online health seekers and these forms of logic there is a balance of power to be negotiated between patient and health care professional. Consumer and community logic can often draw credibility from health forums, which are largely user generated. This may create tension in the dynamic between patient and health professional which requires both parties to renegotiate traditional roles, for instance, health professionals are not the only source of health information for patients. Furthermore, online information and social support is encouraging patients not to adhere to physician advice [14], to which health care professionals must adapt [15].

The online health seeker expects convenience, to be a partner in decision making, and almost instant service in all aspects of their health care [16]. However, the health seeker must pass through a series of complex processes in order to access and utilize health information [6]. Barriers in language, information and communication technologies (ICTs) knowledge, or the ability to weigh up sources and formulate a reasoned perspective can all limit the positive outcomes of health seeking online. Trust has also been identified as a key barrier to improving the online health information-seeking experience [17].

Making a primary care appointment can be highly bureaucratized, often with considerable waiting times. Access to primary care for patients within the United Kingdom is guaranteed within 48 hours of contacting their general practitioner (GP) [18]. In Scotland, 29% of adult patients reported that they can wait up to a week for an appointment [19]. However, time constraints, busy lives, and anxiety about symptoms mean that when it comes to medical advice, people want it here and they want it now. Not only do they want instantly available advice, 75% of consumers want access to monitoring devices and online tools [20], thereby allowing visits to the doctor, or other health professional, to be reduced.

The point of origin for this initial exploratory study is concerned with the effect of online health information on primary care services in Scotland and the potential impact this has on the doctor-patient relationship. As stated previously, health seekers often want to be partners in their health care; as Ball and Lillis [16] stated:

> The empowered, computer-literate public is exerting tremendous influence on healthcare delivery. Consumer interest in and demand for online administrative processes, information-rich Internet health portals, and access to physician web pages and e-mail has introduced a new dimension to maintaining wellness and treating disease.

Objective

There is a growing body of literature that is concerned with the prevalence and patterns of online health information seeking. This study hopes to contribute to that body of knowledge by providing an overview of online health information seeking

among a patient population in Scotland. It is hoped that this information will create a baseline indicating what is happening in relation to online health information seeking, rather than an explanation of patient motivation to do so. By simply discovering what is happening, for instance, how many and who, the authors hope to provide a starting point for future research focused on finding out what motivates online health seekers and gain a deeper understanding of the behavior involved. The findings of this study will also be useful to health policy makers and health website content regulators.

Methods

Overview

This study involved a cross-sectional survey and data were gathered using a self-completed questionnaire. The questionnaire was adapted from the Pew Internet and American Life Project [4] (see Multimedia Appendix 1 for the full text of the questionnaire). Questions were closed response and patients were asked to select one response from a range of categorical options. Additional questions were inserted in order to gather data on whether online health information was sought prior to the patient's current appointment and the importance of privacy, convenience, and confidentiality to the patient. The questionnaire was pilot-tested on a sample of students attending the University of the Highlands and Islands (UHI).

The timetable for this cross-sectional study was at the health care center manager's discretion, but no more than one calendar month as per ethical approval. A total of 800 questionnaires were distributed to 10 medical centers in Moray, Scotland, and yielded a response rate of 71.4% (571/800). This sample of 571 patients represented 0.10% of the total population in Grampian (N=581,198 [21]).

Respondents

All adult patients (aged 18 years and over) attending the medical center were invited to participate. The definition of a patient within this study is a person who is attending a medical center on the day surveyed. Table 1 indicates the demographic data from patients who completed the questionnaire.

Procedure

Questionnaires were placed in health care centers with the permission and ethical approval of NHS Scotland, the National Research Ethics Service (NRES), and the University of the Highlands and Islands. Health care center personnel handed the questionnaires out to patients as they waited to see a health professional. A study brief and consent form were read and completed prior to the patient completing the questionnaire to ensure that only adult patients responded.

Anonymized self-completed questionnaires were deposited in a post box in the medical center and collected by a researcher. The software program Statistical Package for the Social Sciences (SPSS) version 22 was used to perform statistical analysis. As the data were nominal, nonparametric tests were employed. Chi-square tests with 95% confidence levels were used to identify differences among the patient demographics. Cramer's V and phi were calculated to indicate the presence and strength of any relationship between variables, as even though the confidence interval is high, the strength of the effect is only indicated by the appropriate coefficient (phi for 2x2 tables or Cramer's V for larger tables).

Table 1. Demographic data of patients surveyed in Moray, Scotland (n=571).

Characteristics	Frequency, n (%)
Age groups (in years)	
18-25	82 (14.4)
26-35	89 (15.6)
36-45	107 (18.7)
46-55	94 (16.5)
56-65	88 (15.4)
66-75	51 (8.9)
76-85	15 (2.6)
86+	2 (0.4)
Not completed	43 (7.5)
Gender	
Male	186 (32.6)
Female	325 (56.9)
Not completed	60 (10.5)
Employment status	
Full-time paid employment	246 (43.1)
Part-time paid employment	71 (12.4)
Full-time student	24 (4.2)
Part-time student	3 (0.5)
Home duties	26 (4.6)
Retired	122 (21.4)
Unemployed	19 (3.3)
Caregiver	2 (0.4)
Ill	1 (0.2)
Not completed	36 (6.3)
Educational attainment	
No formal qualification	52 (9.1)
Standard Grade, "O" grade	102 (17.9)
Highers	75 (13.1)
Vocational qualification	73 (12.8)
Higher National Diploma	2 (0.4)
Undergraduate degree	63 (11.0)
Masters	18 (3.2)
Doctorate	1 (0.2)
Professional qualification	98 (17.2)
Not completed	70 (12.3)
Location	
Rural	90 (15.8)
Village	172 (30.1)
Town	200 (35)
City	69 (12.1)

Results

Demographics and Prevalence of Online Health Information Seeking

Table 1 presents the demographic data gathered on the patients who responded to the survey and Table 2 contains the patient responses to the survey. A total of 554 patients responded to a question asking if they had previously searched for health information on the Internet. Of these responses, 379 (68.4%) had previously searched for health information online, with 63.7% (353/554) of patients doing this by themselves and 4.7% (26/554) doing so on behalf of someone else.

Furthermore, 25.4% (136/536) of patients had consulted the Internet for health information in relation to their appointment on the day surveyed. This was either by themselves—21.5% (115/536)—or someone had done so on their behalf—3.9% (21/536). Of the patients who consulted the Internet for health information prior to their current appointment, 34.6% (47/136) stated that the information they had found online had influenced them to attend their current appointment and 15.4% (53/344) also indicated that they would not have otherwise attended the current appointment.

A large proportion of patients (211/483, 43.7%) stated that they had found information online which had helped them to improve their health, and 90.0% (376/418) believed the health information that they found online was useful. Tables 3 and 4 present the channels and specific sites used. There was a very low response rate (16/571, 2.8%) to specific sites used by the patient sample; this may have been due to issues with memory recall. Table 3 shows that almost half of the patients (53/108, 49.1%) used a search engine, 33.3% (36/108) used NHS sites, and 17.6% (19/108) used a health forum.

The age range dispersion between 18 to 65 years was relatively equal given that opportunity sampling was employed. Patients who took part in the survey were predominantly female (325/571, 56.9%), in full-time employment (246/571, 43.1%) or retired (122/571, 21.4%), and educated to Standard Grade or Highers (177/571, 31.0%)—equivalent to Advanced Subsidiary (AS) level in England and Northern Ireland—which is a reflection of general survey response bias [22]. The classification of patient home location was a relatively even divide between rural and urban. However, it should be noted that the geographical location of this study is generally classified as being a rural area.

Table 2. Patient responses to the survey.

Questions and responses	Frequency, n (%)
Q1. Have you or someone acting on your behalf previously used the Internet to look up health information? (n=554)	
Yes, myself	353 (63.7)
Yes, someone on my behalf	26 (4.7)
No	175 (31.6)
Total	554 (100)
Q4. Did you or someone acting on your behalf search for health information recently with regard to your current appointment? (n=536)	
Yes, myself	115 (21.5)
Yes, someone on my behalf	21 (3.9)
No	400 (74.6)
Total	536 (100)
Q6. Did the health information influence your decision to attend your appointment today? (n=398)	
Yes	47 (11.8)
No	351 (88.2)
Total	398 (100)
Q7. Would you have attended this medical center today if you had not found this information? (n=345)	
Yes	292 (84.6)
No	53 (15.4)
Total	345 (100)
Q8. Have you previously found information on the Internet which has helped you improve your health? (n=483)	
Yes	211 (43.7)
No	272 (56.3)
Total	483 (100)
Q9. Overall, how useful was the health information you got online? (n=418)	
Useful	376 (90.0)
Not useful	42 (10.0)
Total	418 (100)
Q10. Did you talk to a health professional about the information you got online? (n=430)	
Yes	146 (34.0)
No	284 (66.0)
Total	430 (100)
Q11. Did you learn anything new from the information you got online? (n=432)	
Yes	290 (67.1)
No	142 (32.9)
Total	432 (100)

Table 3. Channels used by patients to search for health information online (n=108).

Channels	Frequency, n (%)
Health forum	19 (17.6)
Search engine	53 (49.1)
National Health Service website	36 (33.3)
Total	108 (100)

Table 4. Specific sites used by patients to search for health information online (n=16).

Specific sites used	Frequency, n (%)
BBC.co.uk [23]	1 (6)
Menopausematters.co.uk [24]	1 (6)
Boots.com [25]	1 (6)
CDC.gov [26]	1 (6)
Public Health England (GOV.UK) [27]	1 (6)
Fibromyalgia.co.uk [28]	1 (6)
Google [29]	5 (31)
JustAnswer.co.uk [30]	1 (6)
NHS24.com/SelfHelpGuide [31]	1 (6)
Patient.co.uk [32]	3 (19)
Total	16 (100)

Characteristics That Influence Online Health Information Seeking

As shown in Table 5, a weak association was found between employment status and those who previously searched for health information online. Results also revealed a weak association between employment status and those who were influenced to attend the current appointment as a result of online health information. There was no association between employment status and online health information seeking prior to the patient's appointment on the day surveyed.

A weak association is evident between educational attainment and those who previously searched for health information online. A weak association was also found between educational attainment and those who were influenced to attend the current appointment as a result of online health information. There was no association between educational attainment and online health information seeking prior to the patient's appointment on the day surveyed.

There was a weak association between location and those who previously searched for health information online. A weak association was also found between location and those who were influenced to attend the current appointment as a result of online health information. There was no association between location and online health information seeking prior to the patient's appointment on the day surveyed.

There was a weak association between age and those who had previously sought health information online. There was also a weak association between age and those patients who were influenced to attend the appointment as a result of online health information. There was no association between online health information seeking prior to the appointment on the day surveyed and age.

A weak association was found between gender and online health seeking prior to the patient's appointment on the day surveyed. There was a weak association between gender and those patients who were influenced to attend the appointment as a result of online health information.

As shown in Table 6, a large proportion of patients (357/486, 73.5%) indicated that getting information online, as opposed to other sources, was important. Patients were also concerned about their employer finding out which health sites they visited (55/197, 27.9%), reliability of sources (145/206, 70.4%), and the security of information of their online searches (139/207, 67.1%). However, in relation to concern for security, only a small proportion of patients (36/535, 6.7%) checked the website privacy policy in relation to how their data may be used.

Table 5. Effect of socioeconomic characteristics on health-seeking behavior.

Socioeconomic characteristic and health-seeking behavior effect	χ^2(df)	P	Cramer's V or phi
Does employment status have an effect on online health-seeking behavior?			
Patients who previously searched for online health information (n=554)	23.2 (9)	<.001	.21 (V)
Patients influenced to attend current appointment (n=571)	89.9 (27)	<.001	.23[a](V)
Patients who searched prior to current appointment (n=536)	10.3 (9)	.33	N/A[b,c]
Does educational attainment have an effect on online health-seeking behavior?			
Patients who previously searched for online health information (n=554)	21.0 (9)	<.001	.36 (V)
Patients influenced to attend current appointment (n=571)	76.0 (12)	<.001	.21 (V)
Patients who searched prior to current appointment (n=536)	4.9 (4)	.29	N/A[c]
Does location have an effect on online health-seeking behavior?			
Patients who previously searched for online health information (n=554)	21.0 (4)	<.001	.20 (V)
Patients influenced to attend current appointment (n=771)	76.0 (12)	<.001	.21 (V)
Patients who searched prior to current appointment (n=536)	4.9 (4)	.29	N/A[c]
Does age have an effect on online health-seeking behavior?			
Patients who previously searched for online health information (n=554)	52.3 (8)	<.001	.31 (V)
Patients influenced to attend current appointment (n=571)	94.0 (24)	<.001	.23 (V)
Patients who searched prior to current appointment (n=536)	7.7 (8)	.47	N/A[c]
Does gender have an effect on online health-seeking behavior?			
Patients who previously searched for online health information	N/A	N/A	N/A
Patients influenced to attend current appointment (n=571)	46.5 (6)	<.001	.29 (phi)
Patients who searched prior to current appointment (n=554)	35.1 (2)	<.001	.25 (phi)

[a]A total of 20 cells were expected to have a count less than 5.

[b]Not applicable (N/A).

[c]Too many cells violated the expected count.

Table 6. Attitudes evident among patients in relation to online health information seeking.

Attitudes	n (%)
Concerned that their employer might find out what health sites they visited	55/197 (27.9)
Concerned about getting health information from an unreliable source	145/206 (70.4)
Felt it was important that they could get health information online rather than from other sources	357/486 (73.5)
It is important to be able to get health information online anonymously without having to talk to anyone	357/505 (70.7)
It is important that they can get health information online at any time	433/509 (85.1)
Not concerned about other people finding out what health sites they have visited (1 out of 10 patients were very concerned about this)	130/208 (62.5)
Concerned that a website might sell or give away information about what they did online	139/207 (67.1)
Checked the health or medical website's privacy policy to read about how the site uses personal information	36/535 (6.7)

Discussion

Principal Findings

Patients are searching for health information online and this information influences a small proportion to attend medical centers. Attitudes to online health information seeking suggest a concern for reliability, convenience, privacy, and a preference for online health information above other sources. These results also indicate that location, age, and gender do have an effect on the prevalence of online health information-seeking behavior and the resulting offline behavior.

The Pew Project [7] suggests a slightly higher proportion of Americans are using the Internet to search for health information (80% in 2011). The Oxford Internet Survey (OxIS) [9] reported this figure as 71% in 2011 and falling to 69% in 2013 [10], which is closer to the findings of this study at 68.4%. Cultural

differences and a health care service that is not free at the point of need in the United States may explain the difference between the United Kingdom's and the United States' levels of health information seeking.

This study suggests that online health information seeking influences the offline behavior of this patient sample through patients consulting the Internet for health information either by themselves or on behalf of someone else. Some patients have been influenced to attend a medical center as a direct result of information they found online, with a small proportion of patients reporting that they would not have attended the appointment without this information.

Almost all of the patients in this sample population stated that they found online health information useful. Two-thirds of patients claimed they had not discussed this information with a health professional and the same proportion of patients indicated that they had learned something new from the online health information. It could be suggested that patients who consult the Internet for health information and are satisfied may not feel the need to then consult a health professional. However, further research is needed to explore this finding and investigate whether health professionals are being bypassed by patient online health information seeking. As the Web evolves and attitudes to the Web change, this research needs to be ongoing.

The results from this primary data suggest that location, age, and gender have an effect on health-seeking behaviors and the resulting actions, but the association is weak. In line with the Pew Project [7] and OxIS [9,10], large proportions of those surveyed are searching for health information online. However, it must be highlighted that the findings of the Pew Project and OxIS were both taken from secondary sources of data concerned with overall behavior of Internet users. Health information is influencing patients in Moray to attend medical centers when they would not have done so without the information. Therefore, this study sets a precedent for establishing baseline data for online health-seeking activities among patient populations.

The findings provide support that the digital divide has an impact on health information seeking [11]. In this study, a weak association was found between location and health information seeking. However, the geographical area in this study is considered as a predominantly rural area and, therefore, the self-reported location of patients cannot be truly classified as being within a true rural/urban setting. A national-level study is needed to provide primary data, which would investigate the occurrence of online health information seeking among patients across Scotland focusing on the rural/urban dichotomy.

Confidentiality and privacy is important to patients when they search for health information online, especially in relation to how their personal information may be used and the privacy of their search content. In this instance, "others" are a concern when it comes to people finding out about the content of searches and employers are not a concern. This may suggest

that online health information seeking is not taking place at work, however, this would require further research.

The implications of online health information-seeking behavior on the power dynamic of the traditional health professional and patient relationship should also be the subject of future research as a result of the public availability via the Internet of previously exclusive information (ie, medical information for professionals only). For example, change in the power dynamic because knowledge of the health professional is becoming democratized may cause issues around treatment adherence based on trust and the value that patients place on the knowledge of health professionals.

Conclusions

The findings of this survey provide an indication of how patients' offline behavior is influenced by health information they find online. This study has provided support for the findings from secondary data of previous research which showed that a large number of people are accessing the Internet for health information. This study's unique contribution lies in its presentation of evidence based on primary data, which quantifies patients who are influenced by online health information to interact with health care professionals by attending medical centers. This phenomenon needs to be considered in the context of individual countries and specific populations in order to be useful to policy makers.

Further research is needed to evaluate the impact that the democratization of medical information through online health information seeking among patients has on health care professionals and organizations, including how to access those who sought health information online and did not attend a medical center as a result. Patients want access to health information online at any time, in preference to other sources, and this may be related to increased anonymity and privacy.

The numbers of online health information-seeking patients are increasing; health care professionals and their supporting organizations need to consider how to respond to this. With the increasing amount of user-contributed health information, consideration must be given as to the provision of online health information for digital natives versus digital immigrants, for instance, those who have been socialized in a culture in which digital technologies are part of everyday life compared to those who have had to develop an understanding of digital technologies as adults.

This study provides support for the growing phenomenon of an empowered, computer-literate, health information consumer and the impact of this phenomenon must be considered in the context of the patient-health professional dynamic. The unpredictable nature of human thought and action in relation to this field of study requires a program of ethnographic research, both physical and virtual, to describe how people use the Web for health.

Conflicts of Interest

None declared.

Multimedia Appendix 1

Full text of the self-completed questionnaire.

[PDF File (Adobe PDF File), 104KB - resprot_v4i3e85_app1.pdf]

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Abbreviations

AS: Advanced Subsidiary

ICT: information and communication technology

GP: general practitioner

N/A: not applicable

NHS: National Health Service

NRES: National Research Ethics Service

OxIS: Oxford Internet Survey

SPSS: Statistical Package for the Social Sciences

UHI: University of the Highlands and Islands

Original Paper

Mobile App-Delivered Cognitive Behavioral Therapy for Insomnia: Feasibility and Initial Efficacy Among Veterans With Cannabis Use Disorders

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Abstract

Background: Cannabis is the most frequently used illicit substance in the United States resulting in high rates of cannabis use disorders. Current treatments for cannabis use are often met with high rates of lapse/relapse, tied to (1) behavioral health factors that impact cannabis use such as poor sleep, and (2) access, stigma, supply, and cost of receiving a substance use intervention.

Objective: This pilot study examined the feasibility, usability, and changes in cannabis use and sleep difficulties following mobile phone–delivered Cognitive Behavioral Therapy for Insomnia (CBT-I) in the context of a cannabis cessation attempt.

Methods: Four male veterans with DSM-5 cannabis use disorder and sleep problems were randomized to receive a 2-week intervention: CBT-I Coach mobile app (n=2) or a placebo control (mood-tracking app) (n=2). Cannabis and sleep measures were assessed pre- and post-treatment. Participants also reported use and helpfulness of each app. Changes in sleep and cannabis use were evaluated for each participant individually.

Results: Both participants receiving CBT-I used the app daily over 2 weeks and found the app user-friendly, helpful, and would use it in the future. In addition, they reported decreased cannabis use and improved sleep efficiency; one also reported increased sleep quality. In contrast, one participant in the control group dropped out of the study, and the other used the app minimally and reported increased sleep quality but also increased cannabis use. The mood app was rated as not helpful, and there was low likelihood of future participation.

Conclusions: This pilot study examined the feasibility and initial patient acceptance of mobile phone delivery of CBT-I for cannabis dependence. Positive ratings of the app and preliminary reports of reductions in cannabis use and improvements in sleep are both encouraging and support additional evaluation of this intervention.

KEYWORDS

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Introduction

Cannabis is the most frequently used illicit substance in the United States [1], with rates of cannabis use disorders rising among particularly vulnerable populations (eg, veterans [2]). Recently, rates of use and treatment admissions have increased, while public perception of harm associated with cannabis use has decreased. There is clear scientific evidence that long-term, heavy use of cannabis can result in negative health effects including addiction [3]. Although a number of interventions are available for the treatment of cannabis use disorders (eg, contingency management, cognitive behavioral therapy [4]), rates of lapse and relapse, particularly among vulnerable populations, remains remarkably high [5-7].

In light of the relatively poor outcomes associated with standard cannabis use disorder treatments, there has been increasing interest in identifying malleable factors associated with heightened relapse risk among individuals dependent on cannabis, specifically for the purposes of intervention development and refinement [8-12]. Indeed, poor sleep quality has received a considerable amount of recent attention as a malleable factor implicated in the maintenance of, and relapse to, cannabis use [8]. Driven by the observation that cannabis may have acute sleep-promoting effects [13,14] and that individuals dependent on cannabis experience heightened sleep difficulties during abstinence [15,16], recent research has documented that many cannabis users specifically report using cannabis to cope with or "treat" sleep difficulties [17,18].

From these findings, the evaluation of existing sleep treatments as clinical tools to aid in the treatment of cannabis use disorders has been proposed, with the aim of improving sleep and reducing individual "self-medication" with cannabis [8]. Initial work in this domain has focused on pharmacological treatments for sleep. Vandrey et al [19] tested the efficacy of zolpidem for the attenuation of sleep disturbances (ie, sleep efficiency, total sleep time, subjective sleep quality) during a cannabis cessation attempt and found strong evidence for the efficacy of zolpidem in terms of reducing poor sleep during cannabis withdrawal. Vandrey's study was an important first step in determining the efficacy of sleep treatments for those with a cannabis use disorder; however, there has yet to be an examination of behavioral sleep interventions for individuals attempting cannabis cessation.

Cognitive Behavioral Therapy for Insomnia (CBT-I) is the leading behavioral treatment for sleep disturbances [20,21]. Although there has been some initial investigation of the efficacy and clinical benefit of CBT-I among individuals with alcohol dependence [22,23], there has yet to be an investigation of the use of CBT-I among individuals with a cannabis use disorder.

Given identified barriers to substance use disorder care that include access, stigma, supply, and cost [24-27], a mobile phone app could extend reach and utilization of CBT-I among those with a cannabis use disorder. Compared with traditional care, technology can offer personalized treatment for health risk behaviors such as substance use, while using less counselor time and increasing availability at moments of great need. For example, in a randomized trial of 349 alcohol-dependent patients

leaving residential treatment, those who received a mobile phone app intervention for 8 months had fewer risky drinking days at 4 months follow-up than those in a usual care control group (1.39 days vs 2.75 days [28]). In the treatment of cannabis use disorders, one recent study showed that computerized delivery of evidence-based psychosocial therapy (Motivational Interviewing+Cognitive Behavioral Therapy+Contingency Management) was as effective as the same therapy delivered by a counselor [29]. There has been one report of an app to treat cannabis use disorder with promising ratings of ease and overall usefulness from users [30]. However, there has yet to be an evaluation of cannabis use outcomes for those receiving treatment through a mobile phone app.

This pilot study aimed to begin addressing these gaps in the literature by determining the feasibility of providing CBT-I to individuals with a cannabis use disorder engaged in a cessation attempt through a mobile phone app. CBT-I was administered via mobile app instead of in-person sessions as this would allow for greater reach of the intervention (ie, rural areas) and consistent fidelity of the intervention. For the purposes of this feasibility study, we sought to examine mobile app engagement, user-friendliness, and use and future interest in use, in order to provide initial data regarding the feasibility and usability of this technology among veterans with a cannabis use disorder. As a secondary aim, we examined preliminary trends in the impact of app use on cannabis and sleep outcomes. Specifically, we hypothesized that receiving CBT-I through an app, within the context of a self-guided cannabis cessation attempt, would be acceptable to study participants and utilization of the app would correspond with a reduction in cannabis use and an improvement in sleep quality.

Methods

Recruitment and Participants

Recruitment

In terms of recruitment, 40 individuals contacted the lab expressing interest in the study. Individuals leaving a message were contacted up to four times for the purpose of conducting an initial phone screening. Of the original 40 individuals, 28 veterans who contacted the lab were screened over the phone. Of these, 12 individuals were screened out because they did not report current cannabis use, 6 were not veterans, 5 reported no interest in quitting, and 1 individual was eligible but refused to participate. This resulted in a total sample of 4 individuals.

Participants

Study participants (N=4) were adult veterans (18 and over) who reported (1) current sleep problems, defined as a total score of 5 or greater on the Pittsburgh Sleep Quality Index (PSQI) [31], (2) a cannabis use disorder, as defined by the Diagnostic and Statistical Manual of Mental Disorders (DSM), 5th edition (DSM-5) [32], (3) a self-reported interest in making a cessation attempt within the next 30 days, and (4) veteran status. The mean age of the sample was 47 years (SD 16.31; range 27-65 years), and all participants were male. Two participants self-identified as Caucasian, 1 black/non-Hispanic, and 1 black/Hispanic. All met criteria for cannabis use disorder, 1 had

posttraumatic stress disorder (PTSD), and 2 had a current alcohol use disorder.

Measures

The Structured Clinical Interview-Non-Patient Version (SCID I-N/P) for DSM-IV [33] was administered at baseline to determine current Axis I diagnostic status. Diagnosis for substance use disorders was derived from DSM-5 criteria [32], with additional questions added to account for any changes in diagnostic criteria between DSM-IV [34] and DSM-5 (eg, withdrawal for cannabis). Trained research study staff conducted all interviews, with diagnoses discussed with and confirmed by the last author.

A Mobile App Use Measure (MAUM) was developed to gather information about participant use of both the experimental (ie, CBT-I) and control (mood-tracking) apps between baseline and 2-week follow-up, as neither app recorded use data. The MAUM prompted participants to report on (1) frequency of app use, (2) length of use per occasion, (3) components of the app that were used most often, (4) user-friendliness of the app, (5) helpfulness of the app, (6) likelihood of future app use, (7) use of the app for sleep improvement, and (8) use of the app for cannabis cessation. The MAUM was administered at 2-week follow-up.

Sleep quality at baseline and 2-week follow-up was assessed with the 19-item Pittsburgh Sleep Quality Index (PSQI) [31]. Participants indicated their usual bedtime, how long it took them to fall asleep, their usual waking time, and their usual hours of sleep per night, as well as responding to questions such as, "During the past month, how often have you had trouble sleeping because you cannot get to sleep within 30 minutes?" and "During the past month, how often have you taken medicine (prescribed or over the counter) to help you sleep?" on a 4-point Likert-type scale (0=not during the past month, 3=three or more times a week). At baseline, all questions referred to the past month; the questionnaire was modified for follow-up assessment to capture sleep quality only during the time since baseline (ie, 2 weeks). Algorithms were used to generate 7 component scores and a global total score (for scoring algorithms, see Buysee [31]). Components of the PSQI include subjective sleep quality (defined as the overall quality of sleep), sleep latency (amount of time to fall asleep), sleep duration (number of hours of actual sleep per night), sleep efficiency (number of hours of sleep divided by number of hours spent in bed), sleep disturbances (a non-specific index of nighttime disturbances including symptoms of sleep apnea, middle insomnia, disturbing dreams, and physical conditions such as pain), sleep medication (use of prescribed or over-the-counter sleep medication), and daytime dysfunction (trouble staying awake and/or decreased energy during the day). Both component and global scores were calculated. The global score of the PSQI had a high level of internal consistency in this sample (Cronbach alpha=.94 baseline, .81 follow-up).

The Timeline Follow-Back Interview (TLFB) [35] was administered at baseline and 2-week follow-up to obtain data on frequency and quantity of cannabis, tobacco, and alcohol use during the 90 days prior to baseline and between baseline and 2-week follow-up appointments. Average cannabis use was calculated as the mean quantity of use across each day of the given assessment period. As quantity of cannabis used on each day was indexed by a graphical depiction of varying quantities that ranged from 0 (lowest amount) to 8 (highest amount [36]), with the possible range for average cannabis use across any given period being 0-8. The TLFB has demonstrated good reliability and validity across cannabis using and veteran samples [37,38]. Due to an initial variation in the protocol, for Participant 1, the Marijuana Smoking History Questionnaire (MSHQ) [36] was used to assess baseline cannabis use. The MSHQ is a self-report instrument that includes items pertaining to cannabis smoking rate (lifetime and past 30 days). Two questions assessing (1) frequency of use within the past 30 days, and (2) quantity of use on each occasion (identical to the graphical depiction used in the TLFB) were multiplied and then divided by the total number of days in the assessment period to determine the participant's past 30-day mean cannabis use (range 0-8).

Treatment Apps

CBT-I Coach

Cognitive behavioral therapy for insomnia (CBT-I) was administered via the CBT-I Coach mobile app for iOS [39]. The content of CBT-I coach mirrors that provided by traditional CBT-I and includes four main interactive content areas: "My Sleep", "Tools", "Learn", and "Reminders". "My Sleep" provides individualized tracking of sleep and sleep prescriptions for sleep restriction (see Figure 1). Here, individuals can complete sleep diaries, update and track sleep prescriptions, complete sleep assessments to determine patterns in sleep disruption, and obtain individualized suggestions for improving sleep. Guidelines for sleep restriction and determining the prescribed sleep and rise times were completed during the baseline session with study staff. Sleep and rise times were then entered into the CBT-I Coach, which created alarms and reminders as well as tracking wake and rise times for compliance to the sleep restriction prescription. The "Tools" section provides (1) psycho-education consistent with CBT-I strategies and framework including sleep hygiene tips and stimulus control instructions, (2) guided relaxation tools that can be used in the moment to assist in treatment outcomes (eg, guided relaxation, guided worry time, cognitive restructuring exercises), and (3) individualized recommendations for relapse prevention. The "Reminders" section includes menus to customize and set reminders to (1) complete assessments, (2) set alarms for prescription bed and rise times, and (3) begin wind-down time. Finally, the "Learn" section includes psycho-education on stages of sleep, why we sleep, additional sleep disorders, and treatment including CBT-I. A glossary of terms is also provided as well as recommended good sleep habits. Participants randomized to this condition were provided with an iPod touch with CBT-I coach for the duration of the study.
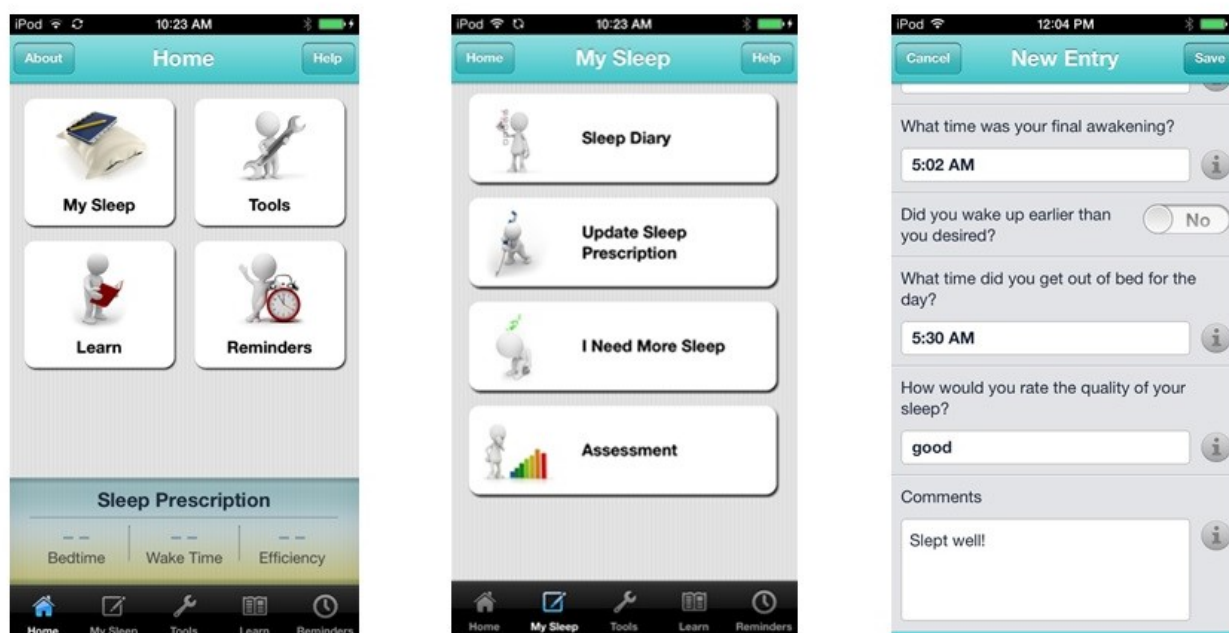
Mood-Tracking App

A self-monitoring mobile app [40] was provided to those randomized to the control condition to test the feasibility of implementing a placebo mobile app. The iOS-based mood-tracking app is a self-monitoring tool, which allows for tracking and referencing emotional experiences (ie, sadness, happiness, stress, anxiety) over time using a visual analogue rating scale. The design of the mobile app is similar to that of CBT-I coach, and symptom rating scales are comparable across apps. Participants randomized to this condition were provided with an iPod touch with the mood-tracking app for the duration of the study.

Procedure

Participants were recruited from a VA hospital in the San Francisco Bay Area via flyers placed throughout the hospital campus and by referrals from clinical staff. Recruitment materials were designed to target veterans interested in making a cannabis cessation attempt. Interested individuals contacted the research lab and completed a brief phone screen to assess for initial eligibility. Those meeting initial eligibility criteria were scheduled for a baseline appointment 1 day prior to the date that they would be willing to make an independent, self-guided, cannabis cessation attempt.

On arrival for the baseline appointment, individuals provided written informed consent. Individuals consented to participate in a cannabis cessation attempt and to engage with a behavioral program via mobile app. The inclusion of a sleep intervention was not discussed in recruitment or consenting procedures. Following informed consent, participants were interviewed with the SCID I-N/P and then completed a battery of self-report measures. Following the completion of the baseline assessment, participants were randomly assigned, by coin flip, to receive either the CBT-I (experimental condition) or mood-tracking app (control condition). Following randomization, participants

were then loaned an iPod touch with charger, trained on how to use their assigned mobile app (which was pre-installed), and instructed to (1) make a cannabis cessation attempt beginning the following morning, and (2) use their assigned mobile app during the first 2 weeks of their cessation attempt. At the end of the baseline assessment, contact information was obtained for each participant to allow for reminder calls regarding app use and follow-up appointment date. Participants were then scheduled for their 2-week follow-up and compensated US $45 for completion of the baseline appointment.

Two weeks following baseline, participants returned to the research laboratory to complete a self-report assessment battery that was similar to the baseline assessment, with the exception of the SCID I-N/P and addition of the MAUM. Following the 2-week follow-up assessment, participants were instructed to relinquish their iPod touch devices and were compensated US $45. All study procedures were approved by the VA Palo Alto and Stanford Institutional Review Boards.

Data Analytic Plan

Based on the small sample size of this pilot study, study outcomes (cannabis use, sleep, and metrics of mobile phone app use) were examined qualitatively for each participant separately.

Results

Information regarding baseline and follow-up scores on study variables can be found in Table 1. Below is an overview of cannabis use and sleep for each participant during baseline and follow-up assessments.

Individual Results

Participant 1

Participant 1 was a 42-year-old single Caucasian male veteran who met DSM-5 criteria for current cannabis use disorder and alcohol use disorder. Participant 1 was a non-smoker and did not meet criteria for any mood or anxiety disorders. He was a novice with mobile technology and did not own a smartphone. As noted in the Method section, the MSHQ was administered instead of the TLFB for this participant. Based on the number of reported days using cannabis during the prior month, coupled with the quantity reported, we were able to extrapolate this participant's cannabis use during the 30 days prior to baseline (see Figure 2). From this, we were able to determine that the participant's mean cannabis use for the 30 days preceding his baseline appointment was 0.40 (on the 0-8 visual scale [36]). In terms of baseline sleep, a total PSQI score of 9 was observed, with a notable impairment in sleep efficiency (ratio of time asleep to time spent in bed trying to sleep; 58%). He reported

no use of medications (prescription or over-the-counter) for sleep.

Participant 1 was randomly assigned to receive CBT-I coach. He reported using the mobile app daily over the 2-week course of his cessation attempt. On average, Participant 1 used the app for 5 minutes at a time and typically interacted with the app in the morning. He reported the most helpful aspect of the app as allowing him to track and view his sleep over the 2-week period. He reported the app as user-friendly and indicated interest in using it in the future. Participant 1 also reported that the app helped his sleep because it provided daily accountability to the intervention components. He also noted that it helped with the cessation attempt because it made him more aware of when and how much cannabis he was using. At 2-week follow-up, Participant 1 had self-reported no cannabis use during the 2-week study period. His total PSQI score did not change from baseline (total score=9); however, his sleep efficiency increased from 58% to 80%, bringing it to just below the normal range (85%). At follow-up he reported using medication (prescription or non-prescription) less than once a week for sleep.

Figure 2. Quantity of cannabis use during each day of the 90-day (30-days for participant 1) baseline and 2-week follow-up periods for each participant, as measured by the MSHQ (Participant 1) and TLFB (Participants 2-4). Vertical dashed line indicates the cessation day for each participant. Because Participant 2 did not complete the follow-up assessment, his data are not presented. Horizontal gray solid lines represent mean cannabis use during the represented timeframe (baseline, 2-week follow-up).
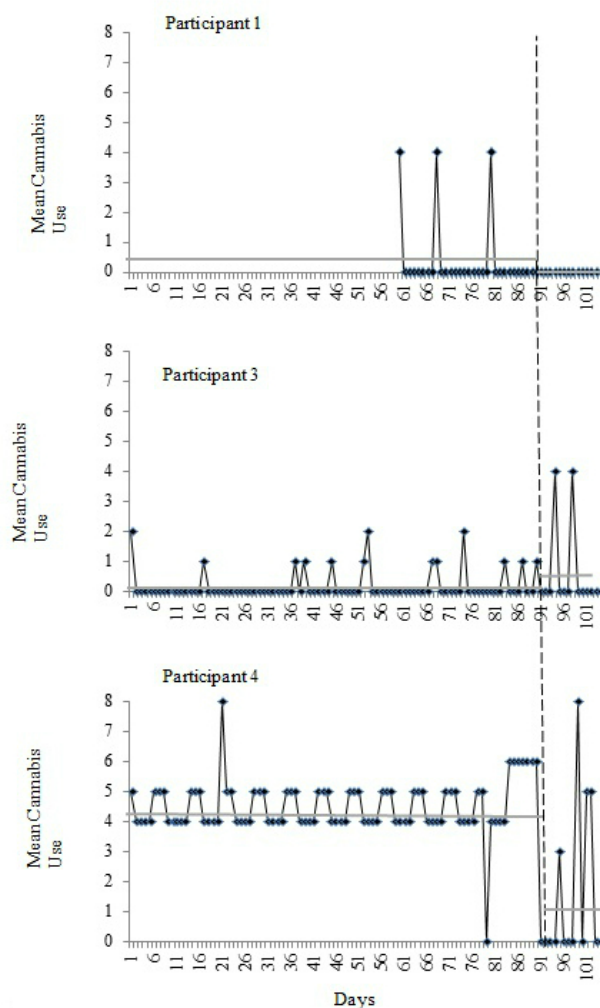
Participant 2

Participant 2 was a 54-year-old widowed black/non-Hispanic male veteran who met DSM-5 criteria for current cannabis use disorder and alcohol use disorder. He did not meet criteria for any mood or anxiety disorders. Participant 2 was a tobacco smoker, consuming an average of 4 cigarettes per day. His mean cannabis use over the 90 days prior to the baseline appointment was 0.71 (on the 0-8 visual scale [36]) and his baseline PSQI total score was 19, with a sleep efficiency of 28%, which indicates a clinically significant level of sleep disturbance [31]. He reported using medication (prescription or non-prescription) once or twice a week for sleep.

Participant 2 was randomly assigned to the control condition (mood-tracking app). This participant dropped out of the study (ie, did not complete his 2-week appointment), thus follow-up data are not available.

Participant 3

Participant 3 was a 65-year-old married black/Hispanic male veteran who met DSM-5 criteria for cannabis use disorder. He did not meet criteria for any mood or anxiety disorders. Participant 3 was also a novice with mobile apps and did not own a smartphone. His mean cannabis use over the 90 days prior to the baseline appointment was 0.18 (on the 0-8 visual scale [36]; see Figure 1). The participant's sleep at baseline was consistent with significant sleep disturbance (PSQI total score=17 [31]) and impaired sleep efficiency (29%). He reported using medication (prescription or non-prescription) less than once a week for sleep.

Participant 3 was randomized to the control condition. He reported using the mood-tracking app minimally (less than once per week) over the 2-week cessation period. Participant 3 reported the app as extremely user-friendly, though he indicated that he would not use it in the future and felt that it did not help at all with his cannabis cessation attempt or sleep. On follow-up, Participant 3 reported an increase in cannabis use (mean use

0.57; on the 0-8 visual scale [36]), as compared to baseline. A slight improvement in sleep was observed (PSQI total score=14), though overall sleep remained indicative of clinically significant levels of sleep disturbance. Sleep efficiency also improved, with his self-reported sleep efficiency score increasing from 29% to 41% at follow-up. He also reported that he did not use medication (prescription or non-prescription) for sleep.

Participant 4

Participant 4 was a 27-year-old divorced Caucasian male veteran of recent conflicts in Iraq and Afghanistan. SCID I-N/P assessment indicated that he met criteria for current PTSD and cannabis use disorder; he was a tobacco non-smoker. Participant 4 had the most experience (of the study participants) with mobile technology, and owned an Android smartphone. He reported the highest amount of cannabis use in the 90 days prior to baseline relative to other participants, with a mean use of 4.51 (on the 0-8 visual scale [36]; see Figure 1). Participant 4's baseline sleep met criteria for mild sleep disturbance (PSQI total=5), with a reported sleep efficiency of 84%. He did not use medication (prescription or non-prescription) for sleep.

Participant 4 was randomly assigned to the CBT-I coach app. He reported using the app daily over the course of the 2-week intervention period. On average, he used the app for 10 minutes during each use, typically in the morning. He noted the app as very user-friendly and indicated that he would use it again in the future. Participant 4 reported that the stimulus control and sleep prescription components of the app were the most helpful, highlighting that the app was useful for sleep, but not for his cannabis cessation attempt. On follow-up, a decrease in mean cannabis use was observed during weeks 1 and 2 (mean use 1.50 on the 0-8 visual scale [36]; see Figure 1). The participant also reported improvement in sleep, with an observed follow-up PSQI total score of 2 and a sleep efficiency increasing from 80% to 100%. In addition, he did not use any medications (prescription or non-prescription) for sleep at follow-up.

Table 1. Participant-level cannabis use and sleep data for baseline and follow-up assessments.

Variable	P1: Experimental		P2: Placebo control		P3: Placebo control		P4: Experimental	
Time of assessment	Baseline	Follow-up	Baseline	Follow-up	Baseline	Follow-up	Baseline	Follow-up
Cannabis use[a]	0.40	0.00	0.71	N/A	0.18	0.57	4.51	1.50
Sleep [b]								
Quality	1	1	3	N/A	3	3	1	1
Latency	30 min	10 min	30 min	N/A	120 min	120 min	30 min	15 min
Duration	5 hours	6 hours	2 hours	N/A	2.5 hours	3.5 hours	8 hours	8 hours
Efficiency	58%	80%	28%	N/A	29%	41%	80%	100%
Disturbances	2	2	3	N/A	3	2	1	0
Med use	0	1	2	N/A	1	0	0	0
Daytime dysfunction	0	2	3	N/A	1	0	1	1
Total PSQI[c]	9	9	19	N/A	17	14	5	2

[a]Mean cannabis use was based on both frequency of use (ie, number of days) and quantity of use per day (scores range from 0-8). Quantity of cannabis used on each day was indexed by a graphical depiction of joints of varying sizes that ranged from 0-8 [36].

[b]Sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disturbances, daytime dysfunction, and sleep med use represent the 7 components of the PSQI [31]. Sleep quality, sleep disturbances, and daytime dysfunction range from 0 "best" to 3 "worst." In terms of sleep medication use, 0=no use in the past month, 1=less than once a week, 2=once or twice a week, and 3=three or more times a week.

[c]PSQI total scores can range from 0 (excellent sleep) to 21 (very poor sleep).

Feasibility

Overview

The current study provided an initial demonstration of using mobile apps for the delivery of psychological interventions among veterans. Feasibility was examined in terms of recruitment, costs, and veteran engagement with the mobile app.

Acceptability Among Veterans

Overall, participants reported interest in using the mobile apps, describing them as easy to use and accessible. Importantly, this feasibility study demonstrated reported app accessibility among veterans without experience with mobile technology. In addition, this study demonstrated the feasibility of using mobile apps among multiple age groups. Indeed, participants ranging from their mid-20s to mid-60s all reported ease in using the mobile apps.

Costs

Individuals were compensated up to a total of US $90 for participation. Additional research costs included iPod touch devices (only 1 individual in the study had their own iPhone) and staff costs.

Mobile App Use

Overall, our sample consisted of novices in terms of mobile technology and mobile app use. Though Participant 4 had experience with using mobile apps, all other participants reported not owning a smartphone or having previous experience with mobile apps. However, all were able to use the apps after a brief explanation. The responses and engagement with the mobile apps was found to vary by treatment condition. Participant 3 (control) reported minimal use of the app (scoring

a 1 out of a possible 4). Follow-up assessment of app use found that this individual did not find the mood tracking app helpful for sleep (reporting 0 out of 4) or cannabis cessation (reporting 0 out of 4) and therefore reported little interest in engaging with the app and low likelihood of using it in the future (reporting 0 out of 4). However, for those who received the CBT-I app (Participants 1 and 4), daily use was reported over the 2-week study period, with an average of 5-10 minutes spent with the app per use session.

Participants assigned to the CBT-I app reported that the most helpful portions of the app were the sleep logs and the exercises for improving sleep. Both reported the app to be very user-friendly (scoring 3 out of 4), found that it was very helpful in improving sleep (scoring 3 out of 4), and reported strong interest in using an intervention app in the future (scoring 3 out of 4). All loaned iPod touches were returned to the study team after completion of the study. Although Participant 2 did not complete the 2-week follow-up, he did return to the laboratory to return his iPod touch.

Discussion

Principal Findings

This pilot study served as a feasibility test of mobile-app delivered CBT-I (and mood-tracking control) for both cannabis and sleep outcomes among individuals engaged in a cannabis cessation attempt. This study indicates that individuals who received the CBT-I app reported daily engagement with the app, while individuals in the control condition either dropped out of the study or reported minimal use. Importantly, regardless of condition, this study provided support for loaning out iOS devices for the purposes of treatment, as all devices were returned following study completion.

Findings support the initial feasibility of providing CBT-I via mobile app to improve outcomes among individuals engaged in a cannabis cessation attempt. Coupled with theoretical and empirical work that has highlighted the pivotal role of sleep in the maintenance and treatment of cannabis use disorders [8], including among vulnerable populations (eg, those with posttraumatic stress disorder [41]), these data indicate the clinical importance of continuing to comprehensively understand the efficacy and effectiveness of CBT-I for cannabis cessation. Indeed, despite its widespread dissemination [42], CBT-I is not currently indicated or utilized as a treatment for substance use disorders, particularly within the Veterans Health Administration. Although these findings are preliminary, this study highlights the potential utility and feasibility of providing CBT-I for patients with a cannabis use disorder. Further, the observation that CBT-I can be effectively implemented via mobile app on loaned devices addresses some of the barriers to care among this population, particularly access and stigma [24-27] and provides additional evidence for the growing movement toward technology-based intervention delivery [28].

Limitations

Although our investigation served as a novel extension of prior empirical and theoretical work, it was not without limitations. First, the small number of participants, all of whom were male, enrolled in this preliminary study limits inference regarding generalizability of findings. Future work would benefit from the replication and extension of this pilot study to a larger and more gender diverse sample. Future work would benefit from focusing recruitment efforts to target female participants. Second, while we screened 40 individuals, due to our inclusion criteria, only four were enrolled. This may have biased the randomness of our sample. Third, given the scope of the study, follow-up data were collected only 2-weeks post-baseline. As the impact of cannabis cessation on sleep can last for over 30-days post-cessation [15], future work should assess patients within a longer follow-up period to determine whether the impact of CBT-I on sleep and cannabis outcomes continues to improve, or begins to abate, as time progresses. Fourth, study participants with the worst baseline sleep problems were randomized to the control condition, a function of the small sample size. Thus, at this point, the efficacy of the CBT-I app for improving severe sleep problems among treatment-seeking cannabis users remains to be determined. Fifth, we examined CBT-I delivery via mobile app and did not include a therapist delivery condition. Future research should compare both methods of delivery as well as including cost-effectiveness analyses. Sixth, while individuals were randomized to groups, we did not have an appropriate sample size to conduct group-based analyses. Future work should include age and other relevant demographic variables as covariates in analyses. Finally, though many of the measures employed for the assessment of cannabis and sleep are considered "gold standard" self-report instruments, the addition of multi-method assessments in future work, including objective measures of cannabis use (eg, plasma, urinalysis) and sleep (eg, actigraphy, polysomnography), would strengthen confidence in self-reported behaviors.

Conclusions

This study provides initial evidence for the feasibility of CBT-I for cannabis dependence delivered through a mobile phone app. Findings support the use of technology to enable easy, affordable access to treatment for substance use disorders [43-45], and small sample studies to address the challenges in testing new technology-based interventions [46]. CBT-I shows promise to treat cannabis use disorder and associated sleep difficulties. Its efficacy should be evaluated in a randomized controlled trial powered to detect treatment effects on cannabis use and sleep.

Conflicts of Interest

None declared.

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Abbreviations

CBT-I: Cognitive Behavioral Therapy for Insomnia
DSM-IV: Diagnostic and Statistical Manual of Mental Disorders, 4th edition
DSM-5: Diagnostic and Statistical Manual of Mental Disorders, 5th edition
MAUM: Mobile App Use Measure
MSHQ: Marijuana Smoking History Questionnaire
PSQI: Pittsburgh Sleep Quality Index
PTSD: posttraumatic stress disorder
SCID I-N/P: Structured Clinical Interview–Non-Patient Version for DSM-IV
TLFB: Timeline Follow-Back Interview

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<u>Original Paper</u>

The Space From Heart Disease Intervention for People With Cardiovascular Disease and Distress: A Mixed-Methods Study

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Abstract

Background: Poor self-management of symptoms and psychological distress leads to worse outcomes and excess health service use in cardiovascular disease (CVD). Online-delivered therapy is effective, but generic interventions lack relevance for people with specific long-term conditions, such as cardiovascular disease.

Objective: To develop a comprehensive online CVD-specific intervention to improve both self-management and well-being, and to test acceptability and feasibility.

Methods: Informed by the Medical Research Council (MRC) guidance for the development of complex interventions, we adapted an existing evidence-based generic intervention for depression and anxiety for people with CVD. Content was informed by a literature review of existing resources and trial evidence, and the findings of a focus group study. Think-aloud usability testing was conducted to identify improvements to design and content. Acceptability and feasibility were tested in a cross-sectional study.

Results: Focus group participants (n=10) agreed that no existing resource met all their needs. Improvements such as "collapse and expand" features were added based on findings that participants' information needs varied, and specific information, such as detecting heart attacks and when to seek help, was added. Think-aloud testing (n=2) led to changes in font size and design changes around navigation. All participants of the cross-sectional study (10/10, 100%) were able to access and use the intervention. Reported satisfaction was good, although the intervention was perceived to lack relevance for people without comorbid psychological distress.

Conclusions: We have developed an evidence-based, theory-informed, user-led online intervention for improving self-management and well-being in CVD. The use of multiple evaluation tests informed improvements to content and usability. Preliminary acceptability and feasibility has been demonstrated. The Space from Heart Disease intervention is now ready to be tested for effectiveness. This work has also identified that people with CVD symptoms and comorbid distress would be the most appropriate sample for a future randomized controlled trial to evaluate its effectiveness.

KEYWORDS

Introduction

Cardiovascular diseases (CVDs) are the leading cause of disability and mortality worldwide [1]. Atherosclerosis is responsible for a large proportion of CVD, including coronary heart disease (CHD). In 2010, heart attacks were responsible for 80,000 deaths [2]. CHD is a chronic condition that affects approximately 3.5% of the UK population [3]. Long-term conditions (LTCs), such as CHD, can be managed but not cured. Making healthy lifestyle choices, such as stopping smoking, eating healthily, drinking alcohol only in moderation, and being active, are important for physical health outcomes as well as for quality of life [4]. Self-management, whereby people take responsibility for their own health and well-being through staying fit and healthy, taking action to prevent illness and accidents, using medicines effectively, treating minor ailments appropriately, and seeking professional help when necessary, is key [5]. However, self-management can be compromised in the presence of comorbid depression and anxiety [6], which is more prevalent in CVD patients than in the general population [7,8].

Symptoms such as chest pain, palpitations, breathlessness, and fatigue are common in CHD and other CVD-related conditions. These symptoms may have a cardiac origin, but patients with CHD also experience symptoms when no cardiac cause can be found [9-12] and often no further physical treatment is available. In a recent cohort study (n=803) of primary care patients living with CHD, 44% reported current chest pain despite receiving treatment for their CHD [13]. Comorbid depression and anxiety can also exacerbate the perceived severity of physical symptoms such as chest pain, palpitations, breathlessness, and fatigue [6]; this often leads to increased primary care [14] and emergency department [15] attendance.

Access to effective psychological treatment for depression and anxiety for people with CVD is limited, such as cognitive behavioral therapy (CBT) delivered by the UK government's Improving Access to Psychological Therapy (IAPT) services, waiting lists can be long, and patients with physical health problems may be unwilling or unable to attend psychological therapy [6,16]. There is evidence that CBT is effective in the management of psychological symptoms of CVD [17], but it is not widely available. In the United Kingdom, the government's IAPT long-term conditions/medically unexplained symptoms (LTC/MUS) Pathfinder Project was established in 2012 to improve access to psychological therapies for people with LTCs and medically unexplained symptoms (MUS). The management of LTC/MUS using behavioral and cognitive behavioral therapy is being tested in a small sample of IAPT services; a recent interim report suggests some clinical and cost benefits, although problems with data collection mean that findings have to be interpreted with caution [18].

Online-delivered interventions can be a low-cost and nonstigmatizing way of delivering therapy and self-management support, and they are easily accessed. Online-delivered therapy is effective for psychological distress [19], although low levels of engagement can lead to poor patient outcomes [20]. Furthermore, established generic computerized cognitive behavioral therapy packages, such MoodGym [21] and Beating the Blues [22], may not be acceptable for people with comorbid physical health problems [23]. A solution that includes disease-specific content is needed to maximize the health benefit.

Our searches of electronic reference databases suggests that interest in Internet-delivered interventions for patients with long-term conditions including CHD is increasing, though data on their effectiveness are scarce. For instance, the E-Rehabilitation intervention [24] includes information regarding cardiac rehabilitation, a discussion forum, and an activity calendar. In a randomized controlled trial (RCT), intervention group participants received tailored content based on models of health behavior through the website and mobile text messages. Short-term results in 69 patients indicated that at 1- and 3-months posttreatment there was a higher median level of physical activity in the active treatment group compared to the control group; this was statistically significant at 3 months. No significant statistical differences were found between the treatment and control groups on self-efficacy, social support, anxiety, or depression [25]. This intervention was not designed specifically to address comorbid psychological distress.

A number of protocols for trials of online CHD self-management support have been published. The InterHerz project from Switzerland [26] will provide an established intervention for depression treatment (Deprexis) to cardiac patients. However, this intervention is not CHD specific, so may lack relevance to this population. In the United Kingdom, a comparison of usual care—National Health Service (NHS)—with usual care plus access to the NHS Helpline service to reduce levels of cardiac risk factors [27] is planned. In Canada, a trial of e-counselling text messages for adherence to lifestyle change in people with hypertension [28] is underway. Neither intervention appears to offer tailored, comprehensive support for both CHD self-management and comorbid psychological distress.

Therefore, it appears that while some interventions are used to address the physical and lifestyle management of CHD and others address psychological distress in this population, there are no products that take a holistic approach to address both self-management and psychological distress in CHD. Informed by the Medical Research Council (MRC) guidance for the development of complex interventions [29], we have developed such a holistic online intervention: Space from Heart Disease. The development phase of the MRC guidelines includes "identifying the evidence base," "identifying or developing theory," and "modelling process and outcomes"; reporting of this phase is important as it informs later implementation and evaluation [29].

Space from Heart Disease uses an existing platform developed by SilverCloud Health which has been shown to be effective for delivering CBT for depression and anxiety [30-32] and which is currently used in 11 NHS trusts. The anxiety and depression platform has demonstrated a three-fold increase in user engagement and a three-fold decrease in user dropout rates compared to other online therapeutic products through the use of a trained supporter who can provide online, timely, personalized feedback [33,30]. This paper describes the development of CVD-specific content, informed by current evidence and by a focus group with CHD patients, and reports preliminary findings concerning the intervention's acceptability and feasibility. Development of the supporter role will be the focus of future work.

Methods

Overview

This work comprises four phases: development of the intervention and three experimental studies. The relation of this work to the MRC Framework for the Development of Complex Interventions [29] is depicted in Figure 1. Ethical approval for the work was provided by the Psychiatry, Nursing and Midwifery Research Ethics Subcommittee at King's College London (KCL) (PNM/13/14-135). The work was funded by NHS England as part of their Small Business Research Initiative scheme.

Figure 1. Medical Research Council development stage of Space from Heart Disease.
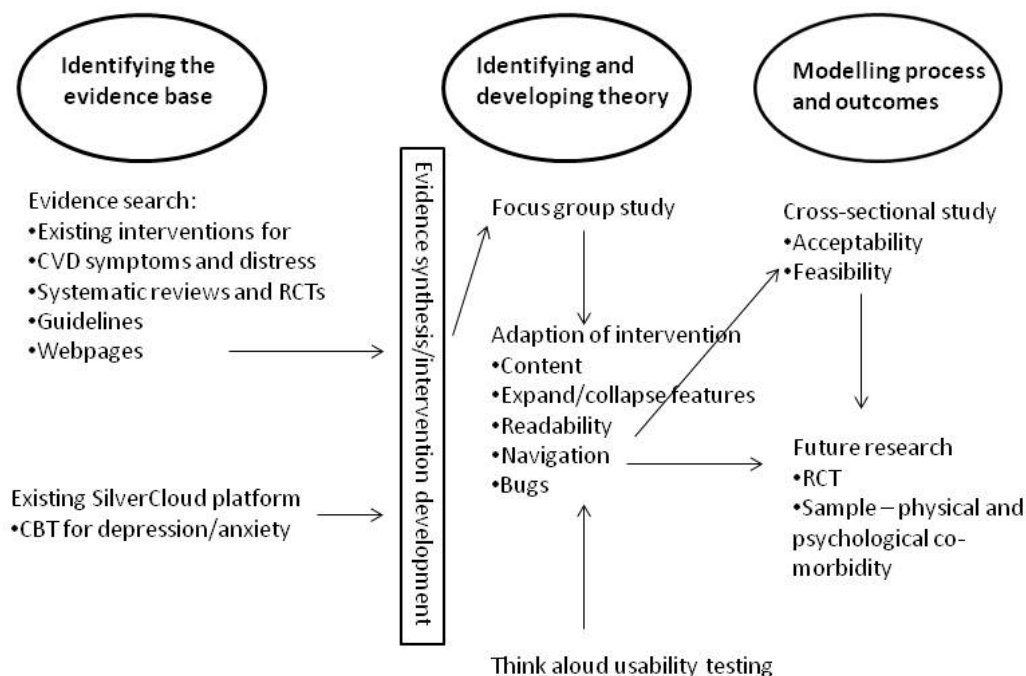
Phase 1: Development of the Intervention

We identified existing evidence-based interventions for common physical (ie, chest pain, palpitations, breathlessness, fatigue) and associated psychological (ie, depression, anxiety, stress, subclinical distress) symptoms of CVD.

We searched electronic databases—Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effects, Embase, Medline, and PsycINFO—for relevant systematic reviews and randomized controlled trials of interventions for CHD symptoms or distress. We also obtained relevant resources currently used in, or recommended for use

by, Southwark IAPT service; this service is participating in the Pathfinder study [18]. National Institute for Health and Care Excellence (NICE) guidelines and high-quality websites, including NHS Choices [34] and the British Heart Foundation (BHF) [35], were reviewed.

This information was then used to adapt the existing SilverCloud intervention for psychological distress so that it was relevant to people with CVD and to develop new CVD-specific content (Figure 1). The intervention content was developed by the research team in conjunction with SilverCloud Health. The research team includes the following: a health psychologist, practitioner psychologist and nurse (EB), a cognitive behavior

therapist and nurse (IN), a cardiac nurse (GL), and a research assistant who previously worked as an assistant psychologist within IAPT (AC). The SilverCloud team included people with expertise in developing and delivering online interventions (DR, KT, DOC).

Phase 2: Focus Group Study

Participants

Participants were recruited via the British Heart Foundation. An email providing details of the project and the researcher's contact details was sent by the BHF support group coordinator to the primary contact for support groups based in South East London. The primary contact for each group was asked to forward the email to their members. The email-recruitment-of-volunteers system at King's College London was also used and a study recruitment poster was placed in a local supermarket.

Those interested in participating were screened to ensure they met the inclusion criteria, which were the following: aged 18 years or over with a self-reported diagnosis of CVD (ie, a diagnosis of one or more of coronary heart disease, atrial fibrillation, stroke, hypertension, diabetes, chronic kidney disease, and/or peripheral arterial disease), able to give informed consent, and able to read and understand English.

Data Collection

A focus group was conducted in the meeting room in the National Institute for Health Research (NIHR)/Wellcome Clinical Research Facility at King's College Hospital. Participants were compensated with a payment of a £20 Love to Shop voucher and travel expenses were reimbursed. The group was facilitated by EB using a topic guide (see Multimedia Appendix 1) informed by literature review and expert opinion—study team and collaborators—to guide the discussion. Topics included current coping strategies (ie, their own or, if not personally relevant, any strategies they are aware of) for chest pain, fatigue, breathlessness, and distress; barriers and facilitators to healthy living (ie, diet, exercise, alcohol); and medication adherence. An example SilverCloud intervention (ie, the online intervention for depression currently being used in 11 NHS IAPT services) was demonstrated by a member of the SilverCloud team and participants were asked whether they thought a similar intervention would be useful to them and, if so, what adaptations would be needed. Example patient stories for use in the intervention were also discussed.

Participants were encouraged to give their opinion so that a wide range of views was understood; it was reiterated that a consensus was not being sought and that all opinions were important. The focus group was audiotaped with consent and transcribed verbatim. Anonymized field notes were made by AC and GL. At the beginning of the focus group session, participants completed a brief demographic questionnaire (ie, age, ethnicity, diagnoses, employment status and occupation, and highest academic achievement). They were also asked to provide their consent to be contacted to take part in the future development studies.

Data Analysis

The focus group transcript was read by two of the authors (EB and AC) to identify key themes. Active searching for disconfirming examples, for instance, statements where participants contradict or disagree with one another, was undertaken. The two researchers compared notes and reached consensus on the themes. Field notes were also considered. Themes were agreed upon by discussion within the multidisciplinary research team. Adaptations were made to the intervention informed by the focus group data (see Figure 1).

Phase 3: Think-Aloud Usability Testing

Participants

The most vocal member of the above focus group was asked to return to test the intervention once changes had been made based on feedback. This person was selected as the participant most likely to be able to articulate their actions and choices during the think-aloud test. We also recruited the first female to respond to the invitation to participate via the BHF.

Data Collection

The intervention was made available on a computer in a soundproofed interview room in the NIHR/Wellcome Clinical Research Facility at King's College Hospital. Written consent to videotape the test was obtained from the participants. The participants were asked to spend up to one hour each exploring the online intervention in any way they wanted. Whilst doing so, they were asked to describe aloud what they were thinking and doing. The study research assistant (AC) attended the session in order to answer any questions and to make notes; EB watched the test via closed-circuit television (CCTV) and also made field notes.

Data Analysis

Audio-visual recordings were observed by the study team in conjunction with the anonymized notes; problems with the intervention or difficulties using it were noted to inform changes to the intervention (see Figure 1).

Phase 4: Cross-Sectional Study

Participants

People with CVD were recruited from the pool of participants who participated in studies above and who had given consent to be contacted for future studies. In addition, snowballing (ie, recruitment of people with CVD known to the study team) was employed. An additional inclusion criterion was access to an Internet-connected computer. Travel expenses and a £20 voucher were provided to participants.

Data Collection

Participants were given access to the adapted intervention (ie, the version including modifications made in response to findings of the above studies) via a password, which allowed access from any computer for 2 weeks. Data concerning patterns of usage of, and satisfaction with, the intervention, as well as clinical data were collected electronically via the secure SilverCloud system. All data were anonymized. Usage data collected over 2 weeks were as follows: number of sessions per user, time

spent per session, and total time spent using the intervention. A session was defined as a period of 5 minutes or more of a user being logged onto the system. Log-ins for less than 5 minutes were also recorded. Session time estimation will always be an imperfect calculation, as users may be interrupted or take breaks within a session, and may not formally log out of the system. All user activity within the system, such as reading a content page, saving a journal entry, or updating an activity, was logged with a time stamp. Starting with the log entry of the user logging on, the total time was calculated by adding up the time that elapsed between each subsequent log record (in the same manner as popular Web analytics software). On its own, this will yield a result vulnerable to overestimation of session time, so to avoid counting periods where the user is not actively engaged with the system, any inactivity (ie, lack of "clicks" within content) longer than 30 minutes was counted as 1 minute. Any period of inactivity longer than 3 hours started the count on a new session, rather than extending the time of the current session. Use of different program components (eg, modules, tracking tool) was measured.

Clinical data were collected using brief, well-validated measures of depression (Patient Health Questionnaire [PHQ-9] [36]), anxiety (the Generalized Anxiety Disorder 7 [GAD-7] scale [37]), quality of life (European Quality of Life-5 Dimensions [EQ-5D] questionnaire [38]), and chest pain (modified Rose Angina Questionnaire [39]). The PHQ-9 [36] and the GAD-7 scale [37] are self-reported measures of severity of depression and anxiety symptoms, respectively. The PHQ-9 consists of nine items and the GAD-7 scale has seven items; for both measures, each item is scored from 0 (not at all) to 3 (nearly every day). The EQ-5D questionnaire [38] is a self-reported measure of health-related quality of life; items relating to mobility, self-care, usual activities, pain/discomfort, and mood are scored to produce a single index score ranging from 0 (worst) to 1 (best possible health). The modified Rose Angina Questionnaire [39] consists of three items designed to detect exertional chest pain which is indicative of angina; respondents report whether or not they have chest pain or discomfort "ever," "walking on the level at an ordinary pace," or "walking uphill or when hurrying." Participants were dichotomized into those who responded positively to any item and those who reported no chest pain in any circumstance. Completion rates and time taken to complete these measures were recorded in order to test their acceptability as outcome measures for a future trial.

Participants were also asked where they accessed the computer (eg, home, friend/relative's house, public space) and whether they had any problems accessing either the computer or the intervention. Participants used Likert items and were able to enter free-text feedback concerning their satisfaction with different elements of the intervention. Within 2 weeks of them completing the trial, we contacted participants by telephone to thank them for their participation and asked if they had any further comments; if we were unable to contact them by telephone, an email was sent. Feedback collected via these methods was recorded verbatim.

Analysis

Descriptive statistics concerning patterns of usage, clinical measures, and their completion and responses to the satisfaction items were produced. Free-text responses (to satisfaction items and verbatim feedback data collected via telephone or email) were subject to content analysis.

Results

Phase 1: The Intervention

Space from Heart Disease is an online psychoeducational and therapeutic intervention designed to support self-management of symptoms and to promote the well-being of people with CVD. A modular design (see Table 1) was used to increase engagement by allowing users to select content relevant to them. The existing SilverCloud intervention for distress delivers cognitive behavioral therapy; we adapted this to include CBT for coping with chest pain, fatigue, and breathlessness. Our literature review also identified specific behavior change techniques—see, for example, the Coventry, Aberdeen and London Refined (CALO-RE) taxonomy [40]—which are effective for CVD-related self-management. For instance, users are helped to apply outcome goal setting (ie, "I will drink no more than one glass of wine on week days") and action planning (ie, deciding in advance what steps to take when faced with a health-related choice, including what to do, where to do it, when to do it, and who will help) to help them to make healthy choices. A summary of module content is shown in Table 1. A tracker app allows users to record their daily activities as part of the therapy, for instance, as a homework task, and a journal function allows users to record free-text thoughts and comments. Standardized outcome measures can also be collected and results displayed graphically; quizzes are used to consolidate learning. Figure 2 shows a screenshot of the home page. Patient stories are used across the modules to provide context. The platform facilitates users to share their work, information, tasks, homework activities, etc, with a supporter, although a supporter was not provided during this development stage.

Findings from the experimental studies are reported below; how these influenced the intervention development is depicted in Figure 1.

Table 1. Space from Heart Disease intervention content.

Module	Module content
Self-management	Medication adherence
(You and Your Health)	Attending and getting the most out of appointments
	Promoting a healthier lifestyle: increasing exercise, healthy diet, reducing alcohol, stopping smoking, stress management
Symptom modules	
1. Chest pain/palpitations	CBT[a] and behavioral strategies for coping with chest pain/palpitations
2. Fatigue	CBT and behavioral strategies for coping with fatigue
3. Breathlessness	CBT and behavioral strategies for coping with breathlessness
Psychological distress	Cognitive behavioral therapy for generalized distress relevant to CVD[b]
Self-monitoring (floating module linked to all others)	Guidance, support, and tools for self-monitoring

[a]Cognitive behavioral therapy (CBT).

[b]Cardiovascular disease (CVD).

Figure 2. Screenshot of Space from Heart Disease home page.
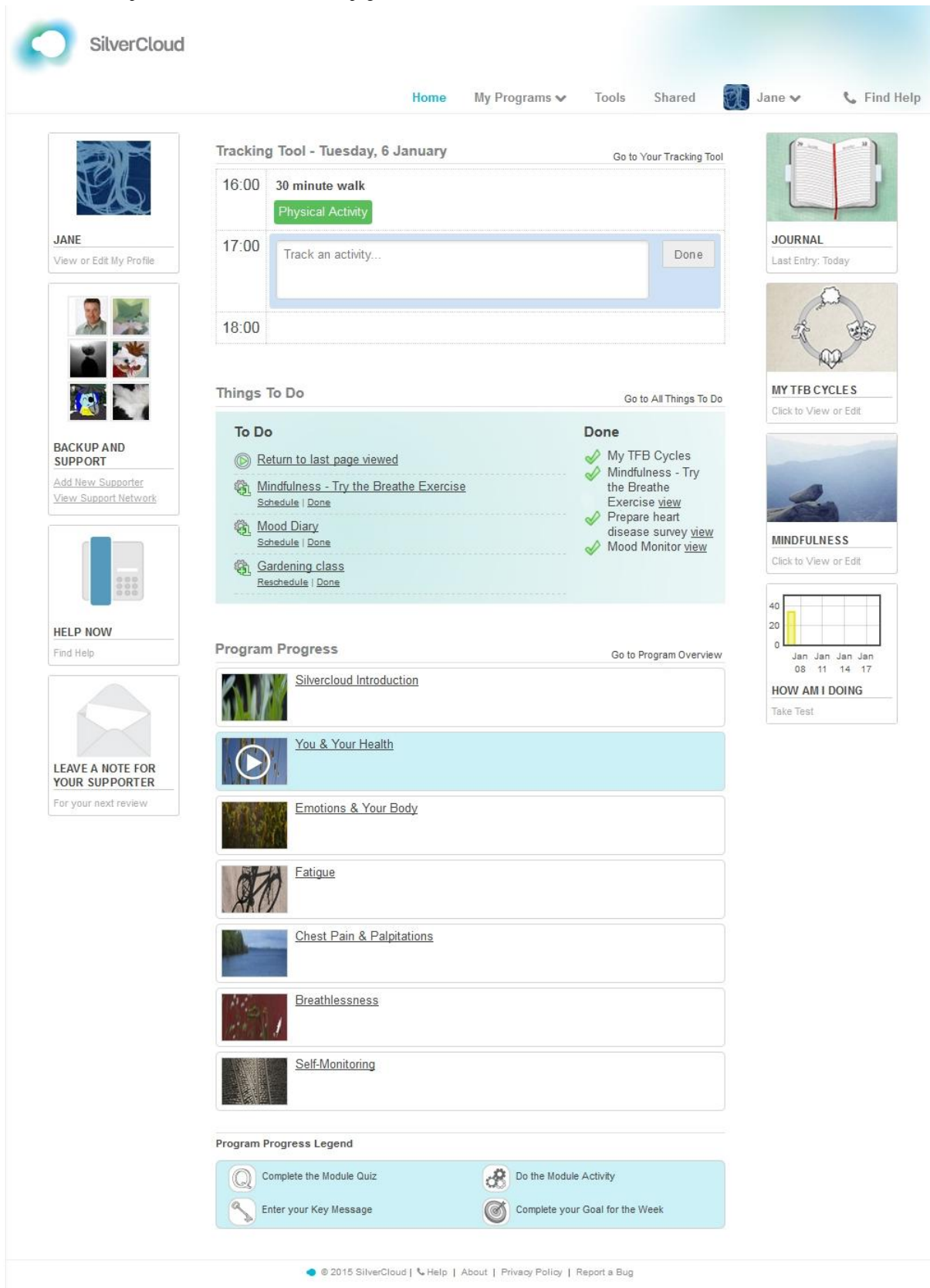
Phase 2: Focus Group Study

Overview

A total of 10 men were recruited from the British Heart Foundation; these represent the total number of those agreeing

to participate. All participants met the inclusion criteria. No women responded to the invitation to participate in time for the discussion. Ages ranged from 53 to 85 years (mean 70 years, SD 11), all participants were Caucasian, 5 of the 10 (50%) were in current employment, and 5 (50%) were retired. Out of the 10

participants, 1 (10%) left school at 16, 4 (40%) had further education qualifications, 3 (30%) had undergraduate degrees, and 2 (20%) had postgraduate degrees. Participants reported one or more of the following: coronary stent inserted (4/10, 40%), coronary artery bypass surgery (4/10, 40%), comorbid type 2 diabetes (2/10, 20%), and chronic kidney disease (1/10, 10%). The discussion lasted 104 minutes.

Four key themes were identified from the discussion: information needs, physical health concerns, mental health impacts, and self-management. Themes are described with supporting quotations identified by participant number (eg, Participant #1 to Participant #10). All participants contributed to all themes and there appeared to be strong consensus within the group.

Theme: Information Needs

Participants wanted information to be presented clearly and to be jargon free. Some participants wanted a lot of information, whereas others preferred to have key facts:

> *Some people are really interested in the full story and others like me would be interested in broad guidance* [Participant #3]

The importance of treating users as individuals was noted:

> *The way you interpret it and manage your life varies absolutely as an individual.* [Participant #8]

> *It needs to be that I can choose I'm not interested in that bit, I'm not interested in that bit, that bit's really relevant to me, and build my own package up from what's available in there.* [Participant #4]

They also wanted to be confident that the information provided was reliable and represented the best advice. There was consensus that there is so much, often conflicting, information available that it can be hard to know what to read:

> *If I type how to avoid type 2 diabetes into Google I will get probably some millions of pieces of advice.* [Participant #8]

> *You get conflicting advice from people...everyone reckons they're right don't they, so how do I know you're going to be right?* [Participant #3]

There was consensus that no existing resource met all their information needs:

> *The difficulty is you do the expert course which just looks at your diabetes and you do the post-operative cardiac care which just looks at your cardiac care and there's nobody ever puts the two together.* [Participant #6]

There was also consensus that ongoing support is required:

> *At the end of that eight weeks [of cardiac rehabilitation classes] I was suddenly told, sorry, finished now, off you go and it was like having the umbilical cord cut, like what's going to happen now?* [Participant #9]

The data from this theme led us to include "expand and collapse" options within the intervention so that users can select the

amount of detail they wish to read. These findings supported the modular design of the intervention whereby users can choose which aspects of the intervention to access according to their needs. We also made the intervention as comprehensive as possible and provided links to reputable websites.

Theme: Physical Health Concerns

On the whole, the participants, who were all active members of a BHF support group, did not report being troubled by physical symptoms:

> *We've learnt to manage it.* [Participant #5]

They were very concerned, however, about the possibility of having a (another) heart attack. They were aware of each other's experiences and knew that each was different:

> *The confusion is that different individuals feel completely different symptoms...X had terrible pain, I had no pain whatsoever and suddenly I collapsed.* [Participant #2]

Even those members who had had more than one cardiac event agreed that no two events felt the same. Participants agreed that they would like information to help them know when to seek help:

> *I'm a little bit confused about people talking about heart attack and angina...when you're getting the pain, which is which?* [Participant #1]

> *I'd like to see something...which would tell me, is this normal or not, or should I worry?* [Participant #6]

Following identification of this theme, we added advice for participants about when to seek help.

Theme: Mental Health Impacts

Participants discussed the impact of CVD on mental health:

> *What I found with people who have heart problems and who have operations or whatever, they have to live with their mortality on a day to day basis.* [Participant #5]

> *...having been fit and thinking I was going to live forever basically, that I then was diagnosed with obviously heart disease then I'm now being told I'm borderline diabetic sort of thing which is another one I do not want to hear. And I don't think the medical profession really appreciate, well we'll tell him and we'll give him all this information and he can go away and he'll be all happy to sort it out. Well I'm not happy really, I didn't want to be diagnosed.* [Participant #3]

Though not currently depressed, several participants reported past low mood associated with cardiac events:

> *I did suffer depression because I couldn't get my (driving) license back so I wasn't working for a year and a half.* [Participant #4, taxi driver]

> *For about two weeks during my recovery program whenever I spoke to anybody about my experiences...I just couldn't stop crying. And this lasted for about*

two weeks. I didn't want to, I didn't feel like I wanted to cry, tears just came. [Participant #9]

It took six years for me to go through the post op depression. [Participant #5]

However, other participants appeared not to want to dwell on this topic and moved the discussion on. It is unclear what help people had received for their low mood; that some reported long durations suggests that effective help had not been available. We have ensured that help for low mood and anxiety is woven throughout the modules.

Theme: Self-Management

These participants agreed with the importance of self-management and that a heart attack could trigger positive lifestyle changes:

...when you walk out of the hospital and you've done the rehab, well the word I use is you're surviving, you're no longer a patient, you're responsible for your own health. [Participant #8]

...the best thing that can happen to you is to have a heart attack because it makes you think about your health. [Participant #1]

As well as belonging to a support group, which they found helpful, some participants used devices to help them to live more healthily:

I mean X's got Fitbit and I've got the same sort of thing and you get an email from them once a week and you can open it if you like and if you open it, it tells you how many steps you've done in the last week, how many times you've been upstairs, it's just a reminder, it's not particularly intrusive but it actually gives you the feeling that you are in a certain sense monitoring your own health. [Participant #8]

Participants liked the idea of an intervention which could prompt them to make healthy choices and monitor their progress:

If there was a program which helped me monitor the sort of things that I ought not to do just to stay off, you know, I've been warned about it and I think that I'm okay, but just to be reminded etc and to track my own progress which means I might set some simple objective for myself. [Participant #8]

However, there was consensus that they did not want to spend too much time using an intervention or on self-management activities:

I don't want to spend my retirement filling in things and trying to work out whether I'm all right or not. [Participant #3]

...the thing is to lighten the load, that's why I say if you have a to-do list have a to-don't list because the fact is we're not going to do all the things on the to-do list or stick to all the resolutions. [Participant #8]

The You and Your Health module provides tools for making healthy choices. The intervention is flexible to allow individuals to spend as much or as little time as they choose using it.

Phase 3: Think-Aloud Usability Testing

One male (aged 60 years) and one female (aged 50 years) each spent 60 minutes using the intervention. Participants were Caucasian, one left school at 16, the other had an undergraduate degree, and both reported having CHD. Overall, the two participants liked the intervention, they continued to use it until the session ended, and were able to navigate without difficulty. User comments and researcher observations are summarized in terms of strengths and weaknesses in relation to "readability," "information," and "navigation," and are shown in Tables 2 and 3, respectively. The intervention was adapted accordingly (see Figure 1). Minor bugs were also noted and fixed.

Table 2. Usability strengths identified in think-aloud testing.

Intervention characteristic	Usability strengths	
	Participant 1	Participant 2
Readability	N/A[a]	Easy to understand
Information	Relevant	Relevant
Navigation	Found commenting easy	Arrows could clearly be clicked
	Used "like" buttons a lot	Used side menu and next/previous buttons without difficulty
	Easy to move between modules	Opened expandable subtopics easily
	Used the side menu and the next/previous buttons without difficulty	True/False buttons easy to use
	Easy to select relevant information to read	
Bugs	N/A	N/A

[a]Not applicable (N/A). Participant did not comment on this aspect of the intervention.

Table 3. Usability problems identified in think-aloud testing.

Intervention characteristic	Usability problems	
	Participant 1	Participant 2
Readability	Font too small in some places	Font too small in some places
		Links and icons should be bigger
		Too much text in some sections
Information	Would like more links (eg, to charities, support services)	Would like more links (eg, to charities, psychological services)
	More content could be given in some places, using a "tiered approach"	Add dietary information for diabetic patients and vegetarians
		Provide more information on medications
Navigation	No problems	"Dots" were confusing (didn't realize they could be clicked)
		Tried to click on some icons, they look too much like buttons
		In self-monitoring module, didn't realize the subtopics were support content
	Difficult to remove comments	
Bugs	"Liking" twice (because of liking something very much) made it "un-like"	N/A[a]

[a]Not applicable (N/A). Participant did not comment on this aspect of the intervention.

Phase 4: Cross-Sectional Study

Overview

A total of 10 participants (2 female, 20%) were recruited; 6 (60%) had participated in the focus group, 1 (10%) had participated in both the focus group and the think-aloud test, 1 (female, 10%) had participated in the think-aloud test, and 2 (20%) (1 female) were recruited via snowballing. Participants were aged from 65 to 85 years (mean 70 years, SD 9). All participants were Caucasian; out of 10, 4 (40%) had left school at age 16, 3 (30%) had an undergraduate degree, and 3 (30%) had a postgraduate degree. Out of 10, 5 (50%) participants were retired, 3 (30%) were working full time, and 2 (20%) were working part time. Self-reported confidence in using the Internet was as follows: out of 10, 2 (20%) participants were "very confident," 3 (30%) were "confident," 2 (20%) were "mildly confident," and 3 (30%) reported "average" confidence. Out of 10, 7 (70%) participants reported having had at least one cardiac event. None reported current depression or anxiety, but in the past, 4 out of 10 (40%) participants had received psychotherapy and/or medication for these conditions.

Usage

All participants reported using their home computers with no access difficulties with either the computer or the intervention. Over the 2-week testing period, there was considerable variation in the number of occasions and amount of time spent using the intervention. The average number of sessions per user was 2.4 (SD 2.2, range 1-8) and the mean time per session was 23 minutes (SD 15, range 5-65). All users also had one or more log-ins of less than 5 minutes (range 1-8). The total time spent using the intervention per participant ranged from 8 to 197 minutes (mean 57, SD 59). All aspects of the intervention were accessed: 43% of time was spent using the content, 26% of time was spent using apps on the platform, 16% of time was spent browsing the home screen, 3% of time was spent using the journal, and 12% of time was spent completing the clinical outcome measures.

Clinical Outcomes

At baseline, all 10 (100%) participants completed all four outcome measures—PHQ-9, GAD-7 scale, EQ-5D questionnaire, and the modified Rose Angina Questionnaire—and at the end of 2 weeks, only 5 (50%) participants returned data for these measures. Measures took a maximum of 1 minute and 9 seconds to complete. There were no missing answers. At baseline, 4 out of the 10 (40%) participants reported current chest pain (modified Rose Angina Questionnaire [39]) and at 2 weeks, 2 out of 5 (40%) participants who responded reported chest pain. Questionnaire scores indicated that the participants were not depressed or anxious and had a good quality of life (see Table 4).

Table 4. Participant ratings of depression, anxiety, and quality of life from the cross-sectional study (n=10).

Clinical outcome	Median (IQR[a])		Range	
	Baseline	2 weeks	Baseline	2 weeks
Depression (PHQ-9[b])	2 (3)	0 (2)	0-8	0-6
Anxiety (GAD-7[c])	2 (3)	0 (0)	0-7	0-5
Quality of life (EQ-5D[d])	0.95 (0.5)[e]	0.90 (0.4)[e]	0.50-1	0.50-1

[a]Interquartile range (IQR).

[b]Patient Health Questionnaire (PHQ-9). Scoring range for the PHQ-9 was 0-27 (depression scores: 0-4 minimal, 5-9 mild, 10-14 moderate, 15-19 moderately severe, 20-27 severe).

[c]Generalized Anxiety Disorder 7 (GAD-7). Scoring range for the GAD-7 scale was 0-21 (anxiety scores: >5 mild, >10 moderate, >15 severe).

[d]European Quality of Life-5 Dimensions (EQ-5D). Scoring range for the EQ-5D questionnaire was 0-1 (quality-of-life scores: 0 worst, 1 best possible health).

[e]For this measure, there were 5 participants.

Satisfaction

Out of 10 participants, 8 (80%) responded to the questions concerning satisfaction with the intervention. Overall, 7 out of 8 (88%) reported being "satisfied" with the intervention and 1 out of 8 (13%) reported being "very satisfied"; 7 out of 8 (88%) would recommend the intervention to someone else. Participant responses to the intervention use and satisfaction items are shown in Tables 5 and 6, respectively.

Table 5. Participant responses to intervention use items (n=8).

Intervention use items	Yes, n (%)	No, n (%)	Not sure, n (%)
Easy to use	8 (100)	0 (0)	0 (0)
Informative	8 (100)	0 (0)	0 (0)
Helpful with any difficulties you are having	5 (63)	2 (25)	1 (13)
Any changes in any area of your life since using intervention[a]	1 (14)	6 (86)	0 (0)
Would you recommend intervention?	7 (88)	1 (13)	0 (0)

[a]This item had one missing value (n=7).

Table 6. Participant responses to satisfaction items (n=8).

Satisfaction with intervention	Very satisfied, n (%)	Satisfied, n (%)	Somewhat satisfied, n (%)	Somewhat dissatisfied, n (%)	Dissatisfied, n (%)
Overall	1 (13)	7 (88)	0 (0)	0 (0)	0 (0)
You and Your Health (self-management module)	0 (0)	7 (88)	1 (13)	0 (0)	0 (0)
Emotions and your body module	0 (0)	8 (100)	0 (0)	0 (0)	0 (0)
Fatigue module	0 (0)	5 (63)	2 (25)	1 (13)	0 (0)
Chest pain module[a]	0 (0)	5 (71)	2 (29)	0 (0)	0 (0)
Breathlessness module	0 (0)	5 (63)	2 (25)	1 (13)	0 (0)
Tracker app (self-monitoring)	0 (0)	6 (75)	1 (13)	1 (13)	0 (0)

[a]This item had one missing value (n=7).

Content Analysis of Free-Text Feedback

Participants were asked to "use 3 words to describe the intervention" (quotes in this section are representative examples). Out of 10, 5 (50%) people's responses suggested they found the intervention easy to use (eg, "easy," "piece of cake," and "straight forward"), 3 (30%) others focused on the usefulness of the intervention (eg, "helpful, useful, informative"), and 1 (10%) person each described it as "reassuring," and "focused or clear." The only negative words were from 1 (10%) person, who described the intervention as "static, impersonal," but also "good quality."

A final person (1/10, 10%) said "not necessarily relevant." This person also sent a long email explaining that they had had their heart attack many years ago and felt that their condition was under control; they did not enjoy filling in the depression and

anxiety measures and felt that the intervention was too focused on low mood for someone like himself.

The aspects of the intervention which were most liked included the presentation ("The screens are nicely laid out." [Participant #1]), clarity of information ("What was being asked was clear and the information was clear." [Participant #3]), ease of use ("easy to use" [Participant #5]), and the ability to choose relevant aspects of the intervention ("Self-selection helpful as I really only have problems with fatigue and how to deal with it." [Participant #9]).

Aspects least liked included diagrams being "too busy" [Participant #2], "emphasis on depression" [Participant #3], and "uninspiring case studies—however, I can see how they might help others" [Participant #7]. One would have liked "more in-depth information" [Participant #9] and one "didn't dislike anything" [Participant #10].

Out of 10 people, 4 (40%) said that an online supporter (as planned) would be useful.

Only 1 (10%) participant had used an online heart-related website before. In comparison to that (unknown) website, they reported that Space from Heart Disease was "Much better in terms of content, use and appearance. Not as good in terms of interactivity or helping a person achieve changes in life-style." [Participant #1].

Some participants did not think the intervention was useful to them personally as they were not experiencing the mood or symptom problems that it addressed.

Discussion

Principal Findings

This paper describes the development and preliminary acceptability and feasibility of a new CVD-specific online intervention to promote self-management and well-being: Space from Heart Disease. The development process was informed by MRC guidelines for the development of complex interventions [29]. This enabled us to produce an intervention which builds on existing evidence, is theory based (ie, CBT and behavior change theory), and is flexible, personalized, and service-user informed.

For instance, the focus group participants varied in their information needs and said they wanted content to be delivered flexibly in order to increase their control in using the intervention. This feedback led to the use of "expand and collapse" options where users can "click" to see information which is hidden from those who find too much text off-putting. The use of modules allows people to skip sections not relevant to them, for instance, only people experiencing chest pain would use the chest pain module. In our cross-sectional study, only 4 people reported chest pain at baseline; future research will recruit people with CVD symptoms in order to test the efficacy of Space from Heart Disease. The symptoms currently covered by Space from Heart Disease are those which have been found in research to cause impaired quality of life and increased unnecessary health care usage [41,42]; if further problematic symptoms are identified, modules to address them could be

developed. Specific information that was added following feedback included how to recognize a heart attack, when to seek medical help, and information concerning diabetes, which is common in people with other CVD-related conditions [43].

Following the focus group, adaptations were made to the intervention and we conducted think-aloud usability testing. This was a useful stage in the development process as it highlighted potential improvements relating to readability (eg, font size too small) and navigation (eg, confusion around which features were "clickable") that could not have been tested in the focus group. A difficulty in removing comments should the participant change their mind was also highlighted. Using several evaluation methods, therefore, helped us to identify a wider range of potential problems; the benefits of this approach have been noted previously [44].

The Space from Heart Disease intervention builds on a generic online intervention for depression and anxiety that is currently used within the NHS. Space from Heart Disease includes a module on distress, which patients may or may not select, which highlights CVD-related dysfunctional thinking (ie, "catastrophizing"—assuming that chest pain is always serious, leading to panic and inappropriate responses such as avoidance of activity, which can lead to worse health and unnecessary health service use) [45]. However, the impact of low mood and anxiety is stressed throughout the intervention; feedback from the cross-sectional study of participants suggests that people who are not currently experiencing distress may not consider the intervention relevant to them. A cohort study of 548 people with CHD [46] found that 22% of participants reported that life was better since their diagnosis supports this. Those participants reported that diagnosis of CHD had led to healthy lifestyle changes, reduction of stress, and recognition of their mortality; such people would be unlikely to benefit from Space from Heart Disease. This suggests that future research to test the effectiveness of Space from Heart Disease should target only CVD patients who report comorbid distress; studies such as one that tested a telephone intervention for primary care patients with CHD and distress [47] indicate that this is feasible.

It is sometimes assumed that older or less-educated people will not be able to access or use technology. In this work we recruited people with a range of educational backgrounds and self-reported levels of confidence using a computer; an important finding was that no participant reported problems either using or accessing the intervention. This is a preliminary indication of the feasibility of the intervention in this population.

Finally, the focus group data indicated that users would appreciate a tailored approach. In future, we plan to develop a supporter role to facilitate the intervention. The original SilverCloud intervention employs such a supporter who is able to provide tailored encouragement and feedback, for instance making suggestions regarding which elements of the intervention the user may find helpful. Future work will determine what skills are needed for a supporter of a CVD-specific intervention—that is, whether medical or psychological skills are most needed. Candidate professionals to fulfil this role may be nurses or psychological well-being practitioners as employed

within the UK Improving Access to Psychological Therapies service.

Strengths and Limitations

Informed by the MRC guidelines for the development of complex interventions [29], we used multiple research designs to develop and make systematic, service-user informed improvements to a new CVD-specific intervention for the promotion of self-management and well-being. To our knowledge, Space from Heart Disease is the first online intervention in CVD which addresses self-management, symptom management, and psychological distress. Use of the MRC guidelines [29] enabled us to develop content which builds on existing research and uses evidence-based CBT and behavior change techniques. We used the existing SilverCloud online platform for delivering CBT as the basis of our CVD-specific intervention. The SilverCloud intervention was developed with extensive user input and is known to be effective for improving psychological distress [30-32]. Our approach, therefore, differs from that of others who have used focus group data as the basis of their intervention. For instance, Antypas and Wangberg [48] conducted a focus group to determine user needs and combined findings with a theoretical review of health behavior models to develop a novel online intervention for physical activity in cardiac rehabilitation.

Our sample sizes were small, so the participants may not be representative of the larger population of people with CVD and, in particular, the views of women are lacking since only two were recruited. Our use of the large body of existing literature on distress and symptoms in CVD was designed to ensure that Space from Heart Disease meets a range of needs, however, the needs of women are often neglected in CVD research [49] and in future, researchers should make additional efforts to address this. Future trials of Space from Heart Disease will determine whether there was sufficient input from the range of people with CVD to produce an effective intervention. Nevertheless, the level of patient and public involvement in the development of the intervention is high as adaptations to the intervention were made as a direct result of in-depth participant feedback. Our use of a series of studies using different designs ensured that all aspects of the intervention were tested.

Our cross-sectional study provides preliminary support for the acceptability and feasibility of Space from Heart Disease in people with CVD—patients did not report problems using the intervention and feedback indicated that the content was felt to be relevant. However, none of our participants was currently experiencing depression or anxiety, so further work is needed to test the acceptability of the intervention in people with CVD and comorbid psychological distress using a much larger sample. Space from Heart Disease builds on an existing, effective, generic intervention for depression and anxiety which is designed to be facilitated by a professional "supporter" who provides timely and personalized feedback; future research will test the effectiveness of Space from Heart Disease delivered with online support.

Conclusions

Health information technology can improve health care quality and safety [50,51]. Online-delivered therapy is effective for psychological distress [19]. However, generic computerized CBT packages may not be acceptable for people with comorbid physical health problems [23]. We have developed an evidence-based, theory-informed, user-led online intervention for improving self-management and well-being in CVD. The use of multiple evaluation tests has informed improvements to its content and usability, and preliminary acceptability and feasibility have been demonstrated. This is important since the effectiveness of online interventions may be hampered by design and usability problems [44]. This development work also identified the most appropriate sample (ie, people with symptomatic CVD and comorbid distress) for a future RCT of the effectiveness of Space from Heart Disease.

Conflicts of Interest

Intellectual property (IP) for the SilverCloud platform is owned by SilverCloud Health. A license agreement in relation to KCL IP is currently being negotiated with SilverCloud to allow them commercial exploitation of the final intervention. The license has revenue-share obligations due to KCL. Some of the authors (DOC, KT, DR) of this paper are employees of SilverCloud Health.

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Multimedia Appendix 1

Topic guide for focus group.

[PDF File (Adobe PDF File), 7KB - resprot_v4i3e81_app1.pdf]

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Abbreviations

BHF: British Heart Foundation
CALO-RE: Coventry, Aberdeen and London Refined
CBT: cognitive behavioral therapy
CCTV: closed-circuit television
CHD: coronary heart disease
CVD: cardiovascular disease
EQ-5D: European Quality of Life-5 Dimensions
GAD-7: Generalized Anxiety Disorder 7
IAPT: Improving Access to Psychological Therapy
IP: intellectual property
IQR: interquartile range
KCL: King's College London
LTC: long-term condition
LTC/MUS: long-term conditions/medically unexplained symptoms
MRC: Medical Research Council
MUS: medically unexplained symptom
N/A: Not applicable
NHS: National Health Service
NICE: National Institute for Health and Care Excellence
NIHR: National Institute for Health Research
PHQ-9: Patient Health Questionnaire
RCT: randomized controlled trial

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Defining the Content of an Online Sexual Health Intervention: The MenSS Website

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Abstract

Background: Health promotion and risk reduction are essential components of sexual health care. However, it can be difficult to prioritize these within busy clinical services. Digital interventions may provide a new method for supporting these.

Objective: The MenSS (Men's Safer Sex) website is an interactive digital intervention developed by a multidisciplinary team, which aims to improve condom use in men who have sex with women (MSW). This paper describes the content of this intervention, and the rationale for it.

Methods: Content was informed by a literature review regarding men's barriers to condom use, workshops with experts in sexual health and technology (N=16) and interviews with men in sexual health clinics (N=20). Data from these sources were analyzed thematically, and synthesized using the Behavior Change Wheel framework.

Results: The MenSS intervention is a website optimized for delivery via tablet computer within a clinic waiting room setting. Key targets identified were condom use skills, beliefs about pleasure and knowledge about risk. Content was developed using behavior change techniques, and interactive website features provided feedback tailored for individual users.

Conclusions: This paper provides a detailed description of an evidence-based interactive digital intervention for sexual health, including how behavior change techniques were translated into practice within the design of the MenSS website. Triangulation between a targeted literature review, expert workshops, and interviews with men ensured that a range of potential influences on condom use were captured.

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Introduction

Background

Sexually transmitted infections (STI) are a major public health problem, with high social and economic costs [1]. Diagnoses in England increased by 5% between 2011 and 2012, rising to 450,000 annual diagnoses of STI in 2013 [2]. Condoms are effective for prevention of STI; however, there are many barriers to successful use, for example decrease in sensation, interruption of sex, incorrect size or fit, or use of alcohol/recreational drugs [3,4]. Men have more power to influence use (given that it is them who wears the condom), so risk reduction and prevention efforts should be targeted at this group [3]. While there are many interventions aimed at improving sexual health for men who have sex with men (MSM), interventions specifically aimed at men who have sex with women (MSW) are lacking [5,6]. MSW report much less consistent condom use than MSM [7]; furthermore, men may be reluctant to discuss their sexual health with health professionals, partners or friends [8]. An interactive digital intervention may address this unmet need.

Interactive Digital Interventions for Sexual Health

Interactive digital interventions are computer-based programs that provide information and one or more of: decision support, behavior change support, or emotional support for health issues' [9]. Interactive digital interventions offer personally relevant, tailored material and feedback. Delivery via the Web and mobile devices offers private, anonymous, convenient access [10,11], which is particularly advantageous for sexual health content. Interactive digital interventions can potentially save clinic staff time as they require minimal delivery and training time compared to one-to-one structured discussions with patients, which is the current practice recommended in sexual health clinic settings [12]. Interactive digital interventions have been shown to have a moderate impact on condom use (d=0.259; 95% CI 0.201 - 0.317) [13], as well as increasing knowledge, self-efficacy and safer sex intention [9,13,14].

Behavior Change Theory

Interventions that make more extensive use of theory and involve a higher level of user involvement in development tend to be more effective [15,16]. Such interventions tend to be complex; if we are to learn about "what works", it is essential that such interventions are reported in enough detail to allow replication, implementation, and exploration of the mechanisms of action of an intervention [17]. A method developed for this purpose is to specify intervention content in terms of behavior change techniques (BCTs). BCTs are active components of an intervention designed to change behavior [18], and are applicable to a range of health behaviors [17]. A comprehensive theoretical framework which guides the intervention development process and suggests appropriate behavior change techniques (BCTs) is the Behavior Change Wheel (BCW) [19]. Intervention designers using this approach can select BCTs, considering the appropriateness for the population, setting, and intervention format. Despite using an established development framework, a creative leap is still needed to actually make an engaging, relevant intervention. User input is key to this process.

The Men's Safer Sex (MenSS) website aimed to increase condom use in MSW, and was designed following extensive fieldwork with service users, using the Behavior Change Wheel to guide the development process and select appropriate BCTs (for details regarding the development process, see Webster and Bailey [20]). The website was designed to be viewed on a tablet computer in the clinic waiting room, thus utilizing the time that patients are waiting to be seen. This paper describes the content of the MenSS website, and the rationale for it.

Methods

Procedure

Three sources of information were used to determine the intervention content, format, and style (see Figure 1): research literature, expert views, and interviews with the target population (men in sexual health clinics). This evidence was discussed and evaluated in two expert consultation workshops. The development process was iterative, seeking comment and refinement of prototypes of website content from service users. The intervention took the form of an interactive website, rather than a mobile phone app, due to issues of privacy (ie an app would need to be stored on a user's phone, which could be accessed by other people) and availability (ie not all users may own a mobile phone which could run an app).

Ethical approval was provided by the London – City and East NHS Research Ethics Committee (Reference number 13/LO/1801).

Figure 1. Flow diagram of data collection processes.
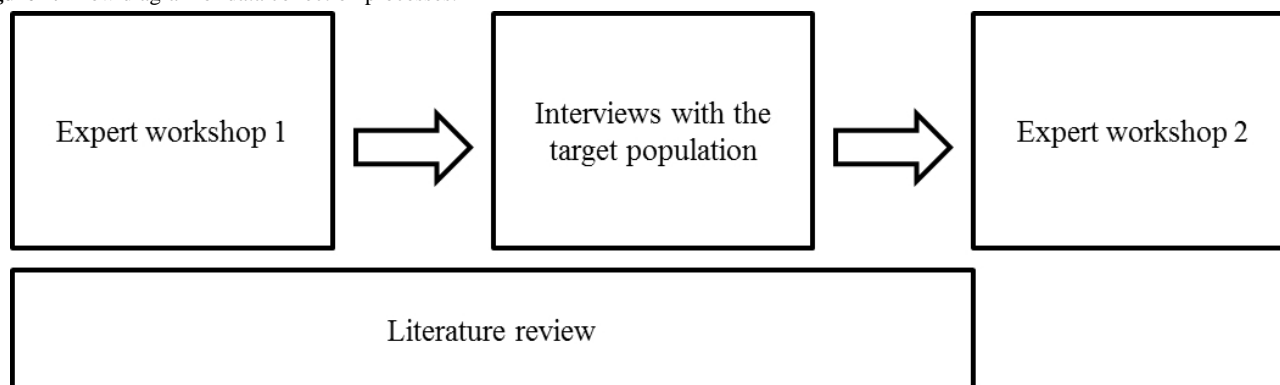
Research Literature

A targeted literature review identified research on men's barriers to condom use. Search terms included "men", "heterosexual", "condom", and "barriers". Databases searched included Web of Knowledge databases (including MEDLINE, EMBASE, and PsycINFO) and Google Scholar; selecting articles on risk factors for condom nonuse, theoretical correlates of condom use, and men's barriers to using condoms. The full text of 27 papers was included, consisting of reviews, qualitative studies, and cross-sectional, longitudinal, population based, and experimental designs [21,22,23,24,25,26]. The findings of these papers were summarized and synthesized into themes and subthemes (see Table 1).

Table 1. Barriers and facilitators for condom use identified in the literature.

Theme	Subtheme
Barriers to condom use	Reduced pleasure or sensation when condoms are used
	Condoms cause interruption of sexual activity
	Condoms reduce intimacy
	Judging the risk of STI using appearance or behavior
	Saying one thing and doing another – the intention-behavior gap
	Partner perceptions/influence
	Difficulty using condoms
	Having sex under the influence of alcohol
	Low perceived susceptibility to STIs
	Condom problems (e.g., breaking, discomfort)
	Lack of awareness about risk of oral sex
Facilitators to condom use	Condoms as prevention against pregnancy
	Reflection on past behavior as a motivator
	Awareness/close personal experience of pregnancy or STI
	Seeing condom use as an "essential behavior"
	Desire to avoid STI
	Dislike of visiting clinics
	Having condoms available
	Communication about condoms with partner
Theoretical/psychosocial predictors identified in quantitative studies	Norms surrounding condom use
	Attitudes towards condom use
	Self-efficacy about using condoms
	Perceived susceptibility/risk
	Perceived benefits of and barriers to using condoms
	Outcome expectancies

Expert Consultation

Two expert workshops were held to inform decisions, and to refine the focus, form and content of the intervention.

Attendees at the first (one day) workshop included 13 experts in the area of men's sexual health and/or behavior change, including sexual health clinicians, health advisors, researchers, academic professors, and technology experts. The workshop was facilitated by RW and JB. Participants were asked to select the most important barriers and facilitators to condom use, and potential approaches to changing behavior. Participants were asked to work in small groups (2-5 people) to discuss tasks, and then give feedback to the whole group, which was audio recorded. Participants were also asked to write down their own personal views on individual worksheets.

A second (half day) workshop was held to guide final decisions regarding the intervention design and content and to inform the creative process of designing intervention features. This workshop included five experts in the fields of sexual health, sex education, and Web development (two of whom also attended the first workshop). Informed by the findings from the interviews with male clinic attendees, participants were asked to prioritize potential intervention content, and discuss the potential intervention features.

Interviews With the Target Population

Semistructured qualitative interviews were conducted with 20 men who visited sexual health clinics, to gain information regarding barriers to and facilitators of condom use, potential intervention design, content, and mode of delivery.

Participants were recruited from two sexual health clinics in central London. Men attending sexual health drop-in clinics between February and April 2013, who were aged over 18 and had not been diagnosed with HIV or hepatitis, were eligible to participate. They were given a leaflet about the study and asked to approach the researcher if they wished to take part. Participants were aged between 20 and 52 (mean 31, SD 10.08); 7 identified as White British, 9 as Black (Black African or British), 2 as European, 1 as Chinese, and 1 as mixed ethnicity; 17 interviewees were currently sexually active with female partners, and 3 with male partners. The decision to focus solely on men who have sex with women (MSW) was made partway through the fieldwork process, hence a small number of men who have sex with men (MSM) were included in the sample. There was considerable overlap between MSM and MSW regarding the most prominent determinants of condom use. Some determinants were specific to MSM (e.g. a greater concern

about contracting HIV), and so these were disregarded when synthesizing evidence.

Participants were asked about their experiences and views on using condoms and their interest in a potential sexual health website. Interviews lasted between 30 and 60 minutes, and were audio recorded. The recordings were listened to, initial themes summarized, and then analyzed using qualitative thematic content analysis [27], allowing inductive themes to emerge and using categories provided by the BCW to organize them [19,28].

Results

Overview

The development process of the intervention content, with reference to behavior change theory, is described elsewhere [20]. Here we describe the content and functionality of the intervention website, by providing each intervention topic, the rationale for it, the relevant behavior change techniques and the subsequent content included in the intervention.

Barriers to Condom Use

Rationale

The interviews and literature review identified a multitude of potential barriers to condom use, and these barriers varied between individuals. Such barriers must be addressed in order to instigate behavior change; however, overwhelming all users with all content addressing all barriers may be off-putting. Interventions which are tailored to users are more likely to be effective [10].

BCTs

The relevant BCT was problem solving.

Content

On first using the website users were asked to select the reasons why they personally did not use condoms from 12 possible options, which were identified through the fieldwork (condoms too tight or uncomfortable; reduced pleasure; not knowing when or how to suggest it; being drunk or having taken drugs; losing erection; being in a relationship; difficulty stopping in the heat of the moment; partner not wanting to use condoms; partner might be offended; sex doesn't feel as good; STIs are easily treated; they often break or slip off). The homepage (see Figure 2) was then tailored to each individual user by ensuring that the content that addressed the barriers selected was displayed prominently in the centre of the page (although all users could access all content through the global navigation bar).

Figure 2. MenSS homepage with carousel of personalised tailored content.

Condoms: The Basics

Rationale

Although data from the workshops and interviews suggested that men feel competent in applying condoms, the literature review identified high rates of errors and problems in condom use [29,30].

BCTs

Relevant BCTs included instruction on how to perform the behavior and demonstration of the behavior.

Content

This section included a short video demonstration and a click-through slide show, which provided advice about using condoms correctly, highlighting the key steps in condom use and areas where people often make mistakes (see Figure 3).

Figure 3. Condoms: The Basics – skills in correct condom application.
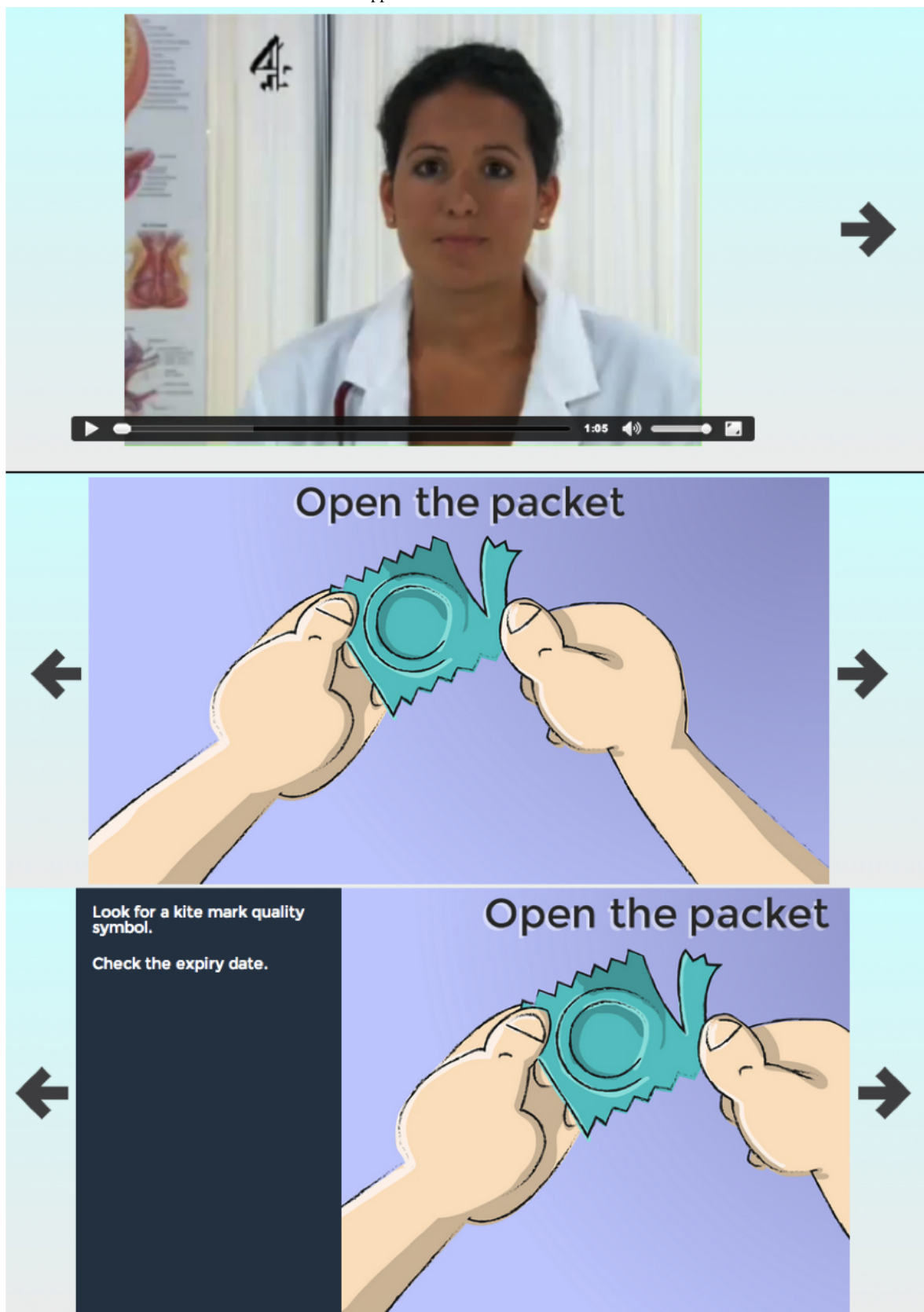
Condoms: Tailored for You

Rationale

Evidence from our qualitative work and the literature suggested that condom size and type impact strongly on acceptability of condoms, with poorly fitting or thicker condoms being viewed more negatively. Incorrect condom size was also related to problems such as breakage [31].

BCTs

The relevant BCT was problem solving.

Content

The intervention website aimed to educate men about different sizes and types of condom, using a tailored feedback activity. In this activity, users were asked to identify problems they had with condoms, and then offered tailored advice about and recommendations for condom types to help address those problems (see Figure 4). For example, men suggesting that condoms were uncomfortable, small, or problematic due to breaking were offered advice about larger types of condoms. The format of this activity was similar to the "Barriers to condom use" activity (above); but focused on problems with the actual condom (rather than problems surrounding condom use in general), and gives specific condom-related feedback and recommendations.

Figure 4. Condoms: Tailored for you – tailored feedback on selected barriers to condom use.
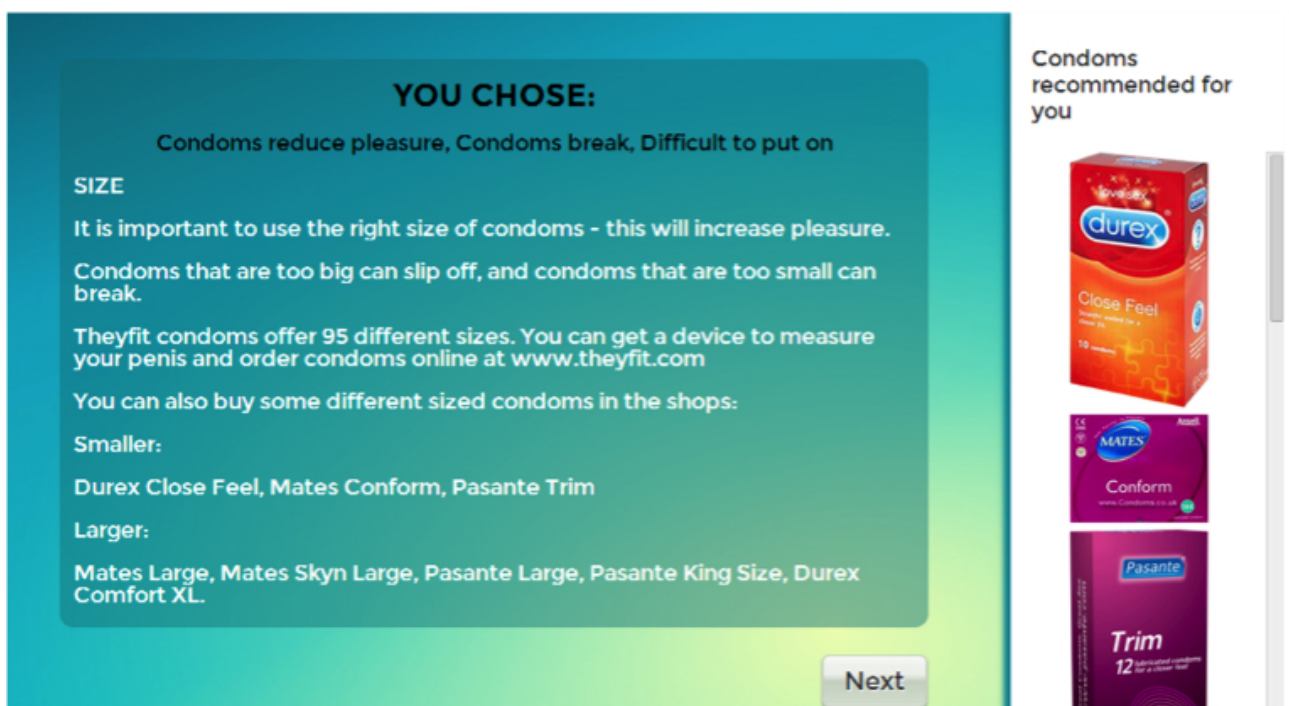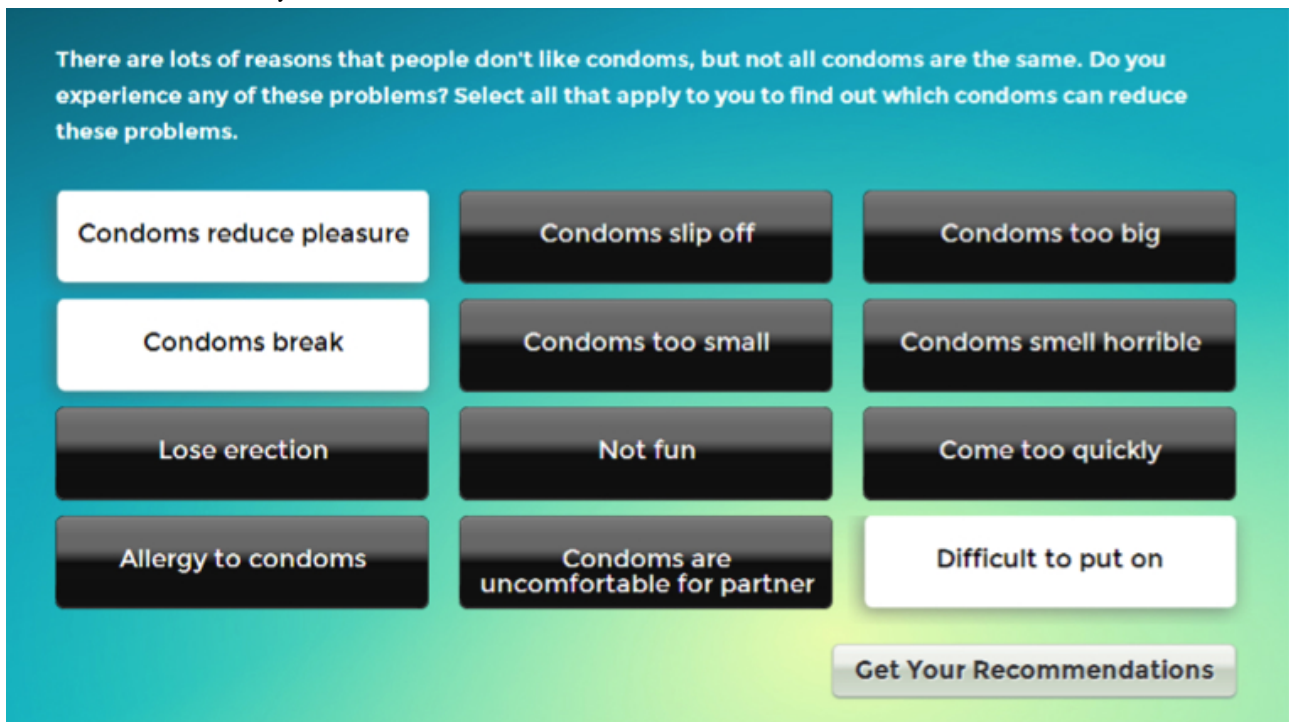
Pleasure

Rationale

All data sources indicated that the belief that condoms reduce the pleasure of sex is a very important and common barrier to condom use.

BCTs

Relevant BCTs included the use of nonspecific incentive, restructuring the physical environment, instructions on how to perform the behavior, behavior substitution, information about health consequences, focus on past success, distraction, behavioral practice/rehearsal, anticipated regret, information about social and environmental consequences, and social incentive.

Content

This section incorporated written advice and videos. It gave advice about how to improve pleasure with condoms, how sex with condoms might be preferable to sex without condoms, for example by reducing worry (nonspecific incentive), how there are types of condom that may be more pleasurable, and how to enjoy nonpenetrative sex (behavioral substitution). BCTs were conceptualized within written text; for example, the "anticipated regret" technique encouraged users to focus on avoiding the worry and hassle that may follow an episode of unprotected sex; the "focus on past success" technique was incorporated by encouraging men who had previously had problems with loss of erection to focus on occasions when they had not lost their erection.

STIs: Are You at Risk?

Rationale

All the data sources suggested that men were aware of the benefits of using condoms and of some of the risks of unprotected sex [21]. However, our interviews highlighted a number of widespread incorrect beliefs about the risk of STIs (e.g. partners who are known to them or "seem clean" are viewed as less risky).

BCTs

Relevant BCTs included receiving information about health consequences and the experience of vicarious consequences.

Content

The intervention included two interactive activities addressing STI risk, emphasizing that risk levels cannot be judged (see Figure 5). First, in "What's the risk of STIs?" a quiz presented facts and figures regarding STIs and their transmission (e.g. the number of people with undiagnosed HIV). This conceptualized the BCT of "information about health consequences" in an interactive and visually appealing manner. Second, in "Are relationships safe?" two animated diagrams demonstrated the way that STIs may spread within a network, common methods of transmission that people may not be aware of (e.g. oral sex), and how relationships may not be "safe". This activity encompassed the BCT of "information about health consequences", and also used "vicarious consequences", by demonstrating the impact of risky sexual behaviors on others.

Figure 5. STIs: Are you at risk? – infographics illustrating potential risks of STI.

What Women Think

Rationale

Both our interviews with men and the literature [24] identified fear of partners reacting negatively to suggestions of condom use as an important barrier. The literature also suggests that self-concept and personal values are related to carrying and using condoms [24,32]; if a healthy behavior is consistent with one's identity, one may be more likely to perform the behavior [33]. Our workshops and interviews identified fostering a sense of responsibility towards others as a potentially important factor in condom use.

BCTs

BCTs considered relevant included receiving information regarding others' approval and social incentive.

Content

This section included articles and videos portraying women as approving of men taking the responsibility for condom use and women not being offended by the suggestion of condoms. It also provided advice on responding to women who appeared to be offended. BCTs were conceptualized in written text and in videos; for example, "social incentive" was offered by suggesting that women would view men positively if they suggested condom use.

Slip-Ups

Rationale

Pleasure or lust (being caught "in the heat of the moment") was a widely quoted reason for non-use within our interviews with men and in the literature. All data sources identified alcohol as a strong barrier to condom use. The importance of carrying/availability of condoms has been related to condom use in the literature, and lack of availability was identified as a barrier by experts in the workshops.

BCTs

A wide number of BCTs were used here, including problem solving, verbal persuasion about capability, information about health consequences, instruction on how to perform a behavior, information about antecedents, restructuring the physical environment, anticipated regret, mental rehearsal of successful performance, information about social and environmental consequences, and nonspecific incentive.

Content

This section included articles and videos giving specific advice about how to overcome barriers due to the "heat of the moment" and intoxication by discussing condoms with a partner in advance (instruction on how to perform the behavior), considering potential regret (anticipated regret), and avoiding sex when under the influence of alcohol (information about antecedents). It also provided advice regarding making condoms available (e.g., carrying them, having them near the bed) (restructuring the physical environment). Again, BCTs were conceptualized in written text; for example, the "verbal persuasion about capability" technique included messages that men would be able to use condoms, despite high levels of arousal or intoxication. The "nonspecific incentive" technique was incorporated by telling users that if they wait to have sex when they are not intoxicated, they may perform better, please their partner more, and get a better reputation for being a good lover.

STIs: The Facts

Rationale

In the qualitative interviews, men showed a lack of concern for catching STIs, as they did not feel that they had substantial negative consequences for men.

BCTs

The relevant BCT in this case was information about health consequences.

Content

Users were presented with common misconceptions or questions about STIs and their transmission (e.g. "STIs are easily treated, aren't they?"), which could be clicked to reveal the answer and some brief information.

Communication

Rationale

While the literature [21] and the experts in our workshop suggested that difficulties in negotiating condom use were a more salient barrier for women, evidence from the interviews with men suggested that for some this was an issue, and for most men the opinions of their partner were important when deciding whether to use a condom or not.

BCTs

Relevant BCTs included instruction on how to perform the behavior, information about social and environmental consequences, information about others' approval, information about health consequences, and verbal persuasion about capability.

Content

This section offered information about specific strategies for suggesting, discussing, and negotiating condom use. BCTs were conceptualized in written information; for example, "information about social and environmental consequences" included giving advice that talking about condoms before sex would mean both partners can relax and enjoy it, rather than worrying about STIs or pregnancy; "information about others' approval" included reassurance that most women would not be offended by the suggestion of condom use.

Reminders and Plans

Rationale

Based on evidence from the literature [34,35] and our workshops, goal setting was identified as an important method of encouraging behavior change.

BCTs

Relevant BCTs were goal setting (behavior), action planning, and reviewing behavior goals.

Content

In each section of the website, users were offered goals to set which related to the website content (see Figure 6). When selected, these goals populated users' own personalized "Reminders and plans" page. Users could opt to receive a reminder by email at a specific time, set time-limited goals (e.g. "I will purchase my recommended condoms" by a selected date), or choose event-specific goals, by forming an implementation intention [36] ("if-then plan"), identifying a potential situation where condom use may be unlikely, and then selecting a response to that situation.

Figure 6. Reminders and plans feature.

Strategies for Engagement

Rationale

Whilst access to the website was provided at baseline in the clinic setting, the website was extremely comprehensive, and so most users would not have time to explore all content in one visit. Furthermore, the goal setting tasks were designed to support change over time, through users returning to the website to review their goals. It was therefore important to encourage repeated visits to the website. Increased engagement with an interactive digital intervention can lead to increased effectiveness [37]. Encouraging users to engage in interactive digital interventions, particularly over a long period of time, is notoriously difficult [38]. Email prompts can be used to increase engagement with the intervention [39].

BCTs

Relevant BCTs included the use of prompts and cues, information about health consequences, and reviewing behavior goals.

Content

Users were sent monthly emails, prompting them to visit the intervention website again, in the hope that they would explore content that they had not previously viewed. These engagement emails contained "teasers" regarding website information and links to the website (e.g. "Do you know how many people have Chlamydia? Find out here"). In addition, if users set goals or implementation intentions within the website, they could select the option of being reminded via email. These emails asked users if they had achieved their goal, and prompted them to return to the website to review their goals.

Discussion

Principal Findings

This paper provides a description of the content for an interactive digital intervention aimed at increasing condom use in men, and the rationale for it. Triangulation between a targeted literature review, expert workshops, and interviews with the target population, all led by a multidisciplinary team, ensured that a range of potential influences on condom use were captured and that feedback to men on barriers to condom use was relevant to them. The resulting intervention is extensive, tailored to individual needs, and targets a wide set of influences on sexual behavior. This is in line with recommendations that sexual health interventions should use a holistic approach to sexual health and well-being [40].

As with many complex interventions, the MenSS website contains multiple components, targeting a number of influences on behavior. It can therefore be difficult to determine which part(s) of the intervention are effective, via what mechanisms. Online interventions offer the possibility of easily monitoring patterns of intervention use, including its component parts, which can assist in the analysis of the mechanisms of action of an intervention. Clearly describing the intervention aims and content can assist in this analysis. BCTs provide a standardized method for this process of describing intervention content.

The use of standardized BCTs to specify the intervention content provided two advantages. First, the BCTs provided ideas for website features and health promotion messages (so the authors did not start with a "blank canvas"). Second, the BCTs were used to specify the content in standardized terms to facilitate replication, make judgments regarding quality, and allow comparisons with other interventions [18]. Translating BCTs into interactive website features can be a difficult process, requiring a certain level of creativity. Given that the content of complex interventions is often not described in detail [41], building a repository of examples of such features would be a valuable resource for intervention designers.

Limitations

The study had some limitations. For example, while we collected detailed data to specify intervention content, the literature review was targeted, rather than fully systematic, due to time and resource constraints. This means some relevant evidence may have been missed. However, the inclusion of a number of systematic reviews within the literature review mitigates this concern. A second limitation is that all men interviewed during the development process were sampled from sexual health clinics within inner London, thus potentially limiting the transferability to other populations and settings. However, the findings from our literature review confirmed the importance of the emergent themes from the interviews.

Conclusions and Future Work

This paper provides a detailed description of an evidence-based interactive digital intervention for sexual health, including how BCTs were translated into practice within the design of the MenSS website. It is hoped that this will assist intervention developers in their development work and reporting in terms of BCTs. A pilot study is currently underway to determine the feasibility of evaluating the intervention in a full scale randomized controlled trial.

Conflicts of Interest

None declared.

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Abbreviations

BCT: behavior change technique
BCW: behavior change wheel
IDI: interactive digital intervention
MenSS: Men's Safer Sex
MSM: men who have sex with men
MSW: men who have sex with women
STI: sexually transmitted infections
HIV: human immunodeficiency virus

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<u>Original Paper</u>

Development of Motivate4Change Using the Intervention Mapping Protocol: An Interactive Technology Physical Activity and Medication Adherence Promotion Program for Hospitalized Heart Failure Patients

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Abstract

Background: It is important that heart failure (HF) patients adhere to their medication regimen and engage in physical activity. Evidence shows that adherence to these HF self-management behaviors can be improved with appropriate interventions.

Objective: To further promote medication adherence and physical activity among HF patients, we developed an intervention for hospitalized HF patients.

Methods: The intervention mapping protocol was applied in the development of the intervention. This entailed performing a needs assessment, defining change objectives, selecting determinants and strategies, and developing the materials.

Results: The resulting intervention, Motivate4Change, makes use of interactive technology and provides HF patients with personalized feedback and advice. Specific change objectives were defined. The relevant behavioral determinants for the physical activity program were practical knowledge on physical activity performance and self-efficacy for, and perceived benefits of, physical activity. For medication-taking, the selected determinants were practical knowledge on medication-taking, perceived barriers to medication-taking, beliefs about the necessity and harm regarding the medication prescribed, and beliefs about overprescribing and harm of medication in general. The change objectives and behavior change determinants were translated in feedback and advice strategies in an interactive technology program that included tailored feedback and advice, and role models in videos in which the behaviors and overcoming barriers were demonstrated. Relevant stakeholders were involved in the interventions development process. The intervention was pretested among HF patients and adjustments were made accordingly.

Conclusions: The interactive technology physical activity and medication adherence promotion program for hospitalized HF patients was systematically developed using the intervention mapping protocol and was based on the available theory and evidence regarding HF self-management behavior change. The intervention's efficacy is yet to be determined in evaluation research.

Introduction

Background

Heart failure (HF) is a chronic condition, affecting primarily older patients [1]. Although HF is usually irreversible, it can be effectively managed with medication and behavioral treatment, including physical activity [2]. HF medications have proven effective in various clinical trials [2], and medication adherence among HF patients is related to event-free survival [3]. However, in studies that use objective measurement techniques, low medication adherence rates are demonstrated [4]. The physical activity recommendation for HF patients specifies performance of at least 30 minutes of moderate intensity physical activity daily [5] . Performance of physical activity among HF patients was found to be related to reduced readmission rates in contrast to the other studied nonpharmacological self-care behaviors (daily weighing, fluid restriction, low-salt diet) [6]. Despite the potential benefits, HF patients report insufficient rates of physical activity [7,8]. Interventions that promote medication-taking and physical activity among HF patients are therefore warranted.

Interactive technology is a promising channel for delivery of patient education and health promotion interventions since it may increase interest and recall of information. Using auditory, visual, and interactive learning strategies, knowledge can be transferred to patients with various learning capabilities [9]. Due to constraints of the medical system, currently not all patients may be provided with education, and interactive technology solutions are a feasible alternative [9]. HF nurses name various barriers to provision of patient education in the hospital, including insufficient teaching materials [10]. So far, face-to-face or telephone-based education and counseling programs for HF patients demonstrate promising results [11-13], but interactive, technology-based education and counseling interventions for HF inpatients are scarce. A CD-ROM-based educational program has been developed for HF patients for the hospital setting [14] focusing on providing generic information to patients by displaying animations, photos, and voice-overs. This program has demonstrated similar but not superior results as standard education [15] and patient acceptance of the technology [16]. It could be that addressing patient motivation to engage in the behaviors and tailoring the information to individual needs and barriers may be beneficial in comparison with standard education, and interactive technology provides the opportunity to do that.

When designing an intervention, the setting and timing for intervention delivery should be carefully considered. Hospitalization has been referred to as a teachable moment [17] because patients may be more motivated to change their behavior soon after being confronted with their disease. Moreover, many patients can be reached during hospitalization with relatively little effort (as opposed to, for instance, a home visit by a community nurse). An HF nurse typically provides education in the hospital to patients before their discharge from the hospital [18]. Previous work suggests that hospital nurses may not always provide effective education, because of lack of time and/or training, that individualizing content to patients may be one particular area in which nurses could use support, and that nurses do not have sufficient materials (teaching aids) to support them [10]. This suggests that although there is potential to reach many patients in the hospital, the education being provided by hospital nurses may not be optimal.

Interactive technology health behavior promotion interventions hold the potential for individualizing content, as the expertise of the health educator is documented in the interactive program and can be used by nurses to supplement their education. With an interactive technology program, patients can use the entire hospitalization period to become informed regarding their self-care because the nurse does not necessarily have to be present, thereby increasing the learning potential. In the current situation, patients are educated by HF nurses about self-care typically just before they are discharged from the hospital and need to start performing the behaviors when they at home. The transition from the hospital to the home environment is reported to be a point of confusion and miscommunication [19], and interventions that assist in supporting learning and reducing the potential confusion are desired.

Objectives

We aimed to develop an individually tailored interactive technology program for the promotion of medication adherence and physical activity among HF patients, for delivery in the hospital setting. The goal of the program, which we named Motivate4Change, is to educate and motivate patients to engage in physical activity and medication adherence after their discharge from the hospital. To increase the level of confidence that the intervention we develop would be efficacious, we worked according to the intervention mapping protocol. The intervention mapping protocol is a stepwise method (Figure 1) used to develop interventions systematically using relevant theory and evidence [20]. By going through the steps and creating matrices, decisions are made regarding the specific behavioral change objectives and how to achieve these changes by identifying theory and evidence-based strategies and behavior change techniques. This allows targeting the behavioral determinants and using behavior change strategies that are most likely to affect the desired outcomes. In the current paper we report on the design of Motivate4Change using an intervention mapping approach.

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Figure 1. The intervention mapping protocol. Source: Bartholomew et al (2001) [21].
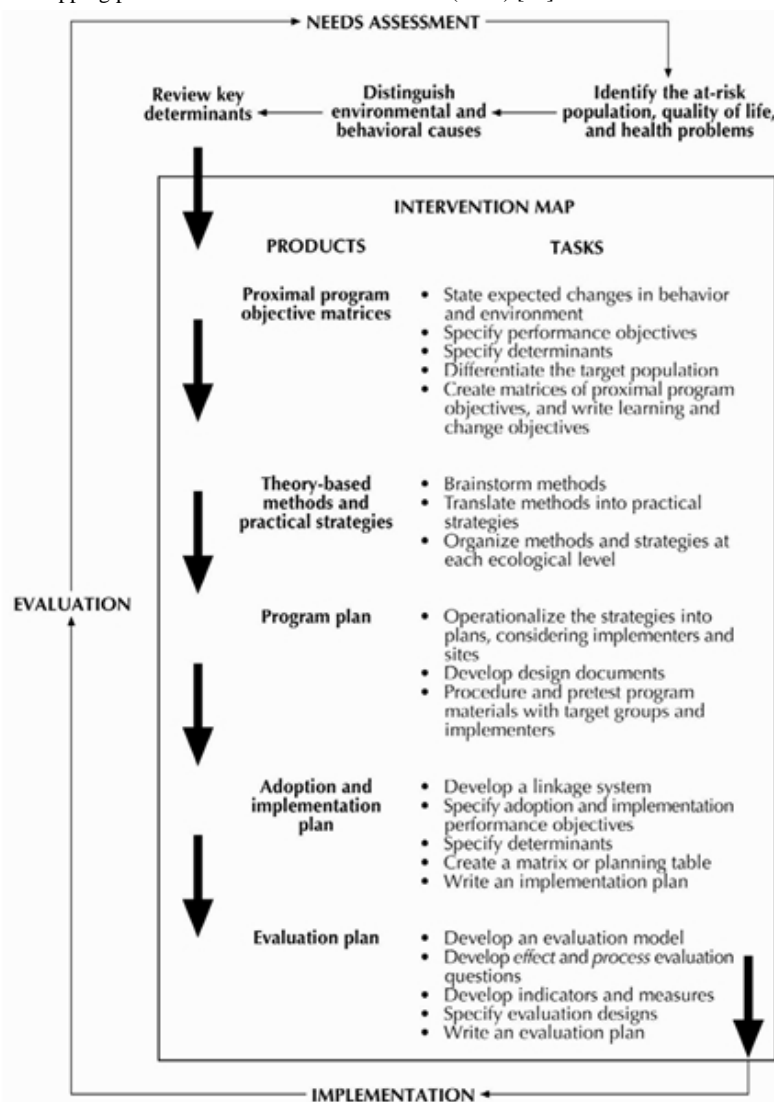
Methods

The intervention mapping protocol specifies six steps for the development of theory and evidence-based health promotion interventions [21]. We implemented the first four steps in the development of Motivate4Change, including (1) the needs assessment, (2) the definition of the performance objectives, selection of behavioral determinants, and definition of matrices of change objectives, (3) selection of methods and behavior change strategies, and (4) the translation of these into an actual intervention program. To define the program objectives, relevant literature and medical guidelines were consulted. This led to a definition of the performance objectives. To define the important and changeable determinants for these performance objectives, systematic literature reviews were conducted [22,23]. Based on the performance objectives and selected behavioral determinants, matrices of change objectives were created. Strategies for behavior change were selected by consulting literature and behavioral theories to identify strategies that target behavioral constructs. After these steps were taken, the intervention program and materials were devised. These included the

program structure and sequence, assessments, tailored messages, and functional research prototype of the program.

Results

Step 1: Needs Assessment

Management of Heart Failure

Effective management of HF is needed to curb adverse outcomes. Reported HF prevalence rates in men are 8 per 1000 at age 50 to 59 years, increasing to 66 per 1000 at ages 80 to 89 years (similar values (8 and 79 per 1000) were noted in women) [24]. Poor health outcomes include high mortality [25], frequent acute episodes leading to hospital readmissions [26], and low levels of quality of life [27] and wellbeing [28] for patients and caregivers. In addition, the costs of HF are high, approximately 1%-2% of the total health care budget in developed countries, primarily due to the readmissions [29]. The management of HF primarily includes medication prescriptions and self-care behavior although in some cases surgery may be possible [2].

Promotion of Medication Adherence

Evidence-based pharmacological treatment is common practice in the management of HF. Commonly prescribed drugs include diuretics, angiotensin-converting enzyme inhibitors, and beta blockers, among others [30]. Medication adherence, when measured with the Medication Event Monitoring System (MEMS), was found to be related to event-free survival [3]. However, for the medications to be effective, patients need to take them as prescribed. Although research on medication adherence using self-report measures demonstrates that adherence to HF medication is adequate [8], studies that use more objective measurement techniques such as claims data demonstrating prescription fillings [31,32] and MEMS data [4] demonstrate low adherence rates and thus room for improvement.

Promotion of Physical Activity

It is recommended that HF patients perform moderate intensity physical activity for at least thirty minutes daily [5]. There is evidence that performance of physical activity among HF patients can lead to a reduction in readmission and mortality rates [33]. Despite the promising effects, numerous studies show that adherence to physical activity recommendations is inadequate among HF patients [2,7,34,35]. In addition, health care providers do not always promote physical activity among HF patients. Reasons include lack of knowledge on behalf of the health care providers and financial reasons [36]. Education on self-care behaviors, including physical activity, is often not provided for hospitalized patients due to lack of time [18].

Needs in the Hospital Setting

As previously mentioned, Motivate4Change was developed for delivery in the hospital setting, although patients would perform the self-care behaviors after they are back at home. As such, we assessed the needs of patients during hospitalization, when they would be engaging in the intervention. Patients' needs for completion of an interactive technology health behavior promotion program may be different in the hospital setting than in the home setting. The needs assessment for the hospital setting revealed that the short length of stay and high symptom acuity level [10] are challenges that are specific to the hospital setting. These challenges could lead to patients experiencing negative emotions and feeling less focused and more confused, in addition to having only a short period of time to engage in the intervention. Based on these identified issues, specific requirements for the intervention were defined including a short length for the intervention program and clear and simple content and user interface. An intervention meeting these requirements was considered more likely to be suitable in light of the state of confusion and symptom acuity that patients experience in the hospital.

Based on the needs assessments, we defined the aim of the intervention. For a health behavior promotion intervention provided in the hospital setting, the behavioral objectives can only be achieved some time after the provision of the intervention; it is unlikely that patients will take their medications independently or perform physical activity during hospitalization. Therefore, the aim of Motivate4Change was that "patients have the *intention* to take their medications as prescribed and increase the amount of physical activity they perform." According to the theory of planned behavior (TPB) [37], intentions to perform a behavior are the closest factor to actual behavioral performance. We found in the scientific literature that many patients perform very little physical activity, and this information was also verified by a cardiologist and a HF nurse. Based on their input, we defined the physical activity aim loosely and not specifically according to the recommendation for this patient population because for patients who perform very little physical activity, an increase to the recommended level of at least 30 minutes of moderate intensity activity daily was perceived an unrealistic aim for a brief intervention, to be delivered only during hospitalization.

Step 2: Definition of Performance Objectives, Selection of Behavioral Determinants and Creation of Matrices of Change Objectives

Definition of Performance Objectives

Performance objectives are the specific cognitions and/or actions required towards intentions for behavior change. Complex behaviors often need to be changed by addressing their components and making a change in each of these components. The performance objectives (Textbox 1), corresponding to the program objectives mentioned above, were cognitive because the program objective was cognitive.

Textbox 1. Performance objectives for intentions to take medications as prescribed and to perform more physical activity.

Performance objectives for intentions to take medications as prescribed:

- Patients describe how to take their medications

- Patients identify solutions to their barriers to taking medications

- Patients specify counterarguments to their concerns to taking medications

- Patients specify reasons why their medications are necessary

Performance objectives for intentions to perform more physical activity:

- Patients describe how to perform physical activity

- Patients identify solutions to their barriers to performing physical activity

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Selection of Behavioral Determinants

Health promotion interventions should address the most important and modifiable behavioral determinants so that the behaviors are influenced and the health problem diminished [20]. The identification of behavioral determinants and the translation of these determinants into intervention strategies and techniques should be guided and informed by behavioral theories as well as scientific evidence. Since the targeted delivery setting was the hospital, determinants had to be changeable in a brief intervention in the hospital setting. Theoretical health behavior models and scientific literature were consulted in the selection of determinants.

Theoretical Indications

After reviewing prominent health behavior theories, two were selected to be used for guidance in the selection of determinants: TPB [38] and social cognitive theory (SCT) [39]. These were selected in part because they describe cognitive determinants of behavior that were deemed changeable in a brief intervention and are widely used in the design of new health promotion interventions [40].

The concept of perceived self-efficacy, or one's confidence in being able to perform a specific behavior, is central in SCT [41]. Another key concept is outcome expectations. SCT postulates that behavioral motivation is generated through cognitive representations of future outcomes of performing the behavior. According to TPB, three cognitive factors influence intentions for behavior: behavioral attitude (ie, one's beliefs regarding the behavior), subjective norms which results from someone's normative beliefs, and perceived behavioral control, which is based on control beliefs and considered similar to the self-efficacy concept of SCT.

Scientific Literature

We conducted two reviews in which the determinants of self-care [22] and adherence to medication [23] were investigated. Self-care consists of multiple behaviors including self-care management; self-care maintenance; sodium, fluid, and alcohol intake restriction; physical activity; smoking cessation; monitoring signs and symptoms; and keeping follow-up appointments. Overall, important determinants were perceived benefits and barriers (specifically related to sodium intake restriction) and type-D personality (specifically related to keeping follow-up appointments). However, we found inconsistent evidence of any of the determinants investigated in the included studies in relation to increase in physical activity. Having been hospitalized in the past was found in the review to be related to higher adherence to medication. Since we found no evidence of determinants related to increasing physical

activity for HF patients and past hospitalization was not a determinant that we could easily address in our short intervention, we had to expand our search and look for determinants of increasing physical activity and medication adherence in general.

Previous work [42,43] outlines a wide range of potential barriers to medication adherence, including aging-related factors such as cognitive and physical declines, social and economic factors [43], and patients' health condition and treatment [42]. Most of these determinants were deemed not suitable for a brief intervention in a hospital setting because more time and effort would be required to observe a change in them. Beliefs about medications, which are more suitable to target within a brief intervention, are also important determinants of medication adherence [44]. Beliefs may be about side effects of medications, efficacy of medications as well as negative views about medication in general. Knowledge and understanding may also be important for medication adherence because HF patients are prescribed an average of eight different medications and they usually need to take medication more than once per day [45].

Self-efficacy is an important determinant of physical activity in the general population [46] and among older adults [47,48]. There is also evidence that targeting self-efficacy in interventions is an effective means to increase engagement in physical activity [49]. Specific barriers for physical activity that HF patients may feel a lack of confidence overcoming include physical symptoms [50], environmental influences (eg, weather, resources), expectations of others (eg, encouragement of relatives, interest and advice of others), mental outlook (eg, no self-identification as active, lack of motivation for physical activity) and fluctuating health (eg, HF symptoms) [51].

In sum, three determinants of medication adherence were selected, which were deemed important and suitable for targeting in a brief intervention: practical knowledge, self-efficacy for taking medication, and beliefs about medication. Two determinants for physical activity were selected: practical knowledge and self-efficacy to perform the activity.

Creation of Matrices of Change Objectives

Next, performance objectives for the program objectives were created. These are a set of subcognitions, and a change in those would lead to a change in the program objective (Table 2). Finally, the selected determinants and the performance objectives were integrated in matrices of change objectives (Table 2), which demonstrate what is necessary in terms of behavior or cognition to achieve the performance objectives. The change objectives were used to develop the content of the intervention materials.

Table 2. A selection of matrices of change objectives for the five performance objectives.

Performance objective	Knowledge	Self-efficacy	Beliefs
Patients are willing to take their medications	Patients describe the prescriptions of the doctor	Patients express their confidence they are able to follow the doctor's prescriptions	Patients believe that taking the prescribed medications correctly can make them feel better
	Patients describe how they should take their medication	Patients express their confidence that they can take their medications every day	Patients believe that taking medication every day is necessary for them
Patients identify solutions to their barriers to taking medications	Patients recognize the side effects of medications	Patients express their confidence about what to do if side effects occur	Patients believe that if they have side effects this does not mean they should stop taking medications without a consultation
	Patients know which types of memory aids are available	Patients know where they can acquire memory aids	Patients believe that memory aids can be effective in helping them take their medications
Patients are willing to perform physical activity	Patients know they should perform physical activity on most days of the week	Patients identify activities that are enjoyable to them, which they are confident they can perform	
Patients describe how to perform physical activity	Patients know they should perform moderate intensity physical activity	Patients describe the 'talk test' for measuring intensity of physical activity	
Patients identify solutions to their barriers to performing physical activity	Patients list appropriate activities when the weather is bad	Patients express confidence that when experiencing breathlessness or fatigue, they can rest and perform activity again when feeling better	

Step 3: Selection of Strategies for Behavior Change

Tailored Health Communication

Health information which is tailored to patients' relevant psychosocial characteristics has been found to be more motivating than generic health information [52]. Tailoring can be achieved with a computer system and provided through interactive technology and is typically done by assessing patients on relevant characteristics and providing information according to the assessment results [53]. Some of the reported mechanisms for the superior efficacy of tailored information over generic information include personalization of the information, better exposure to the information, more intensive cognitive processing, greater relevance of the information provided to the individual receiving it, and self-evaluation properties of the feedback received [54]. The information in Motivate4Change was tailored to individual patients based on the behavioral determinants identified in the previous step. Specifically, the information was tailored to individual knowledge levels and existence of barriers which may reduce self-efficacy; in the medication adherence module, the information was also tailored to problematic beliefs about medications. Therefore, patients received personalized written and video messages [55].

Instruction

Instruction on how to perform the behavior, including provision of information about the behavior and expected outcome was another strategy used to improve self-efficacy and knowledge. In addition, instruction was provided regarding solutions to overcome barriers. It has been shown that both active and inactive older adults have barriers for performing physical activity, but active older adults recognize solutions to overcome

their barriers while inactive older adults do not recognize solutions [56].

Vicarious Experience

Self-efficacy, as outlined by SCT, can be promoted through three channels: performance accomplishments, vicarious experience, and verbal persuasion [41]. For hospitalized HF patients the first does not apply, because they do not perform the behaviors while in the hospital. Vicarious experience includes seeing others perform the behaviors, leading people to persuade themselves that if others can do it, they should be able to at least partially achieve it too [41]. This strategy was incorporated in the current intervention with a video displaying an actor playing the role of a typical HF patient successfully performing physical activity and taking medication.

Persuasion Techniques

To persuade patients to perform the behavior, we incorporated references to authority [57] whereby people are persuaded to perform a behavior because an authority figure recommends performing this behavior. In Motivate4Change, a professor in cardiology appeared in the videos and emphasized the importance of physical activity and medication adherence for HF patients.

Empathy

In order to increase patient acceptance of the messages being communicated, empathy was an additional strategy used in the current intervention. Hospitalization may be a difficult time for patients [58], and therefore empathic communication was deemed suitable. Also, some of barriers that patients were asked about may be sensitive and/or difficult for patients, and it was therefore appropriate to address them with an empathic tone.

Empathy is one of the main principles in motivational interviewing [59]. Empathic sentences were incorporated in the messages, such as "Many patients feel that…" or "It is understandable that…"

Step 4: Producing Program Components and Materials

In this step the program plan was developed, including the scope and sequence, and the program materials were formulated. Relevant stakeholders were involved in the development of the intervention materials, including cardiologists, HF nurses, and patients (Figure 2). The user interface was designed taking into account the presumed needs of the target group in terms of usability (eg, having a clear indication how to go forwards and backwards in the program, having a large font size), and usability sessions were conducted, leading to an identification of issues which were addressed in the next version. In preparation for the usability session, observation sheets were prepared in which various relevant usability attributes such as learnability, efficiency, and simplicity were specified; for each attribute specific indicators were specified, which could be observed and recorded by the researcher. The researcher observed patients while they were using the research prototype and took extensive notes while completing the usability sheets.

The messages which were created for Motivate4Change addressed the listed determinants and corresponding change objectives. Messages were reviewed by nurses to check for medical correctness and suitability for patients. Feedback sessions with patients took place, in which patients were asked to read the message texts out loud so the researchers could observe and note difficulties. Patients were asked to share their opinions on the content, and the feedback was incorporated (Figure 2). Specifically, based on patient input, messages related to specific barriers to perform the health behaviors were removed or added where appropriate. For example, although at first a message relating only to side effects as a barrier for patients was formulated, it was found in the feedback sessions that medications' desired effects can also be a barrier for

patients, as is the case with frequent urination when taking diuretics in order to reduce fluid buildup. Based on the literature, finding time to perform physical activity was identified as a barrier, but HF patients who participated in the feedback sessions remarked this is not a barrier for them, and the relevant message was thus removed. A cardiologist was asked to provide feedback on the final program and make sure the content was correct from a medical perspective.

The resulting program included an introduction, which included an explanation of the intention of the program and a summary of the key take-away messages in relation to medication adherence and physical activity for HF patients, and two modules, the first on medication adherence and the second on physical activity (Figure 3). Medication adherence was deemed more urgent to address based on input from clinicians, and it was therefore placed first. The medication adherence module included three parts; one which was meant to increase practical knowledge on taking HF medications, another to assess barriers to taking HF medications and provide solutions to identified barriers, and a third part to assess problematic beliefs relating to medications and providing messages to address those problematic beliefs. The physical activity module had two parts; one aiming to increase practical knowledge on performing physical activity and the other another assessing barriers to performance and providing solutions to identified barriers. Within modules, patients are presented with videos followed by assessments and immediate tailored feedback messages (Figures 4 and 5), depending on their answers. The videos were from the Philips Motiva telehealth system.

Assessments for tailoring the content were based on the Beliefs about Medication Questionnaire [60] and the Self-Efficacy to Regulate Exercise Questionnaire [61]. The scales in the original questionnaires were changed to dichotomous scales, and two tailored messaged were constructed for each question. We added and removed items based on input from patients and professionals.

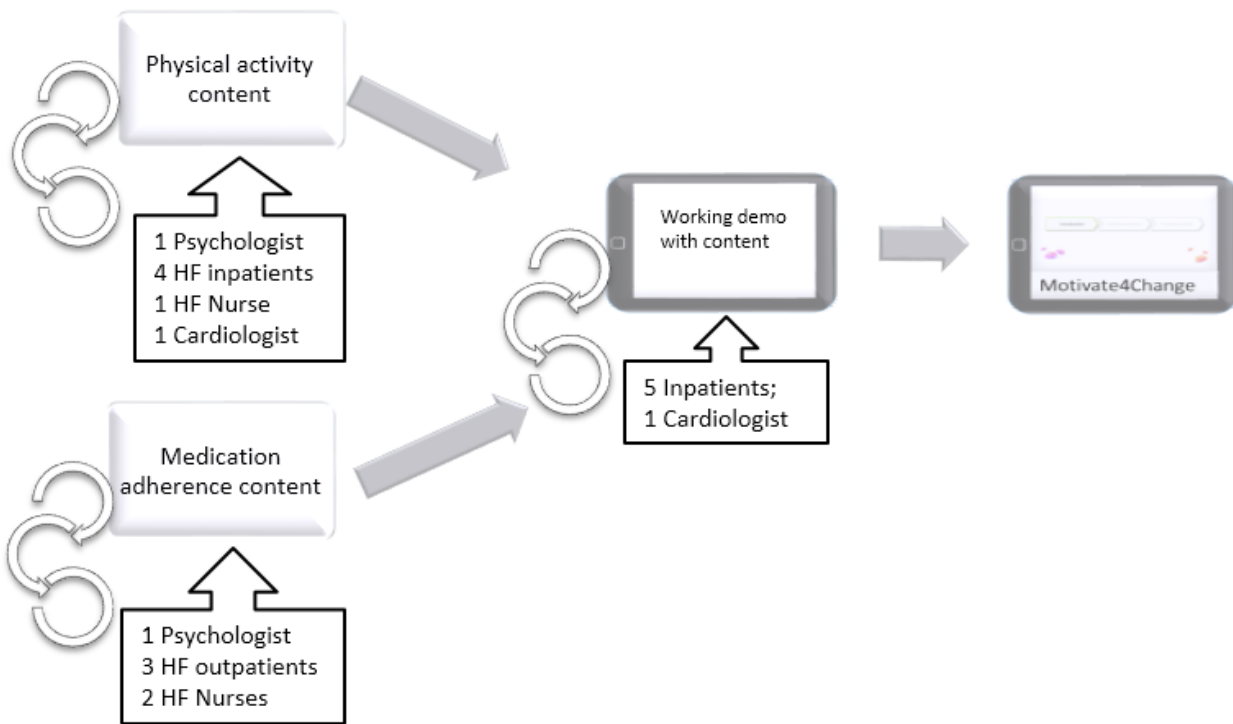**Figure 2.** The iterative process of the intervention content development.

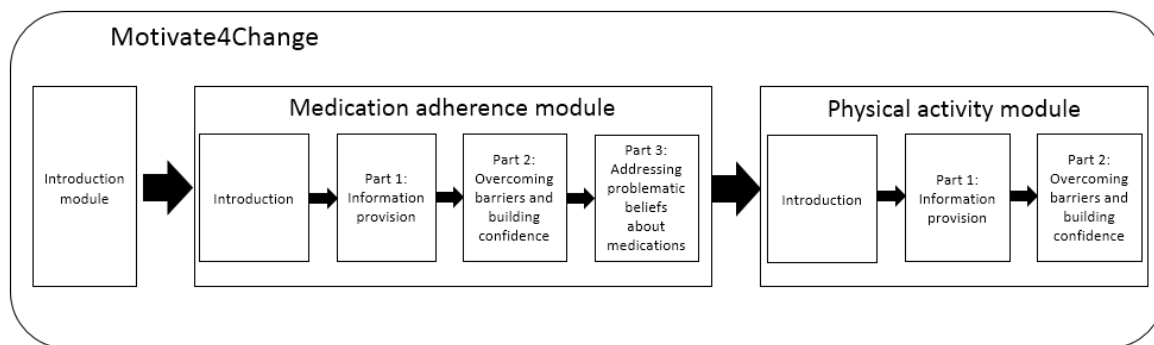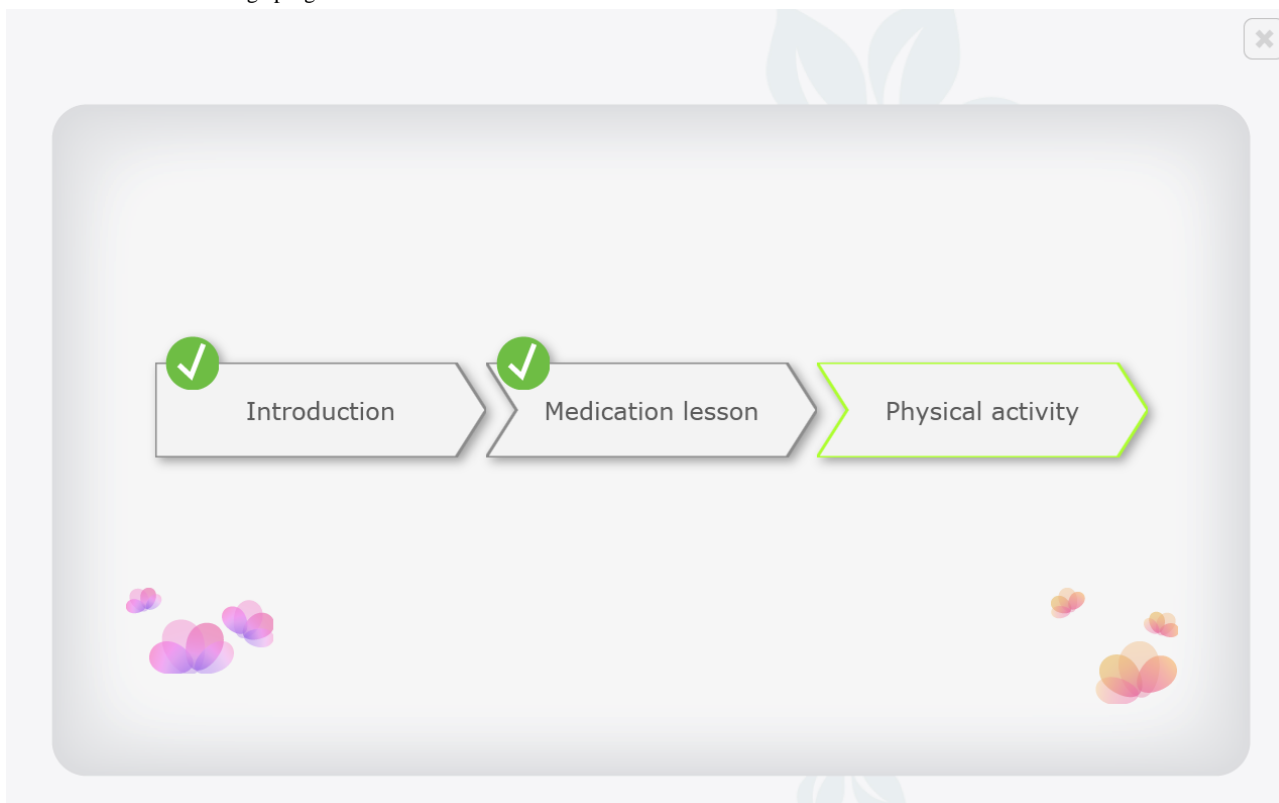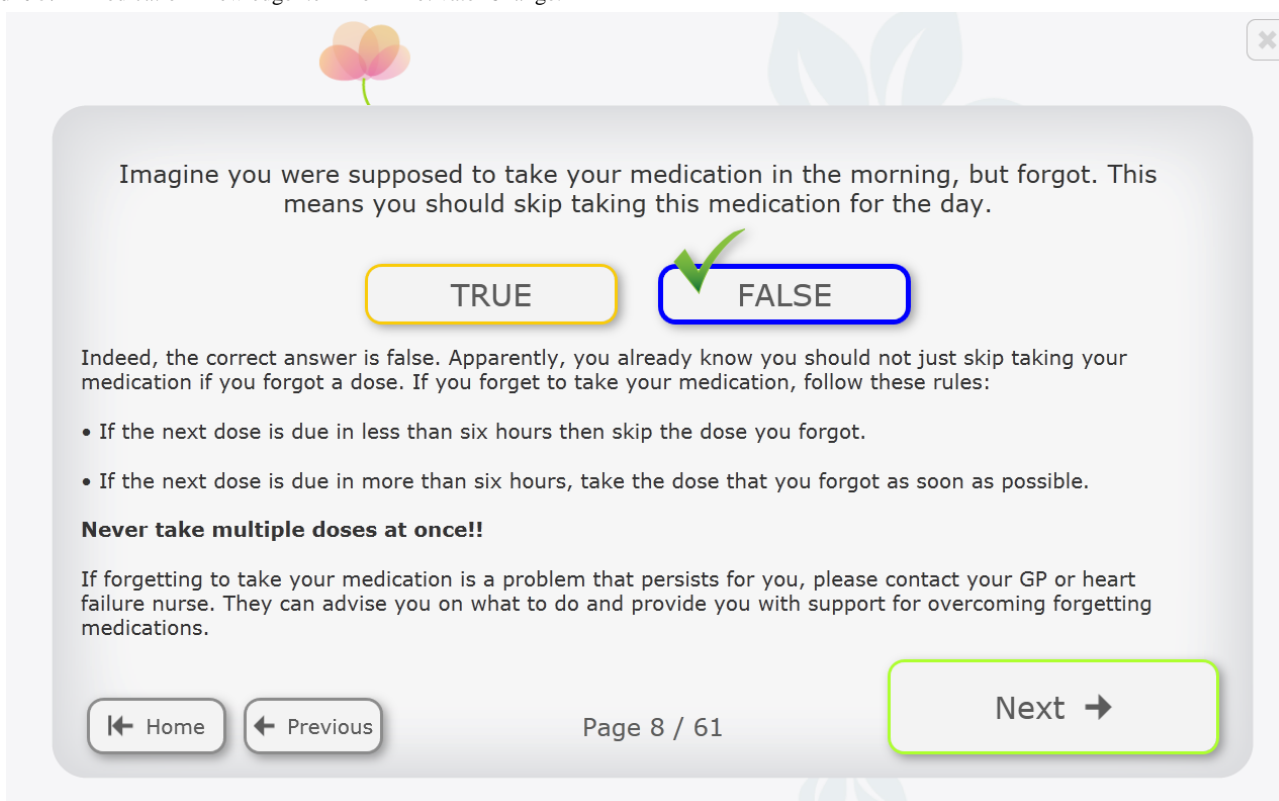**Figure 3.** The Motivate4Change intervention structure.

Figure 4. The Motivate4Change program menu.

Figure 5. A medication knowledge item from Motivate4Change.

Discussion

Principal Findings

In the development of an intervention promoting medication adherence and physical activity targeting HF patients in the hospital setting, a systematic approach guided by intervention mapping was found useful and informative. This process resulted in an intervention, Motivate4Change, which targets knowledge, self-efficacy, and beliefs using a variety of strategies including tailored health communication. We believe Motivate4Change is likely to be effective because its content was guided by scientific literature and behavioral theories as well as input from the potential users. Specifically, this process has resulted in a working research prototype that would be ready for implementation at a hospital. A usability testing of the user interface was conducted demonstrating the intervention can be used by older HF patients. However, it would be necessary to also conduct formative user research investigating the needs and requirements surrounding the intervention's implementation to ensure it is implemented appropriately.

Since intervention development an be time and resource intensive processes, it is imperative to develop interventions that are likely to be effective. To do this, researchers must compile the existing evidence and theory in order to make decisions relating to the intervention's content and structure. As such, researchers may be overwhelmed by the abundance of scientific literature available. A systematic process such as intervention mapping could help them make more informed decisions in a structured and relatively easy-to-follow manner.

Limitations

Although intervention mapping was a very useful tool in the development of Motivate4Change and increased our confidence in the effectiveness of the intervention, it had one drawback. Specifically, although intervention mapping was found useful and informative, it was also a time-consuming and lengthy process in the development of Motivate4Change. There were two limitations to the way in which we implemented the intervention mapping process. First, after discovering that there was not enough available information on the determinants of medication adherence and physical activity among HF patients, we did not conduct additional empirical evidence on this topic, for pragmatic reasons, and instead relied on available evidence from other, similar, populations. In addition, when selecting a digital intervention to address the need for promotion of self-care in the needs assessment stage, we did not assess if the relevant stakeholders have a need specifically for a digital intervention. Instead, we hypothesized such an intervention would be adequate and desirable due to its potential to address some of the observed needs of the stakeholders.

The resulting intervention, Motivate4Change, has a few limitations. Although we believe it would be effective in changing patient behavioral intentions if tested in a trial, it may

be important to combine it with long-term behavior change and adherence support also at home or in an outpatient setting to increase its effectiveness. In a brief intervention for hospitalized patients, only a few change objectives and determinants could be addressed; therefore, we selected the three determinants that were most relevant and changeable according to our research. In addition, the performance objectives were largely restricted to passive performance or actions. The target environment for the intervention delivery is a hospital setting, and the intervention is mainly to help patients plan, prepare, and anticipate actions when back in their home environment. Therefore, the performance objectives were mostly indirect, focusing on describing and identifying specific actions.

One important aspect in the development of the Motivate4Change intervention was the early assessment of the needs of the intended users in the intended setting and the involvement of relevant stakeholders in the intervention development. In the needs assessment phase, it was found that patients the hospital setting are likely to have needs that are specific for this setting, which had consequences for the intervention content, sequence, and structure. Designing the intervention with an early consideration of the needs of the intended users in the intended setting resulted in an intervention that is likely to fit the intended setting, making it more likely that it will affect clinical outcomes if tested in a trial.

Motivate4Change was restricted in its focus because of the predefined setting it was to be implemented in, which reduced the degrees of freedom in applying intervention mapping to come to the best possible intervention. This means that the resulting intervention is likely suitable for the hospital setting, but possibly less effective than an intervention that would have been developed with the intention of having a positive effect on the behavioral outcome, regardless of the setting for intended implementation. Finally, although we believe that Motivate4Change is likely to be effective in changing HF patients' physical activity and medication adherence, the effectiveness is yet to be demonstrated. To assess the effectiveness of an intervention, a randomized controlled trial would be necessary as a next step. Although at this moment a trial assessing the effectiveness of Motivate4Change is not planned, such a trial would consist of an intervention group receiving Motivate4Change during hospitalization and a control group receiving standard care during hospitalization.

Conclusions

In sum, the current work describes the development of the Motivate4Change intervention aimed at promoting medication adherence and physical activity among HF patients. This intervention was developed by following intervention mapping protocol. It was developed for use in the hospital setting and as such would be suitable for implementation in the hospital setting after a formative user needs and environmental requirements study.

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Abbreviations

HF: heart failure
MEMS: medication event monitoring system
SCT: social cognitive theory
TPB: theory of planned behavior

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Original Paper

Patient-Centered mHealth Living Donor Transplant Education Program for African Americans: Development and Analysis

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Abstract

Background: There is a critical need to expand the pool of available kidneys for African Americans who are on the transplant wait-list due to the disproportionally lower availability of deceased donor kidneys compared with other races/ethnic groups. Encouraging living donation is one method to fill this need. Incorporating mHealth strategies may be a way to deliver educational and supportive services to African American transplant-eligible patients and improve reach to those living in remote areas or unable to attend traditional group-session-based programs. Before program development, it is essential to perform formative research with target populations to determine acceptability and cultivate a patient-centered and culturally relevant approach to be used for program development.

Objective: The objectives of this study were to investigate African American kidney transplant recipients' and kidney donors'/potential donors' attitudes and perceptions toward mobile technology and its viability in an mHealth program aimed at educating patients about the process of living kidney donation.

Methods: Using frameworks from the technology acceptance model and self-determination theory, 9 focus groups (n=57) were administered to African Americans at a southeastern medical center, which included deceased/living donor kidney recipients and living donors/potential donors. After a demonstration of a tablet-based video education session and explanation of a group-based videoconferencing session, focus groups examined members' perceptions about how educational messages should be presented on topics pertaining to the process of living kidney donation and the transplantation. Questionnaires were administered on technology use and perceptions of the potential program communication platform. Transcripts were coded and themes were examined using NVivo 10 software.

Results: Qualitative findings found 5 major themes common among all participants. These included the following: (1) strong support for mobile technology use; (2) different media formats were preferred; (3) willingness to engage in video chats, but face-to-face interaction sometimes preferred; (4) media needs to be user friendly; (5) high prevalence of technology access. Our results show that recipients were willing to spend more time on education than the donors group, they wanted to build conversation skills to approach others, and preferred getting information from many sources, whereas the donor group wanted to hear from other living donors. The questionnaires revealed 85% or more of the sample scored 4+ on a 5-point Likert scale, which indicates high degree of interest to use the proposed program, belief that other mHealth technologies would help with adherence to medical

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regimens, and doctors would make regimen adjustments quicker. In addition, high utilization of mobile technology was reported; 71.9% of the participants had a mobile phone and 43.9% had a tablet.

Conclusions: Our study supports the use of an mHealth education platform for African Americans to learn about living donation. However, potential recipients and potential donors have differing needs, and therefore, programs should be tailored to each target audience.

Introduction

Overview

A barrier in the delivery of health education programs is the availability and proximity of the expert or professional to the intended audience, or patient. Technological advances provide opportunities to deliver health-related programs to disparate populations who lack transportation or time to attend sessions at a hospital, clinic, or other traditional health care settings. Educational programs traditionally consist of one-on-one conversations and group interactions where educators and learners can interact directly. Although telephone-based education can be used to reduce geographical barriers, it lacks the personal cues and nuances of in-person contact. Prerecorded video or audio clips can increase a learners' knowledge about a subject, but they usually lack personalization or tailoring to individual needs [1]. Each medium presents a conundrum between costs and the intrinsic reach of the communication method [2].

Health education can now be disseminated worldwide through mobile health (mHealth) platforms, patient-provider telehealth (ie, videoconferencing), and video education using a multitude of Web services that have been increasing worldwide over the past decade [3]. With 92% of US adults owning a cellular phone irrespective of age, sex, or race, and 50-65% with access to a smartphone and/or a tablet, mHealth is a utilitarian opportunistic method for interventions [4,5]. In 2013, 21% of Americans had conducted video calls on cell phones or tablets, a proportion that is projected to grow substantially as smartphone adoption and access to such apps increase [6]. Many individuals use mHealth technologies to assist in making behavioral changes, but inconsistent results in clinical research signal the need for more formative research [4]. Failure to influence behavior change has in part been attributed to the lack of using behavioral theory and technology application models as a foundation for change and not appropriately contextualizing the designs of program apps, user interfaces, or educational content [7].

End-stage renal disease (ESRD) affects the lives of nearly 500,000 Americans [8] and is optimally treated with kidney transplantation. Kidney transplantation has become the gold-standard treatment, with multiple studies establishing its association with superior quality of life, improved life expectancy, and better psychosocial functioning, all at substantially lower cost than dialysis [9-12]. Unfortunately, the number of patients who need kidney transplants at a given point in time far exceeds the availability of deceased donor kidneys

matching patients' tissue type, especially among African American (AA) ESRD patients [13]. The number of living donors is not sufficient to close this gap in need. Increasing living donations is therefore an important health priority in this population. Furthermore, transplants from living donors result in longer and higher quality of life than deceased donor transplants [12,14]. AA ESRD patients experience a lower rate of living donor kidney transplantation compared with whites [15], which is associated with a lower level of engagement in the living kidney donation process [16]. Research suggests that AA ESRD patients are in need of greater support and education to heighten their opportunities to obtain a living donor kidney transplant [17].

Living Kidney Donation Process

The typical living kidney donation process involves a brief group-educational class at a hospital setting in which ESRD patients and potential donors are informed about the medical screening the potential donor engages in to become eligible to donate a kidney, as well as the actual transplant procedures. However, states that include a large rural proportion that have few or only one transplant center, such as South Carolina, require other solutions to educate the populace. Lower national rates of living donor kidney transplantation in AAs compared with other ethnic groups [15] have been associated with lower knowledge levels about the process, as well as lower self-efficacy to discuss with others about considering to become a donor [18,19]. Several programs have successfully increased efforts to engage in the living donor kidney transplantation process and a few have increased rates of living donor assessments. These programs used transplant centers, home visits, and community meetings as the locations to build rapport and educate others about the living donor kidney transplantation process [20,21]. These types of personal contact methods may be replicated and made more accessible through technology when center or home visits are not feasible.

Study Objective

The purpose of this study was to evaluate the attitudes, acceptance, and preferences of AA kidney transplant recipients, kidney transplant donors, and potential donors who learn about living kidney donation through an mHealth program. This study was designed to create a framework that will aid in the decision making and content delivery in support of such an intervention. We used a formative analytic approach to ensure that the program is culturally sensitive, patient centered, and conducive to different learning styles.

Methods

Research Design Overview

This study used a mixed-method design incorporating both qualitative and quantitative methods to assess the attitudes, perceptions, and user characteristics for a future mHealth living donor kidney transplantation program tailored for AA dialysis patients eligible for transplantation. This included use of focus groups with open-ended questions to enable targeted discussions and conversations about mHealth delivery preferences, as well as questionnaire data for quantitative analyses [22,23]. We assessed how technology might be used to educate individuals about living donor kidney transplantation, how such a future program might be designed, and how the contact and communication with the users should be organized. Items from the questionnaire were used to quantify use characteristics of mobile technology and attitudes toward a proposed tablet-enabled video module-based educational program in conjunction with group videoconferencing. Focus groups were used to qualitatively explore the context, perceptions, preferences, and scenarios for using mHealth-delivered education. The results of the study will inform the development of program materials for an mHealth educational delivery and group video chat program about living donor kidney transplantation education among AAs eligible for transplant.

Development of Focus Group Questions

The technology acceptance model [24] and self-determination theory (SDT) [25] guided the development of the focus group interview questions. According to the technology acceptance model, two primary factors influence users' decision as to how and when they will likely use a technology: perceived usefulness and perceived ease of use. These models were chosen to assess which mHealth technologies would be useful in an mHealth program (eg, group videoconferencing, video educational modules, text messaging, and email exchanges), as well as what features of the program may be needed to help motivate those targeted to initiate and continue using the program. In addition, multimedia learning theory [26] was used to frame and expand on the resultant themes to form recommendations for this sample and guide program development and communication for a living donor kidney transplantation program with AAs [24].

We selected SDT as the theoretical underpinning for the development of the program, as it is framed upon the process of fostering participation and sustaining involvement in behavioral change programs through development of competence (akin to self-efficacy in social cognitive theory [27]) and autonomous regulation. Consistent strong effects of these SDT mediators have been observed on sustained adherence to various health behavior programs (eg, smoking cessation, diet, physical activity) [28-31]. SDT conceptualizes a continuum of human motivational regulation, ranging from fully external to fully internal [25,28,30]. *External* regulation, a form of controlled motivation, includes extrinsic rewards and punishments administered by others. This would include, in addition to financial incentives/constraints, pressure from others to change (eg, family members, friends, health care providers). While external or controlled regulation may motivate change

in the short term, such change is less enduring and less stable. The most autonomous form of motivation is internal or *autonomous regulation*. Here the person not only sees the importance of the behavior, but also links the change(s) with their other core values, beliefs, and life goals. Change arising from autonomous regulation is seen as the most stable and persistent [25,28,30]. Autonomy in SDT relates to our need to feel independent in our actions rather than feeling controlled or coerced.

The focus groups scripts were developed incorporating probe questions that identified how living donor transplant recipients developed competence and what factors helped them sustain their efforts to identify their donor. Transplant recipients who received a cadaver kidney provided input on how they may have experienced difficulties establishing competence in approaching others about living donation. Similarly, such information was obtained from the kidney donors and caregivers who were potential donors with regard to their involvement in going through the screening process for donation. In addition, probe questions were gathered from literature reviews and information gathered from prior AA kidney transplant study populations [13,16,18]. A team consisting of transplant surgeons, transplant coordinators, clinical psychologists, and experts in qualitative and quantitative methodology converged to develop the focus group questions.

Questionnaire Selection

A 20-item questionnaire was selected to assess use of cellular technology and attitudes toward use of mHealth technology. The questionnaire was previously used in several studies that evaluated a prototype mHealth system for enhancing adherence to medical regimens with several different ethnic minorities (ie, hypertensive Hispanics, AA, and white kidney transplant recipients) [32,33]. A total of 11 questions used a yes/no response format and assessed patients' access and utilization of mobile phones and mobile technologies, and awareness of telehealth programs (item content presented in Table 2). The remaining 9 items assessed respondents' attitudes toward mHealth- and telehealth-based remote monitoring and used the following 5-point Likert item response format: 1=strongly disagree, 2=disagree, 3=neutral, 4=agree, and 5=strongly agree. Previous studies reported Cronbach alpha internal consistency coefficient of .92 for the 9 items [32,33]. As in previous studies [32,34], the questions were administered following a brief demonstration of an example of the mHealth video module prototype program. A brief video module (approximately 1.5 minutes) was presented on a tablet and addressed the topic of whether a donor had to be a blood relative. It utilized an approach of having a narrator introduce the particular topic domain and then led into a brief interview of a living donor and recipient. The video culminates in the narrator providing a brief summary (along with main points summarized and presented in a bullet framework while the narrator summarized each point). The transplant recipients, caregivers, and potential donors then completed the 9 items, which assessed their level of interest to use such a system if it was available when they were involved in the living donation process or if such a need ever arises again.

Recruitment

Before recruitment, all research activities were reviewed and approved by the Medical University of South Carolina's (MUSC) Institutional Review Board. Recruitment was performed by an AA transplant coordinator from MUSC. A list of living kidney transplant donors, potential donors (who were caretakers), living donor transplant recipients, and deceased donor transplant recipients were invited to participate in the focus groups by phone contact. Comparable numbers of participants were recruited with high-school education or less compared with those with advanced technical trade skills or college education level to ensure diverse education backgrounds in the sample.

Study Implementation

A total of 9 focus groups were conducted and recorded in private conference rooms at MUSC. The focus groups were led by an AA nurse scientist who was a former kidney transplant coordinator and experienced in conducting focus groups. She had no prior contact with the patients and conducted the focus group protocol after obtaining verbal informed consent. Each focus group session started with introducing our concept and rationale for a future mHealth living kidney donor educational program. This was followed by a brief description of a program that would include weekly homework assignments of viewing brief educational video clips developed by AA living donor transplant recipients, AA living donors, transplant health care experts, etc, followed by weekly group videoconference sessions led by an AA living kidney donor transplant recipient. Participants were informed that the proposed group videoconferencing sessions would use a smartphone or tablet with the purpose of reviewing and expanding upon educational video clip assignments. Then, a demonstration of a prototype educational video clip about myths on living donor matching, including testimonials of an AA living donor transplant recipient and his donor was viewed by each focus group using a 10-in (25.4-cm) tablet. Afterward, group discussion commenced with the focus group questions (see Multimedia Appendix 1). At the end of the focus group questions, a questionnaire was given that took approximately 10 minutes to self-administer. A few participants preferred the questionnaire to be read to them. The focus group and completion of the subsequent questionnaire lasted approximately 60-90 minutes. Participants received a US $50 gift card at the end of the meeting to compensate them for their time and travel.

Qualitative Analysis

The focus group audio recordings were transcribed verbatim by a professional transcription company, and the transcripts were uploaded to NVivo 10.0 (QSR International Pty, Doncaster, Victoria, Australia) for qualitative analysis. A directed content analysis was applied to the transcripts, applicable when existing theory guides the investigation [35]. Because the technology acceptance model [24] and SDT [25] guided the development of interview questions, our emphasis was to assess the roles of the underlying tenets of the technology acceptability model (eg, perceived value, easy access and utilization, easy means of rectifying technical problems) and theory (eg, competence in using system, motivation to sustain engagement). This was

framed in the context of the proposed mHealth-technology-enabled combination video module and group videoconferencing educational and motivational enhancement program. In this regard, 2 raters individually searched the transcripts for participants' views on the use of the technology being proposed, its perceived usefulness, ease of use, and intention to use. These were coded to develop the final themes. Coding was conducted on 9 transcripts representing a total of 57 AA focus group participants who were either living kidney transplant donors or potential donors (ie, caregivers of ESRD patients, n=30) or were kidney transplant recipients (n=27). Two of the authors (JS and LN) independently read all transcripts; one of the authors (LN) coded these transcripts using NVivo. Immersion and crystallization [36] were used to validate the analysis. Two of the authors (JS and LN) examined patterns and themes in the data, and integrated them with the primary tenets of the technology acceptance model and SDT [37]. After the initial coding process [38], the 2 qualitative analysts (JS and LN) reviewed the coding results to crystallize the findings through an intensive review of the common themes. *Immersion* entailed examination of the data in detail, involving careful reading to absorb and inductively derive what was important in the transcribed and coded texts, and *crystallization* involved using these coded data to reflect on the analysis, query specific constructs, and identify the key themes noted in the immersion phase [36]. This produced another focused set of iterative codes in which both qualitative researchers reconciled the final themes. The use of NVivo software in the analysis produced an audit trail of the coding decisions, which ensures credibility of findings. The internal validity of findings was ensured using well-known methods for content analysis and the triangulation of the interview findings with the survey results. Iterative questions within the focus group guide were used to probe the participants, which provided the opportunity to corroborate and verify understanding by the interviewers [39].

Quantitative Analyses

The 20-item questionnaire used Yes/No and Likert-scale responses and SPSS v20 (SPSS IBM, New York, NY, USA) was used for the analysis. Item responses were categorized into dichotomous groupings. The 11 cellular technology utilization and prior awareness of telehealth/mHealth questions were readily categorized as yes versus no. The 9 Likert-scale questions had 5 response options to understand the acceptability of the mHealth-enabled group-delivered educational/motivational program. The responses were placed into one of two categories: agree (from strongly agree to agree) versus neutral/disagree (ranging from neutral, disagree, to strongly disagree). Overall group percentages, as well as stratified percentages, were tabulated between transplant recipients and the living donor/potential donor groups. In addition, for the 9 items assessing attitudes toward the mHealth prototype program, stratified comparisons of responses were made to evaluate the potential influence of age (<50 versus ≥50 years) and education (high-school diploma or less versus more than high-school diploma, including technical/trade school, partial college, college graduate).

Independent t tests were used to compare differences between groups on continuous item responses (eg, age). Chi-square tests

were used to examine group differences in responses to categorical data (eg, marital status, ethnicity; Table 1) and the 20 items assessing cellular utilization and attitudes toward

mHealth conceptual program (Tables 2 and 3). Test statistics were reported with *P* values, with *P*<.05 considered significant.

Table 1. Demographics of the participants.

	All N=57	Transplant recipients N=27	Donors/potential donors N=30	*P* value
Sex, n (%)				.26
Male	23/57 (40.4)	13/27 (48.1)	10/30 (33.3)	
Female	34/57 (59.6)	14/27 (51.9)	20/30 (66.7)	
Age, mean (SD) years	46.7 (13.3)	48.6 (14.6)	45.0 (11.9)	.37
Years on dialysis before transplant, mean (SD)		2.8 (2.4)		
Ethnicity, n (%)				.34
African American	56/57 (98.2)	27/27 (100.0)	29/30 (96.7)	
Hispanic	1/57 (1.8)	0/27 (0.0)	1/30 (3.3)	
Marital status, n (%)				.49
Married	31/57 (54.4)	12/27 (44.4)	17/30 (56.7)	
Divorced/separated	10/57 (17.5)	6/27 (22.2)	6/30 (20.0)	
Never married	14/57 (24.6)	8/27 (29.6)	6/30 (20.0)	
Widowed	2/57 (3.5)	1/27 (3.7)	1/30 (3.3)	
Education, n (%)				.64
College graduate	26/57 (45.6)	10/27 (37.0)	16/30 (53.3)	
Trade/technical school; partial college	9/57 (15.8)	4/27 (14.8)	5/30 (16.7)	
High-school diploma	20/57 (35.1)	12/27 (44.4)	8/30 (26.7)	
Less than high-school diploma	2/57 (3.5)	1/27 (3.7)	4/30 (13.3%)	
Annual income				.18
<US $15,000	10/57 (17.5)	8/27 (29.6)	2/30 (6.7)	
US $15,001-29,999	10/57 (17.5)	5/27 (18.5)	5/30 (16.7)	
US $30,000-49,999	13/57 (22.8)	4/27 (14.8)	9/30 (30.0)	
US $50,000-75,000	8/57 (14.0)	3/27 (11.1)	5/30 (16.7)	
>US $75,000	2/57 (3.5)	0/27 (0.0)	2/30 (6.7)	
Prefer not to answer	13/57 (22.8)	7/27 (25.9)	7/30 (23.3)	
Employment status, n (%)				<.001
On disability	17/57 (29.8)	14/27 (51.9)	3/30 (10.0)	
Full time	25/57 (43.9)	5/27 (18.5)	20/30 (66.7)	
Part-time	2/57 (3.5)	1/27 (3.7)	1/30 (3.3)	
Retired	9/57 (15.8)	6/27 (22.2)	3/30 (10.0)	
Unemployed	4/57 (7.0)	1/27 (3.7)	3/30 (10.0)	

Results

Demographics of Study Participants

A total of 57 individuals participated in 9 focus groups between January and March 2013. The demographics of the participants are reported in Table 1. Two groups each of living and deceased donor transplant recipients (n=27) and 2 groups each of living donors and potential donors (caretakers) of prior recipients

(n=30) made up the sample. All were AA except 1 female living donor, who was Hispanic and married to an AA recipient. The overall age was 46.7 (SD 13.3) years with a range of 23-72 years. Most of the participants were married (54%, 31/57), with approximately equal numbers of those with a college education (46%, 26/57) versus those who had a trade-school education or less. A third of the sample (30%, 17/57) was on disability with 47% (27/57) holding full- or part-time employment. There was a wide range of reported personal income between US $15,000

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and US $75,000, with a median income between US $30,000 and US $50,000—23% (13/57) of questionnaires were missing income data. With regard to employment status of the sample, 22% (6/27) of transplant recipients were employed at least part-time, compared with 70% (21/30) of the living donors/caregivers (*P*<.001).

Questionnaire Findings

Several sets of comparisons were made on the questions assessing utilization of cellular technology and attitudes toward the tablet-delivered prototype demonstration of the conceptual educational/motivational enhancement program. The Cronbach alpha internal consistency coefficient was .95 for the items assessing attitudes toward the tablet-delivered prototype program. These results are comparable to previously reported

Cronbach alpha coefficient of .92 [32,33]. No statistically significant differences were found between the transplant recipient and kidney donor/caregiver groups on the 11 questions that assessed cellular technology utilization and awareness of mHealth/telehealth (all chi-square *P*>.09; Table 2). Across the entire sample, most owned a cell phone (91%, 52/57) and 72% (41/57) regularly used a smartphone; 86% (49/57) used text messages, 70% (40/57) used email, and 79% (45/57) routinely accessed the Internet via their phones. After being given a definition of mHealth and telehealth, 74% (42/57) reported they had never heard of mHealth or telehealth concepts before the focus group. Tablets were prevalent in 44% (25/57) of households, and 95% (54/57) reported someone at home could offer assistance with using a smartphone or tablet if needed.

Table 2. Cellular technology-use questions delivered by questionnaire or read-out loud.

% of participants marked "Yes"	All	Transplant recipients	Donors/potential donors	*P* value (chi-square test)
1. Do you already have a working cellular phone?	52/57 (91)	24/27 (89)	28/30 (93)	.554
2. Do you already have a working "smartphone"-capable cellular device (Internet capable)?	41/57 (72)	17/27 (63)	24/30 (80)	.153
3. Does anyone in your household already have a working cellular phone?	52/57 (91)	23/27 (85)	29/30 (97)	.126
4. Does anyone in your household already have a working "smartphone"-capable cellular phone?	45/57 (79)	19/27 (70)	26/30 (87)	.131
5. Do you already have a working tablet computer like an iPad?	25/57 (44)	11/27 (41)	14/30 (47)	.653
6. If you need help with using your cellular phone or tablet, is there someone in your household who can help you?	54/57 (95)	26/27 (96)	28/30 (93)	.617
7. Send or receive text messages?	49/57 (86)	21/27 (78)	28/30 (93)	.091
8. Send or receive email?	40/57 (70)	19/27 (70)	20/30 (67)	.764
9. Use the Internet?	45/57 (79)	20/27 (74)	25/30 (83)	.392
10. Download ringtones or apps?	42/57 (74)	18/27 (67)	24/30 (80)	.253
11. Have you heard of telehealth or mobile health before today?	15/57 (26)	5/27 (19)	10/30 (33)	.205

Following the focus group discussion and demonstration of the prototype video module, participants rated their attitudes toward the conceptual program discussed using the Likert-scale response format from 1 (strongly disagree) to 5 (strongly agree). Table 3 presents the percentage rates of the 5-item format responses placed within 2 categories, namely, agree (strongly agree or agree) or disagree (neutral/disagree/strongly disagree).

Across the entire sample, all scores trended toward acceptability with an agree rating (≥80%). For example, there was a high level of acceptability in being educated remotely by health care providers via technology (93%, 53/57). The entire sample believed that mHealth programs would enable them to both receive information quickly from health care providers (89%, 51/57) and communicate with them when needed (91%, 52/57).

Table 3. Attitudes toward mHealth technology and proposed living donor transplant education program by categories of participants, age and education.

% that marked strongly agree or agree	All[a]	Recipients[a]	Donors and potential donors[a]	Type of participant P value (chi-square test)	Age<50 years[a]	Age≥50 years[a]	Age P value (chi-square test)	High-school diploma or less[a]	More than high-school diploma[a]	Education P value (chi-square test)
Would use mHealth devices if free	49/57 (86)	23/27 (85)	26/30 (87)	.872	31/34 (91)	20/23 (87)	.610	15/22 (68)	34/35 (97)	.002
If someone available to answer questions likely to use devices as directed	50/57 (88)	24/27 (89)	26/30 (87)	.800	32/34 (94)	18/23 (78)	.074	17/22 (77)	33/35 (94)	.057
Comfortable having health monitored remotely by doctor/nurses using mHealth technologies	53/57 (93)	26/27 (96)	27/30 (90)	.352	33/34 (97)	21/23 (91)	.340	20/22 (91)	34/35 (97)	.305
Comfortable using cell phone	51/57 (90)	25/27 (93)	26/30 (87)	.466	32/34 (94)	21/23 (91)	.683	18/22 (82)	34/35 (97)	.046
mHealth technology will help remind me to follow doctor's directions	50/57 (88)	24/27 (89)	26/30 (87)	.800	32/34 (94)	21/23 (91)	.683	19/22 (86)	34/35 (97)	.121
mHealth technology could allow my doctor to make medication changes quicker	51/57 (90)	24/27 (89)	27/30 (90)	.891	31/34 (91)	21/23 (91)	.986	19/22 (86)	33/35 (94)	.303
Confident my privacy is protected when using mHealth devices	47/57 (83)	24/27 (89)	23/30 (77)	.226	33/34 (97)	20/23 (87)	.143	18/22 (82)	33/35 (94)	.135
Important to follow doctor's directions	54/57 (95)	26/27 (96)	28/30 (93)	.617	33/34 (97)	21/23 (91)	.340	20/22 (91)	34/35 (97)	.305
Confident mHealth technology can effectively communicate my medical condition to my doctor	52/57 (92)	26/27 (96)	26/30 (87)	.199	33/34 (97)	21/23 (91)	.340	20/22 (91)	34/35 (97)	.305

[a]All values are presented as n/N, %.

Importantly, there were high levels of comfort in using phone- or tablet-delivered video educational modules and participating in group videoconference sessions with others in the same circumstances (89%, 51/57). The lowest level of acceptability (82%, 47/57) involved their level of confidence that their use of video modules and statements made during videoconference chat sessions would remain secure over the Internet.

We also evaluated the potential modulating influence of age and education on the participants' attitudes. As shown in Table 3, although there were no statistically significant differences between younger and older participants, there was a trend for those aged under 50 to be more likely to engage in mHealth device utilization if technical assistance was available. Level of education was associated with attitudes toward mHealth technology. Participants having high-school diploma or less felt less facile in using a cell phone (P=.046), were less likely to use mHealth technology even if provided for free (P=.002), and if technical assistance was readily available (P=.057). Similar to the entire cohort, there were nonsignificant trends indicating that those aged over 50 years having high-school diploma or less were less confident that their comments over videoconference sessions, etc would remain secure over the Internet.

Qualitative Findings

The following 5 major themes were found to be consistent among most of the focus group participants.

1. Few reservations to use mobile technology
2. Different media formats would be nice to have
3. Willingness to engage in video chats, but face-to-face meetings were sometimes preferred
4. Media needs to work quickly and be easy to use
5. Access to technology help within their immediate circles

There were distinct information needs and preferences between the prior kidney donor/potential donor and the prior kidney transplant recipient groups but there were also many common attributes that were shared from the 5 major themes (Figure 1). It was clear that there should be a co-construction of learning together with others in the same situation to be able to overcome barriers regarding lack of information about the living donor kidney transplantation process. Co-construction of learning places emphasis on learning together, fostering increased clarity, and understanding of others' experiences, perspectives, and viewpoints on the issues under consideration [40]. Potential donors who were typically family members who serve as caretakers and former transplant donors retrospectively voiced preferring to have received information from other donors. They preferred to learn this information in a concise format so that they would be better equipped to make their decision regarding

kidney donation. By contrast, prior transplant recipients (both living and deceased donors) preferred getting information from multiple sources including others like them in addition to medical professionals. They expressed potential benefits from

exposure to learning how to have a conversation with potential donors, address questions they may have, and make the request for a kidney donation.

Figure 1. Similarities and differences between kidney transplant donors/potential donors and transplant recipients in mHealth-based preferences in learning about living kidney donor transplantation.
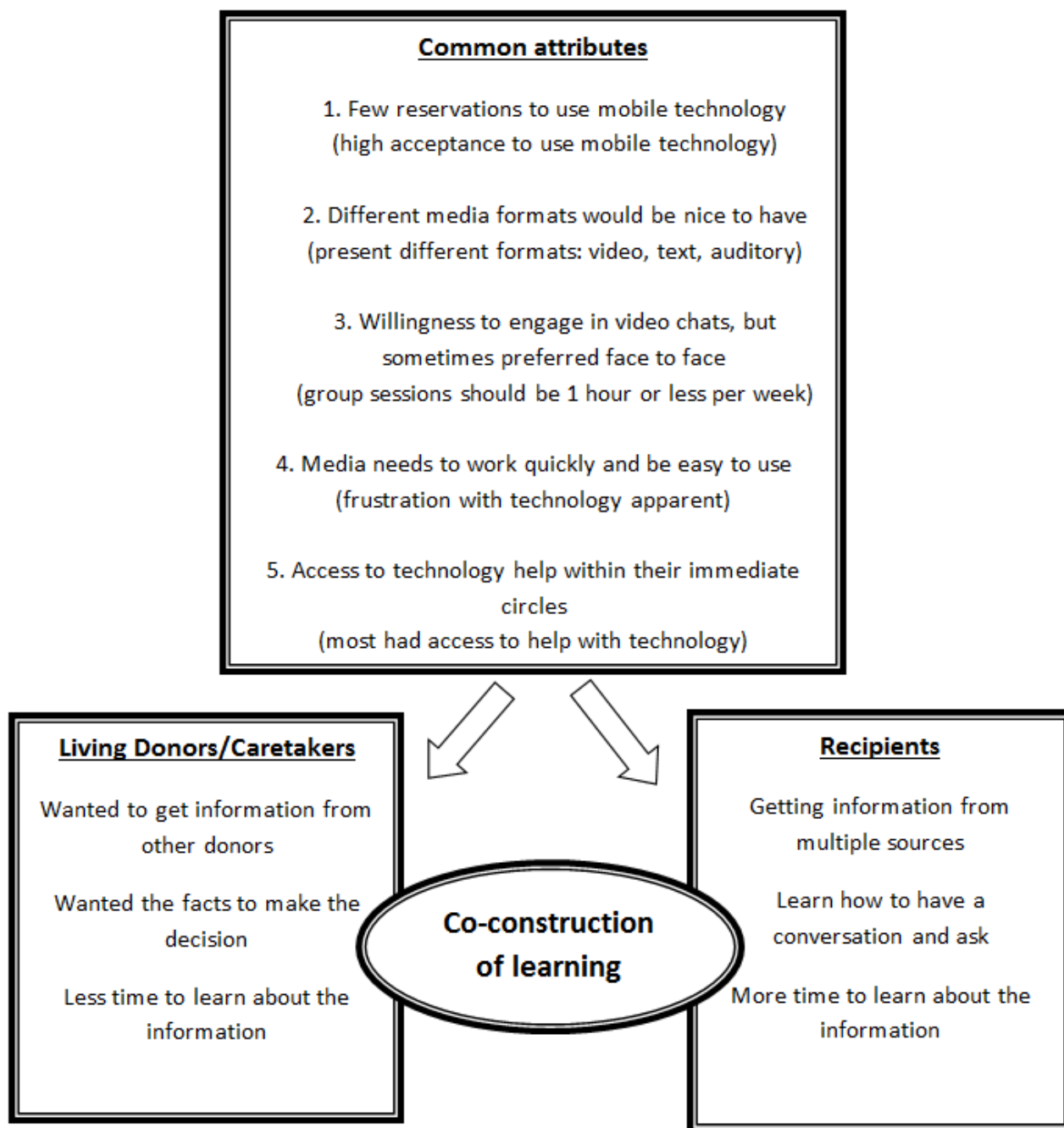
Few Reservations in Use of Mobile Technology

Overall, the participants were familiar with mobile technology such as smartphones and tablets. Participants discussed enjoying video clips as a way to learn quickly from others. Several stated video clips were preferred. Some commented,

I mean the video clip would be good and just put a bit of, not much they have to read, but just enough to know what is going on. A little, just a little video clip and a little note of what's going on.

If I had a choice, then a video is what I would like.

For some people it would be easier to watch a video; it is easier to sit there with some headphones on and just listen to what is being read on the screen.

Different Media Formats Would Be Nice to Have

Others pointed out that text messaging provided helpful reminders and motivators in other health-related programs they experienced. One participant commented,

I would kind of mix it up a little bit, because, like I just registered myself with this Mommy and Me text messages that I get to my phone daily about my pregnancy, and you know they'll be sending me text messages every day about ultrasounds, and to make sure you are eating the right foods, so the iPads plus the text messages to me would, they would both help.

Willingness to Engage in Video Chats, but Face-to-Face Meeting Is Sometimes Preferred

It was noted that there was enthusiasm for having experience in using a tablet (eg, iPad), and with that the willingness to try video chats as it at least provided a way to see the person that you are talking with. Face-to-face meeting was sometimes preferred, but the willingness to try new media was clear from the majority.

With the iPad you said you can do video chats, email, you can set it up where you can call and talk to the person on the phone. I figured, okay, if you can setting up reading and talk to them on the phone, you can always ask, hey can we go meet at Starbucks (coffee shop) or something and have a one-on-one conversation with each other if you're like in the same area or you can, to me you can always, like we have this focus group now, see if you can set up a group like that where everybody can meet together and also share their stories or their concerns about the process.

And as far as like time, you know, if you're super-super busy and your schedules will never link up for you to talk to this person face-to-face, if you have the iPad or something, whenever you do get a moment, you just get the information you need and probably get some of your questions answered that way.

Like if you say you are watching it in another hospital or whatever, just having that direct contact with that person that I can say, I can touch you and see that you are right here and I can ask you questions or whatever. I think that's important.

You're talking about an application like Skype or some other interactive. That would help.

I think it would depend on the person because some people they may have questions that they would be uncomfortable asking someone, you know, face-to-face that they don't really know, unless it's somebody you are comfortable with.

The opportunity to talk with a person who has had the experience was very appealing:

Anything else, it helps if you talked to somebody that's already been there and done that, you're better prepared. Nothing will shock you or, you know, you already know what you're getting into, the beginning, the middle, and end.

Yeah, to talk to somebody that's been there, been through it. That-that would help.

Media Needs to Work Quickly, Be Short, and Easy to Use

It was clear that to some of the participants the bandwidth of Internet connections might be an issue that limits the effectiveness of using video.

I don't think video clips are for me, I don't really click on the video unless it's seriously something like I know for a fact I wanna sit down and watch. I have like slow Internet...a video I'm not as apt to click on it or wait for it to load or do whatever. Just a video clip, like yesterday I was like, okay, it was almost like, it was only two minutes long, but still.

Access to Technology Help Within Their Immediate Circles

Many of the participants had resources that could help with technology barriers through family members, and local stores that offered technical support.

Sometimes there is, especially if they have like a young niece, nephew, grandchild around. If it's an older person like that, or you can always, I've noticed like Best Buy and Office Max and some of those places, they have it where you can come into their establishment with a iPad or a cell phone and the Geek Squad or somebody will help you get the hang of how to use it.

My grandbaby knows how to do all of that stuff and she ain't but nine and I don't know how.

Discussion

Principal Findings

In this study, we assessed rates of AA mobile phone ownership including smartphones and tablets, utilization of the devices' features, awareness of mHealth technology, and attitudes toward use of video modules and group videoconferencing for living kidney donation education. This study identified several themes relevant to designing mHealth programs for potential AA kidney transplant recipients and donors. The focus group members were very familiar with smartphone and tablet technology even if they did not own one. From our findings, there were few reservations in using technology to disseminate education materials. This was especially evident in using brief video education clips to bring up topics and then using video chat sessions to discuss these points more fully. Although the lack of face-to-face content may be a factor in someone choosing to enroll in a program, there was an overall attitude of "Let's try it." Therefore, any program that integrates discussion using such means needs to be clearly defined and tested for the intelligibility of the conversation.

Our qualitative analyses-derived themes support using mobile communication technology in a living donor transplant education program. With increased access to smartphone technologies [5,41], there are fewer concerns with adopting mobile devices for use in programs. Participants who did not own a mobile device were still familiar with them and if supplied, endorsed that they would use them in a program. In addition, if help was needed, there was confidence in the groups that they knew someone who had a similar device to aid them if needed.

The concept of using different media formats is not new [42]. However, combining different methods to communicate messages concurrently may lead to less understanding and confusion [7,26]. For example, cognitive overload, described in learning theory, states that an excessive increase in cognitive load may occur if one has too many teaching methods concurrently presented such as an animation, voice delivery, and text on a video education clip. This is thought to be distracting and may mask the main learning point for those learning new concepts [24]. Limiting the number of communication styles may help in directing focus on the education topic of importance and is helped by cleaning up excessive information [7]. Different education delivery methods may cater to different learning styles, and therefore, reiterating the main concepts using a different delivery tactic, such as when summarizing information, may enhance learning.

There have been several successful programs that instituted face-to-face learning sessions for living donor education, as well as other approaches [2,43]. Rodrigue et al [43] showed an increase in living donor knowledge, patient identification of potential donors, and potential donor engagement in medical evaluations using a home-based visit engaging a transplant-eligible patient and his/her family members and friends in learning about living donation [43]. Although such face-to-face educational approaches were preferred by some in our sample, sending medical staff for home visits across the state or having patients travel to the single transplant medical center in South Carolina or other states with a large service area is not always convenient, easy, or cost effective to arrange. This would be especially noted for those on dialysis with financial constraints, and/or reliance on others for transportation. Many telehealth programs have been used in the past to assess patients' medical status and provide education and medical regimen management with various chronic conditions [44]. The majority of these systems have used traditional telephone communication or desktop computer videoconferencing but with increased access of mobile communication technology in the consumer space, the interface can now be performed using consumer electronic devices such as smartphones and tablets.

Another important theme noted was the usability of the technology. It was important to our sample (participants) that the individual modules and overall program be created in such a way that it is easy to navigate to increase their perceived competence in using the program, as well as help motivate them to sustain using it [24,28,29]. Although smartphone and tablet use was commensurate with the national prevalence rates at the time, not all participants had a data plan through their cellular provider with allowable bandwidth or capacity to accommodate use of video streaming or group videoconferencing. There was

concern on how such a program using a large amount of bandwidth or video would affect monthly service fees. A primary solution is to have the participants access Wi-Fi connectivity; therefore, a data plan is not required and assuring good streaming rate quality. Other solutions include use of lower bit-rate streaming videos optimized for mobile devices using online media distributors or embedding the videos into the app itself if broadband speeds or cellular data networks are too slow.

Although there were many common attributes between the groups, there were noted differences between kidney transplant recipients and living donors/potential donors with regard to preferences for who is going to deliver the video module educational messages. The kidney transplant donors/potential donors mostly wished to receive information from those who had been through the process, whereas the transplant recipients suggested receiving information from multiple sources. The kidney donors/potential donors were also interested in receiving a program's educational modules as quickly as possible and required just the facts to make their decision as quickly as possible. The transplant recipient group differed, preferring to have more time to learn about the living donor transplantation process. In addition, the transplant recipients wanted skill-building learning modules that included passive and active modeling sessions with the transplant recipient navigator and other participants in the program before attempting such activities with family members and/or friends. Other studies have found that transplant-eligible patients benefit from such types of behavioral skill-building sessions [18]. It was also noted that the groups wanted to learn together with those in the same situation and walk through the process and support one another showing they were interested in colearning. This provides an interesting perspective for future studies to provide a social learning setting and may motivate sustained adherence to the programs.

Limitations

Several limitations should be mentioned when interpreting the findings. The focus groups were made up of AA kidney transplant recipients, donors, and potential donors. These findings are context specific and may not be generalized to other ethnic groups or age groups. The sample was also taken from the coastal area of South Carolina and may not be representative of the immediate southeastern states or the rest of the country. Participants may have reacted to the focus group questions with an expectancy bias and given more positive responses due to the study placement conditions. Participants also may have self-selected to be part of the study and may have had a more positive attitude toward living donation when compared with others who may have not had transportation or time to meet for the focus group.

It should be noted that nonsignificant trends were observed, which indicated that the kidney transplant recipients were less likely than the kidney donors/potential donors to own a smartphone, use text messaging, and to have someone in the home with a smartphone. They were also less likely to be employed and as a result tended to earn less than the donors/potential donors. In addition, we did not formally evaluate the impact of limited cellular data plans (or lack of)

with regard to acceptability of the proposed tablet-enabled program. However, as noted earlier, our likely approach to address such issues will be to use Wi-Fi connectivity, which eliminates the need for a data plan.

Although there were high levels of acceptability across participants toward the use of mHealth-technology-enabled programs, level of education and age showed modulating influence on some issues. Participants with high-school diploma or less were less comfortable using a cell phone and reported being less likely to use mHealth technology even if it was free or technical assistance was readily accessible. Similar to individuals aged over 50, those with high-school diploma or less were less confident that their comments during videoconference sessions, personal health data, etc would be kept secure across the Internet. Given the limited sample sizes of these subgroups of AA kidney transplant recipients, transplant donors, and potential donors, further research is warranted with these subgroups, as well as transplant-eligible patients to better understand potential barriers and challenges in the application of mHealth-enabled technologies in future transplant education programs.

Our study's findings support use of tablet-based video educational modules and remote group discussions with an AA living kidney organ recipient as a navigator among AAs eligible for kidney transplantation. This study demonstrates the importance of how patients with chronic diseases are willing to spend more time learning about solutions to their disease compared with those who do not have the disease and could possibly be a potential donor preferring a quicker educational process. Although there was some apprehension in using distance-based group video chat sessions, the sample was optimistic about trying it out. This said, educational message delivery must be succinct and to the point for potential donors, but should be elaborated on for those who need a transplant. This formative research provides insight to be used when tailoring materials for AA populations on issues of living donation. Creative context-specific, mostly brief, segments of video-based education and communication should be developed to include similar people to the patient group who share their life struggles to address educational needs in potential AA kidney donors and recipients. The preliminary findings may spur development of innovative and cost-efficient mobile communication strategies, enhance willingness to adopt these strategies in educating target populations, aid in understanding how these platforms can be used, and determine the preferences of AA ESRD and potential donor populations in receiving these educational materials [13].

Acknowledgments

Conflicts of Interest

None declared.

Multimedia Appendix 1

Focus group questions.

[PDF File (Adobe PDF File), 16KB - resprot_v4i3e84_app1.pdf]

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Abbreviations

    AA: African American
    ESRD: end-stage renal disease
    MUSC: Medical University of South Carolina
    SDT: self-determination theory

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Original Paper

Business Modeling to Implement an eHealth Portal for Infection Control: A Reflection on Co-Creation With Stakeholders

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Abstract

Background: It is acknowledged that the success and uptake of eHealth improve with the involvement of users and stakeholders to make technology reflect their needs. Involving stakeholders in implementation research is thus a crucial element in developing eHealth technology. Business modeling is an approach to guide implementation research for eHealth. Stakeholders are involved in business modeling by identifying relevant stakeholders, conducting value co-creation dialogs, and co-creating a business model. Because implementation activities are often underestimated as a crucial step while developing eHealth, comprehensive and applicable approaches geared toward business modeling in eHealth are scarce.

Objective: This paper demonstrates the potential of several stakeholder-oriented analysis methods and their practical application was demonstrated using Infectionmanager as an example case. In this paper, we aim to demonstrate how business modeling, with the focus on stakeholder involvement, is used to co-create an eHealth implementation.

Methods: We divided business modeling in 4 main research steps. As part of stakeholder identification, we performed literature scans, expert recommendations, and snowball sampling (Step 1). For stakeholder analyzes, we performed "basic stakeholder analysis," stakeholder salience, and ranking/analytic hierarchy process (Step 2). For value co-creation dialogs, we performed a process analysis and stakeholder interviews based on the business model canvas (Step 3). Finally, for business model generation, we combined all findings into the business model canvas (Step 4).

Results: Based on the applied methods, we synthesized a step-by-step guide for business modeling with stakeholder-oriented analysis methods that we consider suitable for implementing eHealth.

Conclusions: The step-by-step guide for business modeling with stakeholder involvement enables eHealth researchers to apply a systematic and multidisciplinary, co-creative approach for implementing eHealth. Business modeling becomes an active part in the entire development process of eHealth and starts an early focus on implementation, in which stakeholders help to co-create the basis necessary for a satisfying success and uptake of the eHealth technology.

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Introduction

Implementation of eHealth

Implementation is necessary to promote the systematic uptake of research findings and other evidence-based practices into routine practice and to improve the quality and effectiveness of health services and care [1]. Attention for evaluating the implementation of eHealth has steadily grown in the last 5 years [2]. Despite this increased attention for implementation, little attention has been given to effects on roles and responsibilities, risk management, engagement of professionals, and transparency of potential benefits of eHealth [2]. Therefore, many implementations are not complete enough when technology "goes live" and its anticipated success is rather a lottery than an actually preplanned implementation. In fact, Black et al [3] concluded in their systematic review that many eHealth projects provide little evidence for actually improving outcomes or being cost effective. Implementation of eHealth has almost universally proven to be more complex and time consuming than anticipated [3]. In addition, many eHealth researchers assume that implementation is an ex-post activity and start preparing implementation when a technology is nearly finished [4]. Many eHealth projects suffer from the "field of dreams" syndrome with the expectation that users will show up as soon as the technology is made available, yet end up having little support, no plans for sustainability, poor uptake, and unknown added value to stakeholders [4,5]. The implementation should not be treated as an afterward necessity, nor treated subordinately to

the design of eHealth technology. "Innovation is not just about technology anymore" [6], and therefore, a well-prepared implementation is just as important as a well-designed eHealth technology.

Business Modeling

In a previous viewpoint paper, we had introduced business modeling as a possible approach to guide the development and implementation of eHealth [4]. Business modeling fosters a ground for dialog regarding the perceived added value and purpose of an eHealth technology [7]. The resulting business model depicts how an organization creates, delivers, and captures value [8]. Such a model can be used as a narrative to explain new ideas [9]. With business modeling, we use this narrative to discuss, plan, and operationalize an implementation of eHealth. Using stakeholder identification, stakeholder analysis, and value co-creation dialog, relevant values can be discussed and then modeled as a business model.

The Center for eHealth Research (CeHRes) road map (Figure 1) introduces eHealth development as a holistic approach integrating eHealth technology design with business modeling for implementation [4]. The road map consists of the following 5 phases: contextual inquiry, value specification, design, operationalization, and summative evaluation. The road map advises research activities that support eHealth research in each of these phases. This paper expands on this road map by demonstrating the research activities that we apply for business modeling.

Figure 1. Center for eHealth Research road map.
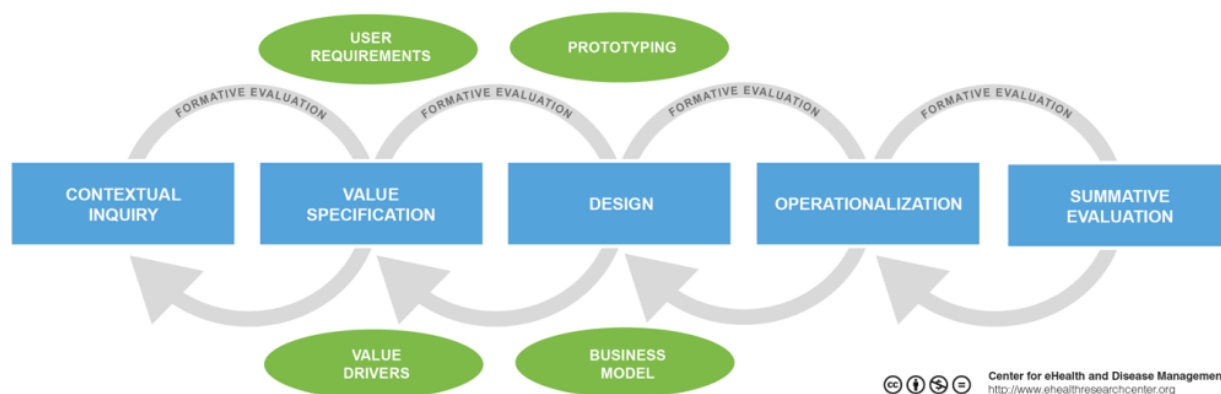
Stakeholder Involvement

Coiera [10] stressed the importance of sociotechnical design in health care. In his paper, he claimed that instead of technology, the social system surrounding that technology should be the central focus. Attention to sociotechnical factors is important to maximize the likelihood of successful implementation and adoption [3]. Academic interest in stakeholder theory started in the late 1970s in the fields of public policy making and business management. The most acknowledged definition for a "stakeholder" in stakeholder theory was established by Freeman as "everyone who affects or is affected by—in this

case—the eHealth technology" [11]. A stakeholder analysis aims to evaluate and understand stakeholders from the perspective of an organization to determine their relevance to a project or policy [12]. In 2004, Bryson [13] reviewed 15 stakeholder methods to identify and analyze stakeholders. Although this review described step-by-step instructions for analysis techniques, these techniques focus strongly on expert-driven stakeholder classification without "true involvement" of stakeholders. To sum up, there is adequate information on expert-based stakeholder identification, yet methods or ideas on "how" to involve stakeholders (eg, users, developers, suppliers) as active partakers in stakeholder analysis

and further co-creation are less established. Likewise, in implementation research for eHealth, the involvement of stakeholders is still relatively unexplored.

Aim of This Paper

This paper presents an approach for implementing eHealth with a strong accent on stakeholder involvement. We demonstrate our business modeling research and stakeholder-centered analysis methods in an example case, its added value to implementing eHealth, and conclude with a step-by-step guideline for stakeholder-centered business modeling for eHealth technology.

Methods

Stakeholder-Centered Analysis Methods

In a learning-by-doing approach to form our business modeling research, we applied various stakeholder-centered analysis methods in an example case study with a strong focus on discovering how stakeholders can best be involved in business modeling. These stakeholder-centered analysis methods are based on stakeholder theory, existing business modeling tools, and paradigms from human-centered design. In the "Methods" section, we present a theoretical overview for each stakeholder-centered analysis method followed by a practical application as an example and reflections on their application.

Example Case: Infectionmanager

The European Union stimulates the mobility of their citizens. Similarly, in health care an increasing number of patients and health care professionals cross the borders and seek or offer health care services abroad. "EurSafety Health-net" has the primary goal to address patient safety in a cross-border context. The EurSafety Health-net consists of 5 "Euregios" or 38 geographical regions, totaling 19.2 million citizens. In these regions, 32 public health organizations and over 300 hospitals participate in the project. Our involvement in this project focuses on developing an Internet-based platform for cross-border infection prevention and control, called "Infectionmanager" (Figure 2). Infection prevention and control is a broad field, and therefore, our eHealth project mainly focuses on antibiotic prescription in hospitals. A change in prescription behavior is urgent, as up to 30-50% of the prescribed antibiotics are either inappropriate or even unnecessary and thereby harming the effectiveness of these antibiotics [14]. Intervening antibiotic use with antibiotic stewardship (ASP) interventions can be a step in curbing antibiotic resistance and hospital-acquired infections, and these can subsequently improve patient safety and reduce costs [15].

The Infectionmanager website is a platform designed to offer eHealth applications that support multiple crucial steps in the antibiotic therapy process and targets multiple, different users and stakeholders. The platform offers eHealth applications with information, decision support, and an overview of the ongoing research and development concerning the platform [16-18]. It targets stakeholders in infection control with currently a specific focus on stakeholders who deal with ASP in hospitals.

The Infectionmanager case is an example of a typical complex eHealth project. First, there is a multitude of stakeholders with diverse stakes, and therefore, an excellent opportunity to try methods for stakeholder involvement. Second, the development options were unlimited, allowing very open discussions with stakeholders to co-create possible eHealth applications and ideas for an implementation. Lastly, the complexity is influenced further by the novelty of ASP in the Netherlands and the novelty of exploring possible eHealth opportunities. Infectionmanager has been researched and developed according to the CeHRes road map [4].

Figure 2. Homepage of Infectionmanager.

Stakeholder-Centered Analysis Methods

Involvement of stakeholders changes over time in the research process. In the beginning of an eHealth project, the analysis focuses on finding the right stakeholders and discussing global problems and opportunities, whereas in the later stages of the project, certain opportunities are combined into a possible eHealth technology and the implementation research moves on to value co-creation with topics that deal with added value, feasibility, sustainability, and costs-benefit issues.

In this section, we present each stakeholder-centered analysis method as listed below. First, we give a short summary of the theoretical background of used methods, followed by the practical application in our example case. We conclude each method with some gaps and lessons learned from use and experience.

Stakeholder Identification

Every eHealth project will have its own unique stakeholder landscape that needs to be understood [4]. As a first step, before analysis *of* or *with* stakeholders can take place, all relevant stakeholders need to be identified. We noticed that stakeholder analysis methods focus more on classification and categorization than identification. Identifying a complete list of the right stakeholders is very crucial for all further analysis. Therefore, the identification step is very important and it is remarkable

that it is not described in depth. Many authors consider stakeholders as a default product of a nonexplained identification process [19].

We explored the following 3 approaches to identify stakeholders in an eHealth project: a literature scan/review, expert recommendations, and snowball sampling of stakeholders. These methods are not mutually exclusive and should be integrated as a mixed-method approach for optimal results.

Stakeholder Identification Method Number 1: Literature Scan/Review

In Theory

There are 2 ways to identify stakeholders with literature:

- Identify stakeholders in stakeholder theory. This can result in a list of general types of stakeholders or stakeholders specifically in relation to eHealth.
- Identify stakeholders mentioned in literature on similar (eHealth) interventions.

Ballejos and Montagna [19] recommend starting with identifying stakeholder types [19]. These types of stakeholders can be very diverse, depending on the desired level of detail. Table 1 lists some literature examples from stakeholder's theory of possible different stakeholders types that can be relevant for eHealth research [19-26]:

Table 1. Overview of stakeholder types in literature related to eHealth.

Study	Research focus/setting	Identified stakeholder types
Volere template [24]	Stakeholder roles in information technology	Clients, customers, business/subject experts, future idea specialists, current system specialists, clerical users, technical users, potential users, sales specialists, marketing specialists, aesthetics specialists, graphics specialists, usability specialists, safety specialists, security specialists, cultural specialists, legal specialists, environmental specialists, maintenance specialists, packaging designers, manufacturers, product installers
Wolper [26]	Stakeholders in a typical, large hospital	Competitors, related health care organizations, government regulatory/licensing agencies, private accreditation associations, professional associations, unions, patients, third-party payers, hospital suppliers, media, financial community, special interest groups, religious organizations, local community, nonmanagement medical staff, hospital board, parent companies/organizations, stockholders/taxpayers/contributors, management
Sharp et al [25]	Baseline stakeholders in requirements engineering	Users, developers, regulators, decision makers (with possible client, supplier, and satellite stakeholders for each of the above baseline stakeholders)
Alexander [20]	Product-centric onion model	Developer, maintenance operator, operational support, normal operator, interfacing systems, sponsor or champion, functional beneficiary, purchaser, consultant, political beneficiary, financial beneficiary, negative stakeholders, regulators, the public
Mantzana et al [22]	Health care actors involved in the adoption of information systems	Acceptors, providers, supporters, and controllers
Mettler et al [23]	A total of 4 key stakeholder types with subtypes for eHealth	Service customer, payer of service, responsible for referral, competitor, supplier of goods, supplier of services, supplier of information, government, and community
Ballejos and Montagna [19]	Stakeholder roles (internal or external)	Beneficiaries (functional, financial, political, sponsors), negatives, responsibles, decision makers, regulators, operators, experts, consultants, developers
Hyder et al [21]	A total of 11 stakeholder categories in health care	Beneficiaries, central government agencies, Ministry of Health, local governments, financiers, civil society organizations, health governing boards, provider organizations, professional organizations and health workers, unions, suppliers

Table 1 demonstrates that the stakeholder types can differ for each chosen focus and that multiple focuses can be used to be thorough in the stakeholder identification. Still, these stakeholders are only stakeholder *types*, and therefore, a researcher still has to identify which of these stakeholder types are present and more importantly, identify who the exact stakeholders are for each stakeholder type. For example, relevant stakeholder types can be "users" or "service customers," but are they patients or specialists? What kind of patients? Which of these patients are included in research and which ones are not?

The second option is to identify stakeholders in the literature on similar interventions. These interventions do not have to be technology per se but are implemented in the same domains as the intended eHealth technology. In this case, very precisely defined stakeholders can be found by looking at the context [27]. This requires sufficient prior knowledge of the domains (medicine, policies, technological) and a clear idea of the goals of the intended eHealth technology. Literature can then be reviewed for mentioned stakeholders (usually professions or organizations); for example, by ranking their occurrence in each publication.

Example Case

When starting with Infectionmanager, our research team decided that ASP was a key intervention for infection control in hospitals and that our main interest was to start exploring eHealth possibilities. We conducted a quick scan literature review on ASP to list possible stakeholders who are relevant for ASP [28]. We performed a quick scan (so not a systematic review or similar strict methods) as this list would provide a general idea of stakeholders who should be involved in our ASP research. We ran a query on "antibiotic stewardship" and selected papers of most cited or key literature from that research domain. We scanned 12 key papers and noted every mentioned stakeholder in these papers. This resulted in a complete list of stakeholders in international hospitals based on the literature scan of ASP.

Textbox 1. List of antibiotic stewardship stakeholders identified in a hospital after a literature scan.

- (Clinical) pharmacists
- Epidemiologists
- Head of pharmacy department
- Infection control nurses
- Infectious disease specialists
- Investigators
- Medical executives
- Medical students
- Microbiologists
- Nurse practitioners
- Nurses
- Pharmacologist experts
- Physicians
- Psychologists
- Software engineers

Gaps/Lessons Learned

- A (quick) literature scan is a good starting point to start with stakeholder identification. It is a fast way to draft a list of stakeholders who may be relevant for further stakeholder identification and later stakeholder analysis.
- An inventory of stakeholder types can be useful as an extra check to see if certain stakeholder types are missing on the stakeholder list or left out for a clear reason.
- Start with a manageable amount of key publications using a simple query in your research subject and list or tally mentioned stakeholders. With 10-20 publications, that stakeholders list will saturate.
- New, innovative health care interventions have limited available literature, especially in an academic context. In our example case, little literature was available for eHealth/health care technology in the field of prescribing antibiotics and stewardship.
- A potential danger with international literature is that it describes various different health care contexts and thus identified stakeholders may not be relevant for local health care systems. To illustrate with examples from our project: Microbiologists in Francophonic countries are called "bacteriologists," and thus, are not 2 different stakeholders; or "infectious disease physicians" do not exist as-is in the Dutch health care system and the closest comparable profession would be an "infectologist," which we learnt afterward through validation of our stakeholder list with experts.
- Policies, (clinical) protocols, and documents are very relevant sources to take into consideration as literature for stakeholder analysis [29], especially when the eHealth intervention is targeted toward supporting tasks performed by health care professionals. Obtaining these protocols and documents requires access via experts or stakeholders who use them.

Stakeholder Identification Method Number 2: Expert Recommendations

In Theory

After exploring stakeholders from a theoretical perspective, the next step is to introduce a practical perspective. Most stakeholder analysis methodologies seem to prefer an expert-driven approach. According to Bryson [13], the "basic stakeholder analysis technique" suggests that the planning team (ie, the eHealth research team in eHealth context) brainstorms which stakeholders should be included for analysis. Depending on the composition of the planning team, one can also ask (external) field experts to nominate stakeholders [21]. The goal of this brainstorming session is to make a complete overview of relevant stakeholders to the eHealth project.

Example Case

We planned 2 brainstorming rounds. The first round started by using specific software that allowed to visualize stakeholder mapping. Our planning team consisted of eHealth researchers and infection control experts affiliated with our EurSafety Health-net project. We conducted 22-hour brainstorming sessions to visualize an overview of stakeholders relevant for infection control and subsequently Infectionmanager. In this early phase of our research, we looked at infection management, which had a broader scope than ASP specifically. We also categorized the stakeholders in stakeholder groups with the mapping software. The Infectionmanager was the central point of discussion, and so, the central question was "Which people or organizations have an influence on Infectionmanager?" And subsequently, "Which people or organizations are influenced by Infectionmanager?." Using these 2 questions, we brainstormed a stakeholder map. In this visual way of brainstorming, the network and relationships of stakeholders become clear. For example, the stakeholder "care recipients" can be categorized into 3 different types of care recipients with

different roles toward Infectionmanager. Or, as another example, we listed possible commercial third parties, possible hospitals, and so on. The visualization aspect of this approach helps to draft a visual representation of the possible stakeholder map, which makes the brainstorming process less abstract and more comprehensive for all participants in the brainstorming team. A global overview of our stakeholder map can be seen in Figure 3.

The second brainstorming round targeted "ASP" more specifically and was a continuation of the stakeholders found with the quick literature scan as described in the previous method. Our team of eHealth researchers asked an infection control expert working at a pilot hospital to help us transpose the theoretical list of (international) stakeholders to stakeholders present at a pulmonary ward. We chose this pulmonary ward, as these wards have a relatively high use of antibiotics and relatively low multimorbidity. In the focus group, we brainstormed about every stakeholder on the list and the stakeholder's possible role in ASP, Dutch analogous profession, and whether that stakeholder was available in the pulmonary ward. Later, for further stakeholder analysis, we organized a focus group with the following stakeholders [30]: clinical microbiologists, pharmacists, (chest) physicians, residents, nurses, nurse manager, ward manager, and staff members of management.

Figure 3. Stakeholder map relevant for infection control and subsequently Infectionmanager.
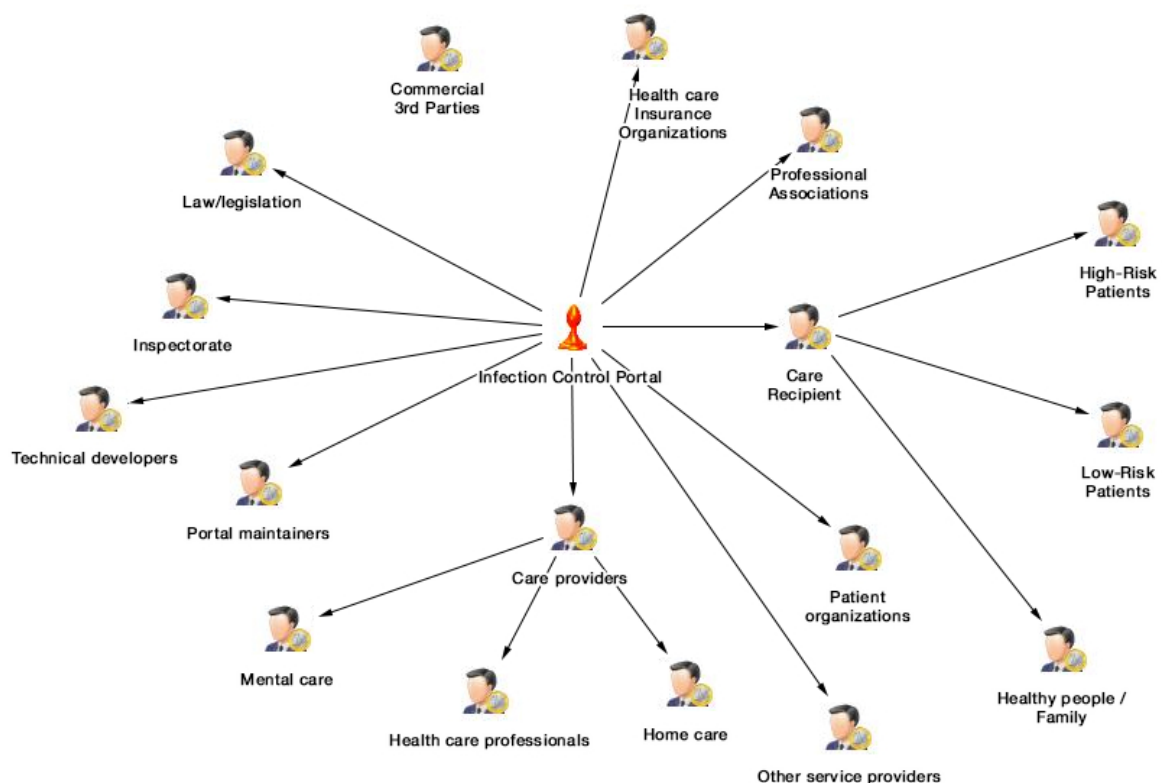
Gaps/Lessons Learned

- Brainstorming with experts is a useful method to bridge the theoretical list of stakeholders with the relevant practice. Experts are active in the field, so a researcher needs to make use of their firsthand knowledge.
- Visualization of the stakeholder map helps making the discussion of relevant stakeholders less abstract and fosters the collaboration and discussion. A map is quick to comprehend and easier to share than long lists, for example. It also visually structures the mentioned stakeholders.
- The more experts involved, the better. Experts are limited to their profession and background and may not know all parts of the stakeholder map. For example, a microbiologist knows all about the laboratory and microbiological diagnosis but has little insight into the daily routine of a nurse during ASP.

- Structure in the focus group is important. Prevent vociferous stakeholders who hijack the session for sharing their views only. Give every stakeholder adequate time and attention.
- Involving more experts also increases validation and paints a broader picture.
- Be open-minded to the stakeholders that experts suggest despite prior knowledge from the literature. In case of questionable or unclear stakeholders, note them and ask why they are relevant and discuss/evaluate their relevance later with other experts.

Stakeholder Identification Method Number 3: Snowball Sampling With Stakeholders

In Theory

Both literature and expert recommendations can still miss certain stakeholders who may be important to the project. A final step, once a list of stakeholders is ready, is to ask these stakeholders

to complete the list. The added value of this step is to validate the list of stakeholders from a stakeholder's perspective and a last chance to identify missing stakeholders. Snowball sampling is a technique where existing participants recruit future participants among their acquaintances. In terms of stakeholder snowball sampling, stakeholders can be asked who the stakeholders are, or, in case of an already available list, which stakeholders are important and which ones are missing. Snowball sampling is one of the common methods used for stakeholder identification [31].

Example Case

In earlier brainstorm sessions (mentioned as a "previous method"), we drafted an initial list of stakeholders in infection control. These stakeholders were sent a questionnaire in which they could rank the importance of stakeholders on our stakeholders list and suggest missing stakeholders [32]. This eventually resulted in the stakeholder map of infection control as depicted in Figure 4. What is interesting is that this map contains some different stakeholders than the ones mentioned by experts and us but above all, it has a broader focus than the expert-based map in Figure 3. For example, our research mostly focused on stakeholders related to infection control in hospitals; yet, these stakeholders also pointed out that dental care and livestock industry deal with infections and antibiotics and are very relevant for infection control as a whole. Therefore, despite having a focus on hospitals (as outlined in Figure 3), there are a lot more other infection control stakeholders to involve in the stakeholder analysis.

As mentioned in the "Stakeholder Identification Method Number 2: Expert Recommendations" section, we further focused on ASP as a key intervention for infection control inside hospitals. Thus, we planned a focus group with stakeholders at a pulmonary ward [30].We also applied snowball sampling to this focus group, and the existing stakeholders agreed that we should additionally contact dieticians, cleaning personnel, and a representative of the information technology department as they may have an influence on ASP.

Figure 4. Example of all the stakeholders relevant for infection control.
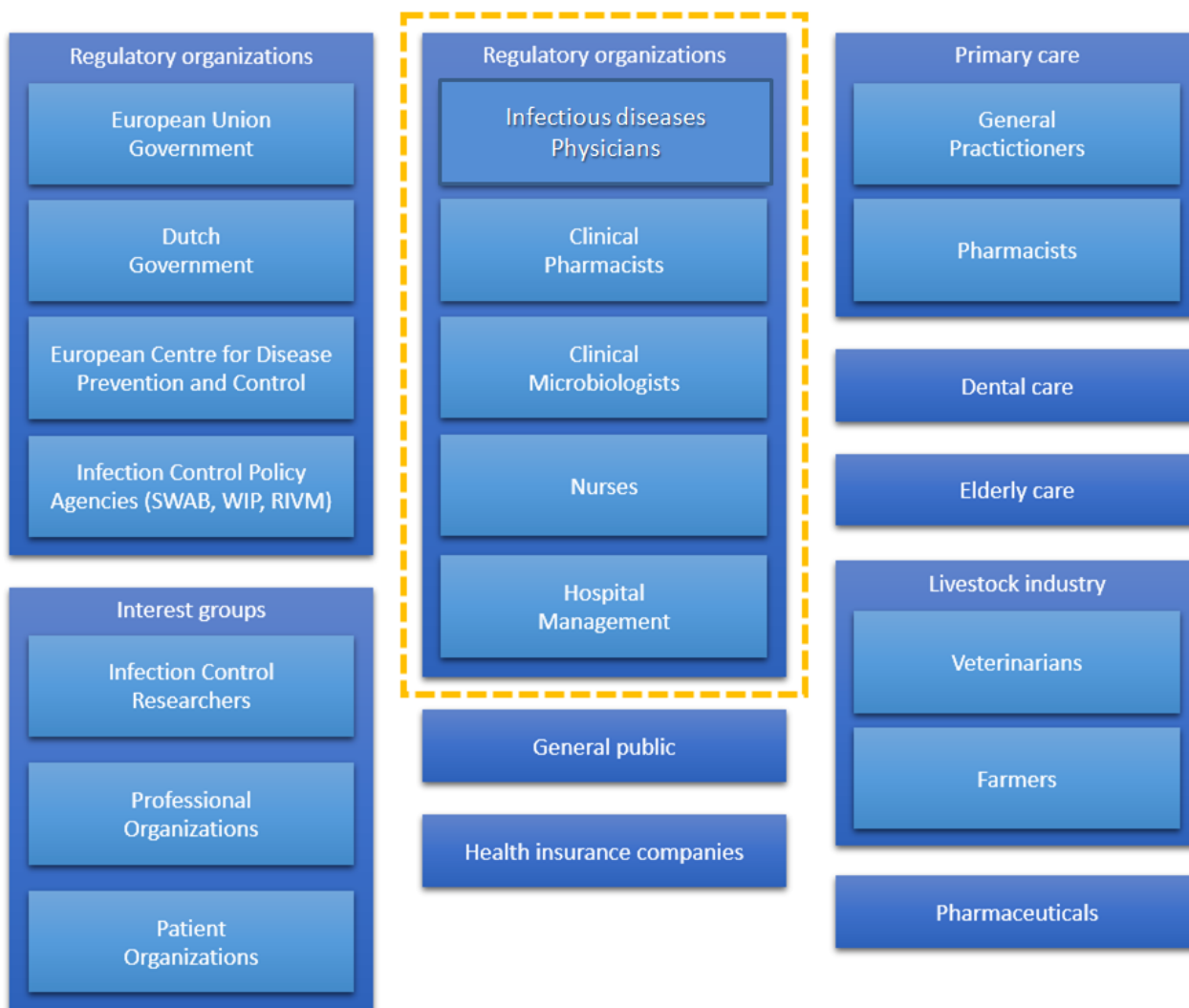
Gaps/Lessons Learned

- Stakeholders have the most direct firsthand experience within the subject domain and thus are crucial in stakeholder identification.
- Snowball sampling is suitable for identifying missing stakeholders. In our case, for example, we identified neither dieticians nor cleaning personnel as relevant stakeholders for ASP via literature.
- Questionnaires are the most convenient method for snowball sampling a complete list.
- Focus groups allow interaction with stakeholders, to iteratively assess conclusions from stakeholders and researchers. Yet, focus groups can be difficult to organize, especially when they consist of a high number of stakeholders. The focus group needs to have something for the stakeholders to be willing to schedule it.

Stakeholder Analysis

After stakeholders are identified, they can take part in the stakeholder analysis. Not every identified stakeholder will be equally important to the implementation of the eHealth technology [4]. In addition, it takes time and resources to interact with every single stakeholder, and therefore, it is recommendable to work toward a selection of key stakeholders. Narrowing the list of stakeholders requires applying some acceptable and justifiable sorting criteria [33]. Again returning to the review by Bryson [13], there are a plethora of stakeholder analysis methodologies to classify stakeholders. In this paper, we demonstrate our application of the basic stakeholder analysis, stakeholder salience (Mitchell's classification), and ranking/analytic hierarchy process (AHP) method.

Stakeholder Analysis Method Number 1: Basic Stakeholder Analysis

In Theory

The basic stakeholder analysis method involves brainstorming expert-based opinions on behalf of each stakeholder [13]. The research team and/or experts can give a global impression from the stakeholders' point of view about what the expectations can be for each possible stakeholder. The analysis aspect behind this method is that a stakeholder with many (important) expectations will most likely be important to the project throughout development. In terms of business modeling, these expectations are related to "values" that we will discuss more in depth later in this paper.

Looking from a research team stance, this overview of possible expectations also allows a first impression on the value proposition possibilities [34]. A value proposition is "the value created for users by the offering based on technology" [35]. In other words, it describes what added value a technology has to offer, as well as possible services around the technology. This value proposition will be the basis for the design and implementation of the eHealth technology.

Example Case

During our brainstorming sessions early on in our research, we examined with experts what possible values each stakeholder could express. We used the same stakeholder mapping software by Inpaqt again to make a value tree for every stakeholder. Value trees can be used to identify a hierarchy of values [36]. For each stakeholder, our project team discussed possible value expectations of Infectionmanager. The next step was to assign a level of importance to these value expectations. We assigned a number between 1 and 5 for each value and its attributes. Not only can this method prioritize stakeholders with many (high-ranking) value expectations, but it can also provide an overview of possible value needs and how these values and their attributes are linked with each other. In this example, providing information for high-risk patients with the Infectionmanager (the attribute "information") would not only affect the value "be informed" but also the values "feeling better," "empowerment," and "peace of mind".

In Figure 5, we show an example of a value tree with possible values (diamonds)—expectations of a high-risk patient group—as well as attributes (blue boxes) that detail these values.

Figure 5. Example of value tree with possible values expectations and attributes for high-risk patients.
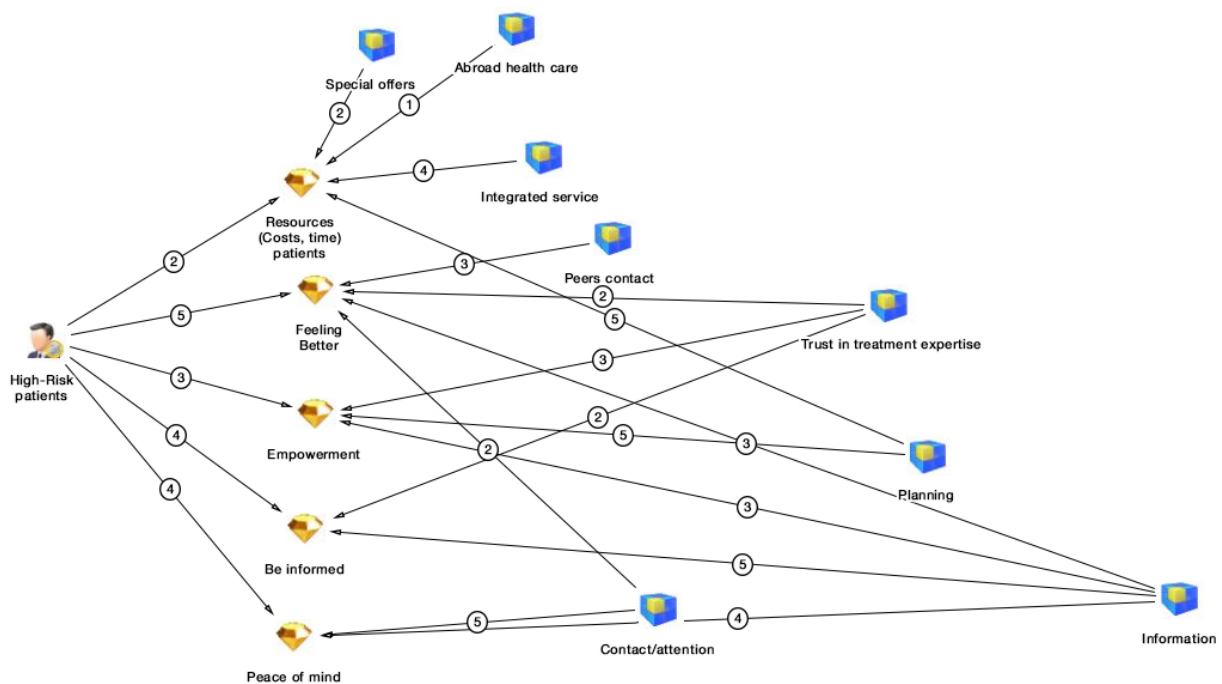
Gaps/Lessons Learned

- This method is a start to understand who the possible important stakeholders are and to prepare a general impression on what to expect as value needs for the technology and implementation.
- It helps to understand the linkage of values. For example, the same values can be shared by multiple stakeholders or values can influence the technology on several places and vice versa.
- Theoretically, this "basic stakeholder analysis" method does not truly involve stakeholders because it is done by experts. To make this method less expert driven and more stakeholder driven, stakeholders can partake in the stakeholder analysis sessions as well.
- Doing this digitally can be a bit more difficult as during the brainstorming sessions a researcher has to real-time model while conducting the discussions, although this is very convenient for continuing and sharing the session results.
- The analysis remains subjective and rather high level or abstract as you try to draw an overall picture of all possible views of all possible stakeholders with experts.
- Experts only see their part of the process, and thus, their conceived values may be biased.

Stakeholder Analysis Method Number 2: Stakeholder Salience

In Theory

A popular method to determine the importance of stakeholders is the stakeholder salience approach proposed by Mitchell et al

[33]. They defined stakeholder salience as the degree to which managers give priority to competing stakeholder claims. Salience is based on 3 attributes that can be classified, namely, power, legitimacy, and urgency (Figure 6). *Power* is defined as "a relationship among social actors in which one social actor, A, can get another social actor, B, to do something that B would not have otherwise done." *Legitimacy* is defined as "a generalized perception or assumption that the actions of an entity are desirable, proper, or appropriate within some socially constructed system of norms, values, beliefs, and definitions." Finally, *urgency* is defined as "the degree to which stakeholder claims call for immediate attention." Based on the 3 attributes, Mitchell et al [33] defined 9 possible stakeholder classes for classification. It is out of the scope of this paper to elaborate on each class, but in short, stakeholders who score on all 3 attributes are definite stakeholders, and thus, key stakeholders. Stakeholders who score 2 of 3 are relatively dominant, dependent, or dangerous stakeholders and should also be included. Stakeholders who only score 1 of 3 are dormant, discretionary, or demanding stakeholders.

Stakeholder salience can be determined by experts in the aforementioned expert brainstorm sessions or project meetings, or by stakeholders themselves using a questionnaire, one-on-one interviews, or a focus group.

Figure 6. Stakeholder salience diagram according to Mitchell et al [34].
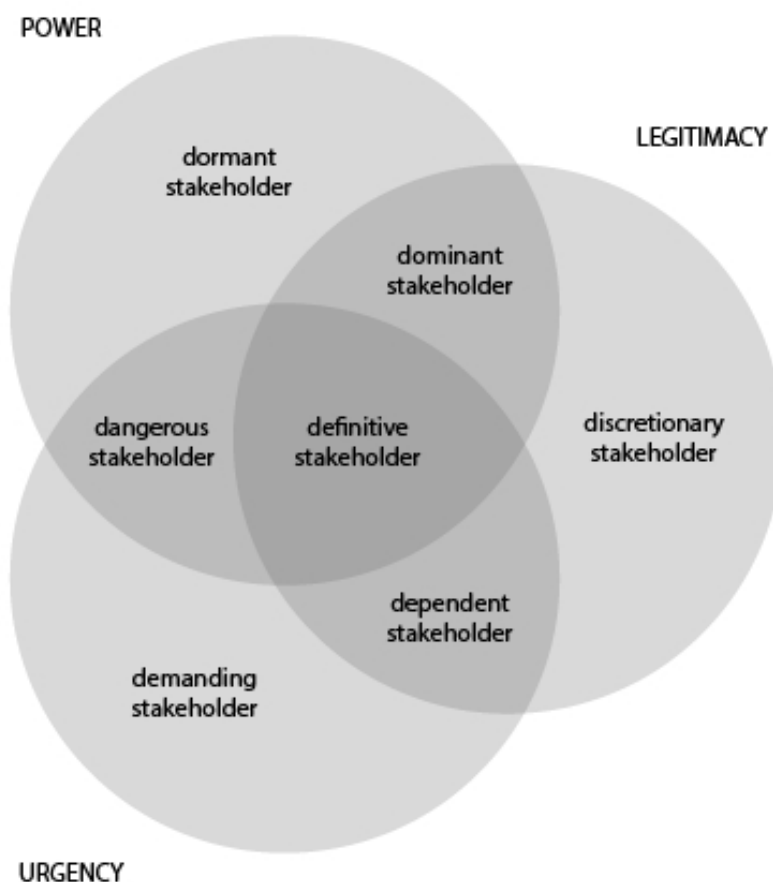
Example Case

We first arranged expert interviews to rate the infection control stakeholders, according to Mitchell's salience. We asked 2 infection control experts to rate stakeholders on whether they have power, legitimacy, and urgency. We then sent a questionnaire to stakeholders who according to experts were the "definite stakeholders" [32]. Table 2 shows a fragment of our salience assessment.

Practically, we learnt that these 3 attributes of salience (ie, power, urgency, and legitimacy) are difficult and had to be explained in more general, nonbusiness-specific terms to the experts and stakeholders: We explained power as "the level of

influence a stakeholder has in infection control." Legitimacy was explained as "the level in which a stakeholder needs to be legally, morally, or contractually involved in infection control." And finally, urgency was "the priority or necessity of the stakeholder in infection control." It is crucial to keep these terminologies and definitions consistent [31].

After comparing the stakeholder salience expressed by stakeholders and by experts, we could validate and draw consensus in both results [32]. The differences were that experts mentioned the Ministry of Health as important and stakeholders did not, and stakeholders found the National Institute for Public Health and the Environment, nurses, and veterinarians more salient. We added these 3 to our final definite stakeholders list.

Table 2. Example of a classification of infection control stakeholders using Mitchell's stakeholder salience.

Stakeholder	Power	Legitimacy	Urgency	Type
Medical specialist/physician	X	X	X	Definite
General practitioner (GP)	X	X	X	Definite
GP assistant	—	X	X	Dependent
Clinical microbiologist	X	X	X	Definite
Nurse	—	X	X	Dependent
Pharmacist	X	X	X	Definite
National Institute for Public Health and the Environment	—	—	X	Demanding
Dutch Working Group on Antibiotic Policy	X	X	X	Definite
Medicines Evaluation Board	X	X	—	Dominant
Insurance companies	X	—	—	Dormant

Gaps/Lessons Learned

- This salience approach is the most commonly used method to assess the importance of stakeholders, and thus, can be seen as a widely acknowledged method. It is also a commonly used method for stakeholder assessment in eHealth research.
- Determining which stakeholders are definite stakeholders—in-turn important for implementation research—is feasible using Mitchell's stakeholder salience. This is especially true when it is necessary to bring the number of stakeholders down to a manageable number to actively involve them in the implementation research.
- The 3 salience attributes (ie, power, legitimacy, and urgency) are difficult concepts. They might overlap and as they are explained in business terms, they are also complex to properly explain to stakeholders. The researchers have to be consistent in the explanation and make sure the stakeholders understand the difference.
- Subsequently, there is also a risk that stakeholders do not fully comprehend the attributes and give answers based on gut feelings or what they expect should answer. Therefore, as the researcher, one needs to be alert and ask for short elaborations.
- The stakeholders who score all 3 attributes of salience are important stakeholders to be involved in the project; however, with a high number of stakeholders, it is important that further analysis is carried out to identify those stakeholders who scored 2 (or maybe even 1) of 3 attributes and include them in the list. This depends on the number of stakeholders and keeping it manageable for research purposes.

Stakeholder Analysis Method Number 3: Ranking/AHP

In Theory

Another way to classify the importance of stakeholders is by attributing an importance score to stakeholders. This scoring or ranking can be done in several ways. In our research, we used a 5-point scale and a derivative of AHP [37] as 2 methods for ranking:

- The 5-point scale is very straightforward. Hyder et al [21] proposed to articulate the power or importance of stakeholders using a 5-point scale. Experts or stakeholders themselves can assign 0 (not important) to 5 (very important) points to a list of stakeholders. Similar methods can deviate from the scale, eg, a 9-point scale [36] but different scales seem arbitrary.
- A mathematically more sophisticated method for ranking is Saaty's AHP [37], which is also applied in health care research [38]. It is out of the scope of this paper to explain how AHP works in full detail. In short, AHP is frequently used in the analysis for decision making. In AHP, the hierarchic relation (an eigenvector approach) of stakeholders weights their relative importance. Saaty's AHP technique becomes especially interesting when the hierarchy expands by also mapping values and attributes to stakeholders (as seen in the value trees in Figure 5). Using a mathematical construction, the number of values and hierarchic relationships determine a weighted outcome for every stakeholder, value, and attribute. It is a sophisticated method, but in our experience the most thorough analysis currently available.

Example Case

The software tool we used for ranking the stakeholders also allowed for a 0-5-point scale to rate the importance of stakeholders. We applied a simple hierarchic calculus based on the value trees. For example, a value with 5 points from a stakeholder with 5 points would get 25 points, a value with 5 points from a stakeholder with 2 points would score 10 points. This is slightly different to Saaty's AHP method as we did not apply relative weights and eigenvectors to avoid overcomplexity in the calculations. We assigned the ranking in a brainstorm session with experts as can be seen in Figure 7 and we did the same to values (as already shown in Figure 5). We did not rank stakeholder or values in an interactive session with stakeholders themselves in our example case, as it would be unfeasible to organize all stakeholders together.

Figure 7. Expert-based stakeholder ranking for infection control portal.
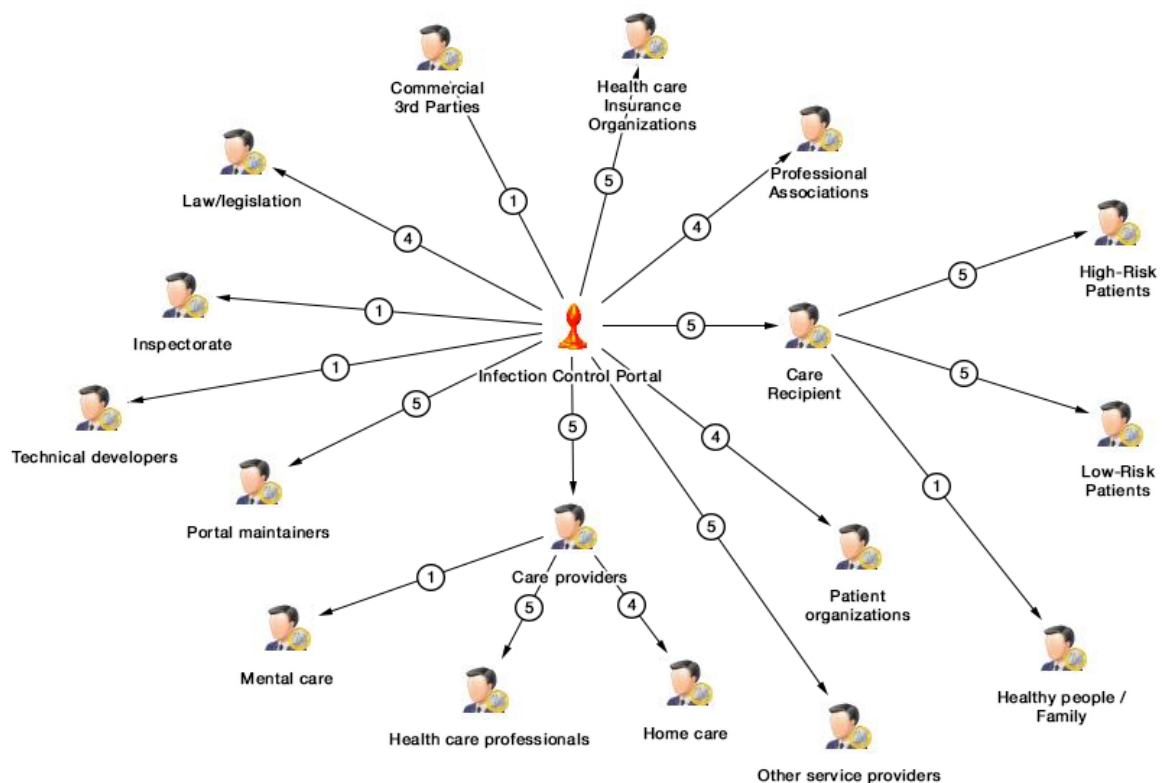
Gaps/Lessons Learned

- Ranking with numbers is a simple yet effective way to quantify and classify the importance of stakeholders.
- AHP can overkill and in practice a simpler calculation of [stakeholder× value × attribute] might be a good alternative.
- The 0-5-point scale is still an arbitrary quantification that is interpreted by stakeholders or experts. For example, what makes a stakeholder a 2 or a 3? The best way to get satisfying results is by validation by either asking multiple stakeholders to rank or to work toward a consensus.
- We did not choose to fully use AHP because it has to be done very thorough, as the hierarchy will determine the importance through eigenvectors. If 1 stakeholder or value is lacking, results may become counterintuitive [37]. More research is needed on this.

Value Co-Creation Dialog

After the stakeholders are analyzed and it is known whose input to the implementation of the eHealth technology is more important than others, it is time to start with value co-creation. We define a "value" as an ideal or interest a (future) end user or stakeholder aspires to or has [29]. These values can be further detailed into "attributes." An attribute is a summary of the need or wish that is spoken out by the (future) end user or stakeholder [29]. Still, "value" remains a difficult concept to concisely communicate as this can elicit philosophical debates on what is good and bad. The eventual eHealth technology and its surrounding services to embed it properly in its intended care setting all encompass the value of the eHealth technology.

Value co-creation is a joint activity involving customers to identify values from their perspective [39]. In other words, with co-creation, stakeholders get an active dialog and co-design the development process of eHealth. In addition, for most stakeholders, value is also a difficult business concept to grasp. One cannot simply ask, "Ok, what value do you expect?" In fact, in most cases the stakeholders cannot even grasp what the technology will be like, nor how it can be used. The researcher has to prepare relevant value co-creation questions and have a discussion with all key stakeholders about their value expectations.

We herein demonstrate 2 possibilities as to how we conducted these value co-creation dialogs: process analysis and stakeholder interviews using the business model canvas.

Value Co-Creation Dialogs Method Number 1: Process Analysis

In Theory

To co-create value, Prahalad and Ramaswamy [39] noted that a joint problem definition and problem solving are required. To facilitate this process, the authors recommend the DART method:

- have "dialogs" with stakeholders about their experiences;
- get "access" to information;
- assess "risks" and benefits with stakeholders; and
- be "transparent" with information.

We combined these 4 with ideas of the contextual inquiry of our road map that recommends performing interviews or focus groups using a scenario-based problem analysis. Focus groups

offer an opportunity to obtain insights regarding the experiences, observations, and opinions of group members [40]. As Prahalad and Ramaswamy [39] point out, to understand the individual experiences for co-creation, the problem analysis, inspired by action research, sense making [41], and previous research [42], should encompass a general discussion of the entire process, including individual tasks, information, and communication needs, as well as the problems experienced and bottlenecks.

Example Case

We organized a workshop for a focus group in a pulmonary ward, inviting stakeholders relevant for ASP [30]. In this workshop, we asked stakeholders about the problems they experienced (general), process bottlenecks (coordination, communication), and information needs (communication, documentation). Stakeholder role playing (enact a situation or process) is mentioned as a possible way to determine importance and value needs of stakeholders [43]. Thus, we started a quick role play of "Who does what?" with the process behind antibiotic prescription for a complex patient. For each topic, we prepared a poster on which stakeholders could stick written Post-its with possible values, and group them in importance. The main problems that were mentioned were regarding the information flow of patient information and insufficient cooperation and consultation between the attending physician and microbiologists again due to inefficient information sharing as well as due to unstructured procedures for consultation. Some stakeholders also noted that an insufficient knowledge of (new) procedures or application of medication might cause problems [30]. An interesting find was that nurses could play a big role in ASP.

Gaps/Lessons Learned

- Value creation with a focus group approach allows for a discussion, and therefore, when talking about processes, problems, or tasks, stakeholders can directly respond to each other, allowing co-creation through agreement and consensus on possible positive and negative values.
- This discussion itself can already be an eye-opening experience for stakeholders. On several occasions, a stakeholder admitted, "I did not know that you were experiencing that (as a) problem," which suggests that discussions create more understanding for each other and willingness for improvement or change.
- Stakeholders might not express all problems or play them down due to the presence of other stakeholders.

- Through this approach, stakeholders will mostly discuss problems and opportunities to change these problems. They might not express them exactly as values but more as attributes. In that case, after recording the focus group sessions, researchers need to extract values from the transcript that are relevant to the technology and its implementation [29].
- In this step also eHealth opportunities can be discussed that can help ideating possible eHealth technology in collaboration with the (technical) design researchers.

Value Co-Creation Dialogs Method Number 2: Business Model Building Blocks

In Theory

For this approach, we started with a business model as a basis to discuss values. A business model mediates between technology development and its intended (economic) value creation [6,35]. In other words, it can be used to explain the value creation logic necessary to create a successful piece of technology. Likewise, a business model can explain the rationale behind implementing eHealth technology [4]. The most commonly used framework for making a business model is the business model canvas by Osterwalder and Pigneur [8]. Their business model consists of the following 9 building blocks: value propositions, customer relationships, channels, customers, key activities, key resources, key partners, cost structure, and revenue streams. These building blocks can guide questions regarding the necessary values for implementing eHealth. Although Osterwalder and Pigneur [8] proposed several questions for each building block, these are targeted toward high-level strategic management. The trick is to transpose these questions to the intended eHealth technology and ask which values are necessary for that eHealth technology to be successful.

Example Case

We took the building blocks of the business model canvas and organized them into 4 main topics for questions on necessary values for implementing ASP, taking the mentioned problems and bottlenecks during the focus group into consideration when preparing questions. Table 3 presents some questions used. Each of the 4 topics has a central question that needs to be answered, with several subquestions. We then organized 1-hour, one-on-one interviews with stakeholders and used this questionnaire as a basis for the interview.

Table 3. Example of topics based on business model components.

Building blocks	Central question	Explanation
Value proposition (the technology and its services)	What value should antibiotic steward-ship (ASP) offer?	The value proposition is basically the to-be-developed platform for ASP. We prepared concrete questions like "What value does ASP need to deliver to you, to your department, and to the hospital?," "What problems does it help to solve?," "What technology and services can we offer to you?," and "What do you deem really necessary to be satisfied with ASP?"
Customers, key resources, and key partners (the stakeholders)	Who are the stakeholders?	Here we focused on all human interactions relevant for ASP. We asked which stakeholders (people or organizations the stakeholder interacted with, or should interact with for ASP). We made a list of stakeholders, described their role briefly, and ranked their importance. We also asked for external stakeholders who may be relevant for ASP as, in general, stakeholders tended to respond from their internal, hospital perspective.
Key resources and key activities (the infrastructure)	What is the required infrastructure?	We asked "How can ASP be integrated with your daily routine?" Regarding possible resources, we asked what tools, means, documents, sources, or people were necessary for ASP and their importance. We had to steer the stakeholder by asking specifically whether a certain technical infrastructure is needed, what technical medium, which data flows and connections or systems are relevant to assess the needs for eHealth technology. We also steered by asking what knowledge is further required, in terms of support from people or literature to have an ASP to assess what resources are specific to ASP.
Costs and revenues (the added values)	What are the success factors?	We avoided monetary discussions with stakeholders. Costs and revenues are always a difficult subject as there may be many benefits not directly linkable to 1 particular stakeholder. In the focus group we organized earlier, stakeholders stated there is a trade-off between quality and efficiency regarding ASP and that they should be balanced [30]. Therefore, we chose to ask for effects and success factors. We asked what the expected effects on patient outcomes (eg, length of stay, mortality, treatment duration, patient safety) would be and their relative importance and whether other quality aspects not directly related to the patient are relevant. We did the same for efficiency, and so, what are the important outcomes for efficiency (costs, less usage of antibiotics, fewer complications, etc) and their importance.

Gaps/Lessons Learned

- One-on-one interviews allow for in-depth analysis of possible values and critical success factors for implementing an eHealth technology and results in a deeper discussion and understanding of each stakeholder's value expectations. Not only are values expressed, but it is also elaborated why they are important.
- From our experience, we advise that the questions need to be concrete enough for stakeholders to give satisfying answers. If the questions are too abstract, the answers will be equally abstract and thus less useful.
- It is important that the interviewer focuses on what the technology should contribute, not design or requirements. It is not about how they want the eHealth solution to be, it is about the why.

Business Model Generation

As "business modeling" suggests, the eventual output is a business model. Exact visualizations of business models are diverse and there is no unanimous agreement on what they exactly should look like or the level of detail they should contain [7]. This is also why there is neither a dominant design nor many tools available for making business models. A popular method for visualizing a business model is the business model canvas [8]. Although this canvas is perfect at abstracting and visualizing key elements that should be *in* a business model,

comprehensive step-by-step instructions on *how* to retrieve the detailed narrative for these key elements remain rather abstract and is therefore mostly targeted at high-level strategic management. However, existing templates or blueprints such as this business model canvas are useful to make a model representation of an implementation of health care technology [4]. We also used this business model canvas as our template for a business model.

Business Model Generation Method: Business Model Canvas

In Theory

The business model canvas (Figure 8) consists of 9 building blocks that can describe the whole rationale of an implementation. In the middle block is the value proposition, the eHealth technology in this case. The top 3 blocks on the left-hand side of the model deal with the required organizational and infrastructural aspects, that is, the key activities, resources, and partners. The top 3 blocks on the right-hand side deal with who the customers/users are and how to interact with them. At the bottom are the financial aspects. Creating and offering values generate costs, and a revenue model is necessary to capture value back to at least cover these costs. This canvas can be used as an empty framework or blueprint to fill with critical success factors that describe the implementation of an eHealth technology.

**Figure 8.** Business model canvas by Osterwalder and Pigneur [8].
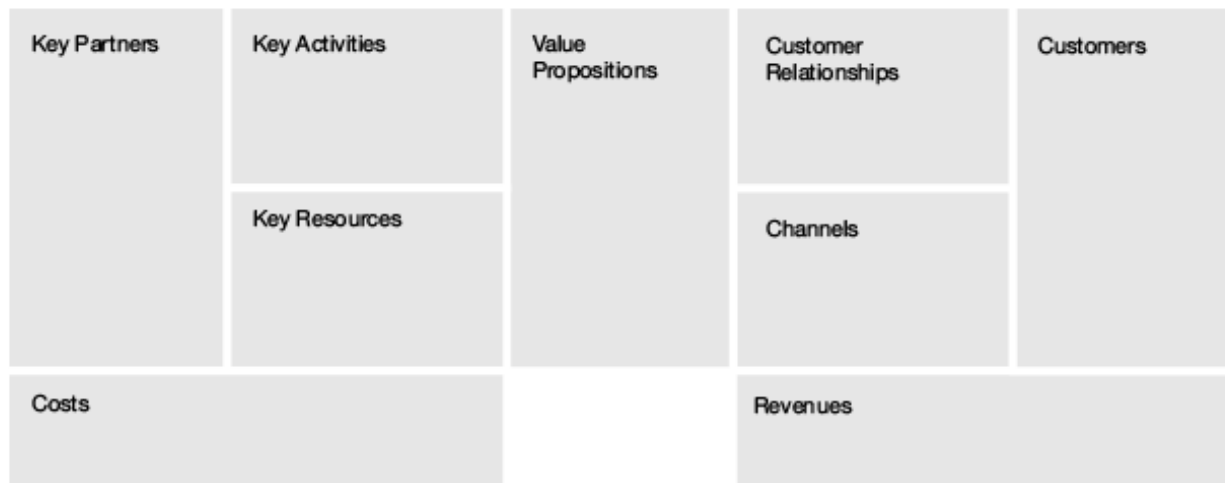
Example Case

We made a business model (Figure 9) filled with the values that were concluded using the focus group and one-on-one interviews as delineated in the previously explained value co-creation methods. We listed critical success factors that are our translation of expressed values and attributes.

This business model in Figure 9 gives an overview of relevant critical success factors that determine the success of ASP and

what role Infectionmanager can play in ASP. It pinpoints critical values that the technology needs to offer to be valuable to stakeholders, critical values that need to be made available in the infrastructure to guarantee feasibility, uptake, and sustainability. This business model also gives an idea about financial opportunities that are available to make Infectionmanager self-sustainable. To sum it up, this business model provides a bird's-eye view of all critical success factors to implement our Infectionmanager.

Figure 9. Business model canvas filled with critical success factors.
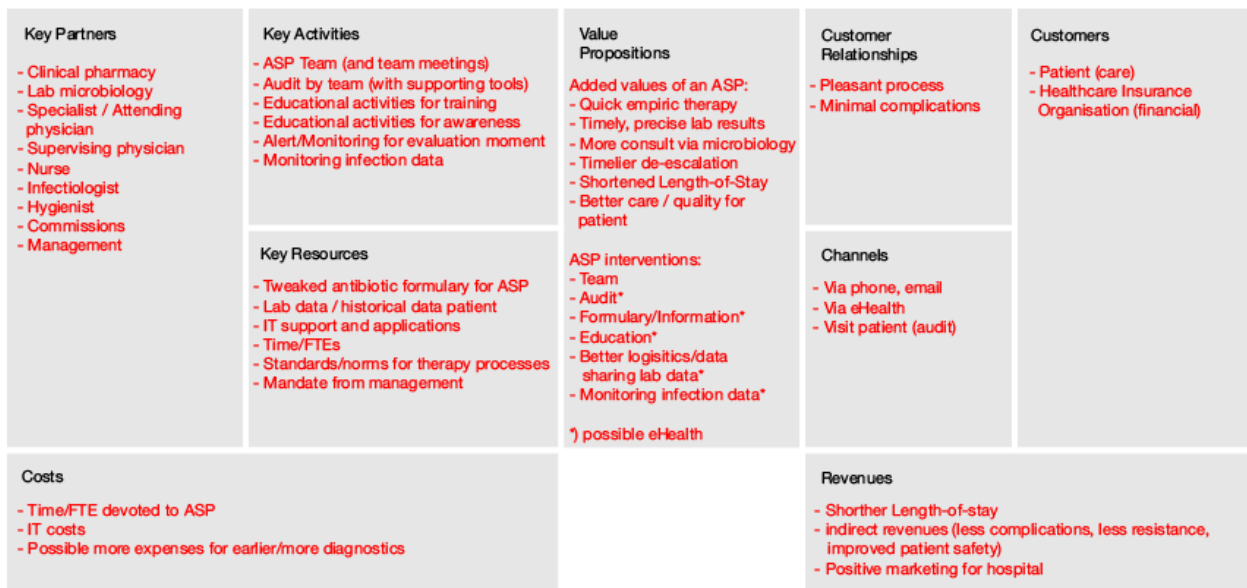
Gaps/Lessons Learned

- A business model can give an overview of the critical success factors for implementing an eHealth technology.
- The level of detail depends on the dialogs with stakeholders, and therefore, the completeness of the business model depends on the (successful) completion of those earlier research steps.

- This is still only a model that reflects a possible (maybe even multiple) implementation. It still needs to be explained to others and practically expanded on to put the eHealth technology "live."

Results

Stakeholder Analysis and Co-Creation of Values

Stakeholder analysis and co-creating values for a business model with them is a progressive journey to understand the global context and problems and to gradually work toward an in-depth, individual dialog with stakeholders to understand what they find important to the technology and its implementation. By exploring several stakeholder-oriented methods as part of business modeling as delineated in the "Methods" section, should we have to start implementation research anew from scratch, we would suggest the business modeling steps presented in Textbox 2.

Textbox 2. Step-by-step guideline for stakeholder involvement for business modeling in eHealth technology implementation.

Business modeling steps for implementing eHealth technology (arranged stepwise):

1. Start with a literature review on comparable interventions to get a feeling for the domains, jargon, and global issues and stakeholders.

2. Involve 1 or 2 domain experts in the research and development team to reflect future findings, ideally experts who have an affinity with technology and research processes.

3. Make an overview of all possible stakeholders based on literature on comparable interventions in the domain.

4. Assign stakeholder types to possible stakeholders, verify if certain types are missing and why.

5. Validate the entire overview by snowball sampling a complete stakeholder list with these key stakeholders.

6. Let experts select key stakeholders from the complete stakeholder list.

7. Organize a focus group with at least one in-person representative of each key stakeholder:

   - Start with discussing each stakeholders' role in the current processes.

   - Let them complete the stakeholder list for missing stakeholders based on the process.

   - Ask stakeholders to rank the importance of stakeholders, or alternatively let experts do it later.

   - Discuss what bottlenecks are experienced.

   - Discuss opportunities for improvement and opportunities for eHealth.

8. Summarize bottlenecks and opportunities and determine with the research team which opportunities are there for eHealth technology and whether these fit the project goals.

9. Ideate an eHealth technology (when possible, make mock-ups or a prototype of the ideas).

10. Plan interviews with stakeholders, or if possible, multiple stakeholders of the same stakeholder type, for value co-creation dialogs for the ideated eHealth technology.

11. Prepare the value co-creation dialog interview with questions that address all business model components (also prepare subquestions that propose possible ideas or values on each business model component to help the interview along. Focus on what the technology should contribute to their daily routines, not technical requirements).

12. Code transcripts of the focus groups and interviews, extract all implementation-related comments and combine all values and critical factors in the business model canvas.

13. Discuss the resultant business model with the research team.

14. Optionally, for transparency and extra validation, explain the business model to stakeholders and let them reflect on it or write a document that explains the implementation strategy based on the business model as the model itself may be unclear to share with the relevant stakeholders.

Gaps/Lessons Learned

To further substantiate the guideline, we conclude the following main lessons from the gaps and lessons learned from our implementation research, for which the aforementioned guideline will help:

- Understanding the context beforehand is crucial to find the right stakeholders and to understand their problems and opportunities for eHealth. As an eHealth researcher, you will have to familiarize yourself with the relevant domains. In our example case, we read up on antibiotics and microbiology literature. If the domain is not your core expertise, involving an expert from the domain is a must to help validating the research.

- Identifying stake*holders* is easier than identifying their *stakes*. Stakeholder analysis is a complex task and needs to be done thoroughly to understand which stakeholders play a key role in the implementation of eHealth technology. Our advice is to discuss it with a group of stakeholder or combine multiple analyses so that outcomes can be compared.

- Co-creation requires incorporating multiple perspectives. Eventually, everything is joined in an implementation. When important stakeholders have different or even incompatible views on the implementation, this will become a huge problem for the technology. All effort should then go toward finding a consensus or a workable trade-off between values.

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- Values are tough constructs. Business modeling is about discussing values, but stakeholders usually do not express their views in terms of "greater goods," but in to-the-point, pragmatic statements of what they want or what should be changed. It is up to the research team to interpret and combine these statements into high-level values.
- Business models are not all about money. Health care is a complex market in which, for example, quality of care or patient safety can be much more important than cost savings or maximized profits. Therefore, the values to discuss are truly "greater goods" and not only money flows.
- An implementation is never finished. Every environment is dynamic, so stakeholders change, business models change, technologies change, etc. The technology needs to be evaluated and when outcomes are getting unsatisfactory it may be worthwhile to redo the business modeling steps iteratively to see what has changed and how these changes can be anticipated.

Discussion

Preliminary Findings

In this paper, we propose a guideline for business modeling with stakeholder-oriented analysis methods for implementing eHealth. The aim of this guideline is to co-create an implementation for eHealth together with stakeholders, by identifying and analyzing stakeholders, discussing co-creation of value with stakeholders, and determining a business model. Once all values are captured in a business model following the step-by-step guide, the model can be used as a basis to disseminate or further detail the design and implementation of the eHealth technology.

We saw that most applications of business models in eHealth (*if* applied that is) are usually based on generic, strategic models or concocted by experts without truly involving stakeholders in the process. In that regard, there is little to no co-creation with stakeholders. The proposed guideline may seem a lot of research and time consuming, but if it can avoid misaligned plans or expectations, lack of uptake, or even design mistakes, it should be worth to spend that time and effort in business modeling.

Because only few frameworks or guidelines are available for business modeling, we chose a pragmatic approach for determining a guideline that can be used in future implementation research. The CeHRes road map (Figure 1) originated in the search to combine "design research" with "implementation research" for a holistic approach for health care technology development. Design and implementation influence each other; hence, a holistic view that combines both is essential for the success of health care technology [4]. Health care technology development is a multidisciplinary process [44]. However, in the field of health care, a multidisciplinary and participatory approach toward development is novel as many of these projects are still expert or eminence driven. This causes problems, as experts also are biased in how they perceive the setting. Policymakers or management see the big picture and understand the global problems a technology needs to address, but still details necessary for implementation can only be understood by talking to those who are directly influenced by the technology.

Stakeholder analysis theory is less scarce than theory on business modeling. In fact, there are many methods in the academic field such as stakeholder theory, policy making, or requirements engineering. Yet, all these possible methods have to be combined in the context of eHealth development. eHealth brings multiple domains of research together; thus, it calls for experimenting with combinations of multidisciplinary research methods. We believe this guideline is a first step toward a very pragmatic approach to think about an implementation for eHealth technology with the essence that stakeholders should be involved in the entire process.

Whereas other implementation theories such as normalization process theory [45], service, technology, organization, and finance model [46], human, organization and technology-fit [47] focus on advising possible factors that influence eHealth implementation, we focused on obtaining such possible factors from stakeholders themselves. Although the aforementioned methods may be successful to find an implementation, we believe that the focus on stakeholders helps to make the technology fit their daily routines and environment in a bottom-up approach. It basically emulates the principles of user/human-centered design, by co-creating an implementation with stakeholders. Instead of a top-down approach in which experts work with a preset of possible critical factors, we apply a bottom-up approach by extracting possible critical factors from what stakeholders deem critical for implementation.

Considering the difficulties with implementation of eHealth as we laid out in the "Introduction" section, we found that describing a pragmatic approach for co-creating an implementation with stakeholders may spur others to be more transparent in how they did it. Instead of reinventing the wheel or repeating the same mistakes again, eHealth projects can learn from each other by giving more insights into the steps that were taken to implement the technology.

Limitations

The presented guideline also has some limitations. First, this paper only demonstrated 1 example case. We applied individual methods or parts from the guideline in parallel to eHealth research based on our CeHRes road map [4,42,48-50], yet further validation of its generic use as a complete framework for other eHealth projects is necessary. It is certainly worthwhile to test the guideline in different research settings as well as compare differences in the results of its methods to see what works best under different conditions.

Second, the proposed activities can be very thorough and time consuming. Going through them faster or being less thorough is an option when time or resources are limiting factors. This suggests opportunities for future research to determine which methods are crucial or which can be left out or possible quicker or discount variants on the methods to find a balance between investing minimal time and satisfactory results. For example, it would not make sense to spend a few years researching the possible relevant stakeholders in a quickly changing environment like eHealth and technology.

Finally, this paper was written over time while exploring all instruments for business modeling, and therefore, our choices for these instruments were based on our good and bad experiences and constraints posed by our projects.

Future Research

We applied the business modeling steps in our example case and also applied them in other projects to test whether they can be used in various projects. In future road map-related publications, we plan to further expand on the business modeling steps and their applications to other eHealth projects. At present, there is 1 eHealth project on zoonoses that is starting with the stakeholder identification and analysis steps. In another eHealth project on dermatology, our business modeling steps are also applied thoroughly and can be published as a second example case.

Conclusions

A successful, sustainable implementation of eHealth technologies is still a tough nut to crack for many eHealth projects and we believe that more involvement of stakeholders in the whole development process of eHealth, and not only designing the actual technology but also designing its implementation can improve the overall success of the eHealth project. Having a dialog with stakeholders about their value expectations will help researchers and developers—as well as all involved stakeholders—to understand what and why they are developing eHealth technologies. We hope we can spark others to work with our proposed guideline, or try stakeholder involvement and business modeling, to advance research in the implementation of eHealth.

Conflicts of Interest

None declared.

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Abbreviations

AHP: analytic hierarchy process
ASP: antibiotic stewardship (program)
CeHRes: Center for eHealth Research

Original Paper

Feasibility of a Website and a Hospital-Based Online Portal for Young Adults With Juvenile Idiopathic Arthritis: Views and Experiences of Patients

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Abstract

Background: To improve knowledge and to encourage active involvement of young adults with juvenile idiopathic arthritis (JIA), an informative website with written and video information and an online portal with access to the personal medical record, self-monitoring, and e-consult functionalities were developed. Before implementing these applications in daily practice, it is important to gain insight into their feasibility in terms of ease of use, perceived usefulness and intention to use.

Objective: The aim of this study was to evaluate and to examine the feasibility of the website and the online portal for young adults with JIA.

Methods: A qualitative, feasibility study was conducted among the first users: 13 young adults with JIA. After provided access to the website and online portal, patients were interviewed on perceived usefulness, ease of use, and intention to (re)use the applications.

Results: Participants in the study considered the website and online portal as useful and easy-to-use. New medical information and feedback would motivate them to revisit the applications again. On the website, videos showing other young adults, telling how they handle their condition, were found as the most useful. On the portal, access to their medical records was most appreciated: it made the young JIA patients feel in control and it helped them monitor symptoms and disease activity. e-consults were thought to facilitate communication with physicians.

Conclusions: The young adults considered both the website and the online portal as feasible, but they also had valuable suggestions to improve accessibility and use. Based on these findings, a news and event section was added on the website and a direct link was made to a discussion board and social media. To provide and support health information, the website is actively used in daily care. Considering the online portal, the use of self-monitoring tools and e-consult can be stimulated if there is direct linkage to treatment and feedback from the multidisciplinary team. Feasibility testing, before implementing the website and online portal in daily practice, has proven to be a valuable step. Results led to improvements in terms of integration into standard care and topics for further research.

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Introduction

Living with a chronic rheumatic disease is challenging at any age. However, these challenges may be particularly difficult for young adults with juvenile idiopathic arthritis (JIA), since their chronic condition and treatment affect both physical and socio-emotional development [1,2]. One of the main challenges young adults with JIA have to deal with is to take over from their parents the responsibility for their own illness and treatment: they have to become a self-manager [3,4].

In general it is believed that eHealth might contribute to self-management, especially for young adults [5-7]. For this study, we followed the definition of eHealth by Eng: "The use of emerging information and communication technology, especially the Internet, to improve or enable health and health care" [8]. The use of health information websites and eHealth applications, including online portals in disease management, disease prevention, and health promotion is well-reported [9,10]. Unfortunately, many eHealth projects fail to survive the pilot phase and studies that focus on the effectiveness of eHealth applications often do not show any long term effects [9-11]. Also, much is developed but not everything is used [10,12,13]. For the actual use and acceptance, evaluation and testing of the feasibility before implementing the techniques in daily practice is crucial [11,14-16]. Several frameworks have been introduced to increase the uptake and to examine the feasibility of eHealth applications. Among them, the technology acceptance model (TAM) [15,17] stands for a prediction and explanation model of the end-users reaction to a technological innovation. The model states that use or acceptance of a particular innovation can best be predicted by an individual's intention to (re) use the innovation. A comparative model, the Holistic Framework of Gemert [11] suggests that developers of eHealth applications should be aware of interactions between technology, people, and their social-cultural environment. Involvement of end-users in developing eHealth applications is considered to be one of the crucial aspects of acceptance of the tools themselves.

In our specialized transition outpatient department, young adults with JIA and their parents receive multidisciplinary care from a pediatrician and a clinical nurse specialist, in order to support the process of acquiring self-management skills and to guarantee a well-coordinated, continuous process of health care between child and adult [5]. To improve knowledge of the disease and to encourage active involvement in this transition process, we developed an informative website and a hospital-based online portal. The website contains information about medical issues and how to deal with consequences of having a rheumatic disease, such as feeling blue, exercise, work, study, relationships and intimacy.

With our secured online portal the young adult has direct access to his medical record; he is enabled to send an e-consult and may use self-monitoring tools including activity diaries and pain questionnaires. These applications were developed in close cooperation with patients to fit the applications to the specific needs and preferences of this group. Therefore, young adults of the Dutch Youth Network of Rheumatology were asked to perform a central role. In interactive workshops, organized by the multidisciplinary team of the transition outpatient clinic, they determined, together with the professionals, the content and structure of the website and portal.

Both applications may be promising to reach young adults with arthritis and to stimulate their self-management behavior, given their access to and high rates of use of the Internet [7,18,19]. Before implementing these applications in daily practice, it is important to gain insight into their feasibility. Therefore, the aim of this study is to evaluate and to examine the feasibility of the website and the online portal for young adults with JIA.

Methods

Design

A qualitative feasibility study with semistructured, (audiotaped) interviews was conducted among the first users of both eHealth applications in order to explore the views and experiences of the young adult JIA patients with regard to the feasibility outcomes: ease of use, perceived usefulness, and intention to use. These outcomes are part of the technology acceptance model [17]. The model states that use or reuse of a particular technical innovation can best be predicted by an individual's intention to (re)use the innovation. This intention is determined by two components: perceived ease of use and perceived usefulness. Perceived ease of use means "the degree of ease, associated with the use of the applications". Perceived usefulness can be defined as the degree in which a person believes that using the technical innovation would enhance his or her personal situation.

Participants were asked to use the applications for three months "as needed", without specific instructions, and were interviewed just before or after their subsequent visit to the clinic.

Study Population

Patients diagnosed with JIA, aged between 16 and 25 years old, being able to read and write in Dutch, with access to a home-based computer with Internet were included in the study. Young adults who already participated in the development of the website and/or portal were excluded.

Recruitment took place at the transition outpatient department of the University Medical Center Utrecht, the Netherlands. All patients who visited the transition outpatient department within a period of three months were asked by their pediatrician or rheumatologist to participate in the study. An information letter and informed consent was handed out which they could return by post.

A convenience sample was used: all patients who returned the informed consent within two weeks after their visit were included in this study. Because it was a feasibility study with a qualitative design, we aimed to include at least 12 participants. According to the ethics guidelines of our hospital, the

nonexperimental and noninvasive nature of this study made ethical approval unnecessary.

Description of the eHealth Applications

The website and online portal are designed to improve knowledge, self-management skills, and involvement in treatment and care. The website (in Dutch) [20] is publicly accessible and contains information and tips on five themes: (1) treatment and medication; (2) physical exercise, holidays, alcohol, and drugs; (3) relations, sexuality, and pregnancy; (4) dealing with pain, fatigue, and emotions; and (5) study and work. In addition, videos and written stories from other young adults talking about their lives with JIA are presented.

For an impression of home page of the Dutch website, see Figure 1.

The portal (in Dutch) [21] is only accessible to JIA patients of the University Medical Center Utrecht with a personal log-in code. By using the portal, patients may have access to the following tools: (1) e-consult, through which patients communicate with a clinical nurse specialist; (2) their own medical record, including all written reports of physicians, laboratory results, present medications and appointments with the outpatient clinic; and (3) online self-monitoring, in which patients can fill out self-tests on pain and activities and diaries to monitor their disease.

For additional general disease information patients are referred to the website [20].For an impression of the portal and the e-consult tool, see Figure 2.

The content of website and portal are outlined in table 1.

Table 1. Content of website and portal.

Website, portal	Content
Website	
Transition	What is transition?
	Practical information about the departments, multidisciplinary team
About JIA	What is JIA?
	Treatment
Leisure	Exercise and sports
	Alcohol and drugs
	Holidays/vacation
Love, sex, and kids	Parents and friends
	Sex and intimacy
	Having kids
	Contraception, pregnancy, and heredity
Feeling blue	Having a rheumatic disease
	Feeling tired or having pain
	Relaxation
	Feeling depressed
	Adherence and treatment advices
School, work, and money	School
	Work
	Social insurance
Portal	
Medical record	Appointments
	Laboratory results
	Written reports of physicians
	Actual medication
e-Consult	Sending and receiving e-consults
Online self-monitoring	Medication diary
	Diary on fatigue
	Pain score
	Activities

Figure 1. Homepage of the Dutch website.

Figure 2. Portal and e-consult tool.

Data Collection

First, participants were asked to complete a brief questionnaire on demographics, illness characteristics, and their general Internet use. Subsequently, a semistructured interview was conducted at the transition outpatient department in a separate, quiet room, by a young independent interviewer (LWS), who was not involved in the care of the young adult.

The first part of the interview was directed at the informative website; in the second part patients' opinions and experiences about the portal were assessed. For both applications, open-ended questions, deriving from TAM were used to get insight into ease of use, perceived usefulness, and intention to (re)use (see Table 2 for an overview of questions). The interviewer encouraged participants to elaborate on all issues, using probes such as: "why?", "please, explain…", "Can you give an example?", "Can you think of any other …" At the end, the participant was asked to grade the applications with a number, where "zero" stands for "not useful" and "ten" stands for "the most useful".

Table 2. Interview questions on feasibility of the website and portal.

	Interview questions
Use	Have you visited the site/portal?
	Did you visit the site/portal with a specific reason?
	Which parts did you visit?
Perceived ease of use	Did you experience any difficulties in use of the site/portal?
Perceived usefulness	How useful is the site/ portal for you?
	Which parts are most/ least useful?
	Can you describe any benefits, or drawbacks?
	What are the most and least appealing parts?
	Do you miss anything?
Intention to use	Would you visit the site/portal again?
	Would you recommend the site/portal to others?
Suggestions	Do you have any suggestions for improvement?

All interviews were audiotaped. Field notes were made immediately after the interview to record the interviewer's impression of the responses to the questions and comfort level of the participants with the interview process. An interview lasted between 30 and 45 minutes.

Data Analysis

All interviews were transcribed verbatim. A generic qualitative approach was used for data analysis, including coding, constant comparison, and categorizing. Data collection and analysis were handled as an iterative process [22]. The first participant was interviewed with open-ended questions on feasibility and suggestions for improvement of the website and portal. In the following interview, the feasibility was asked again and the suggestions made by the former participant were checked. Then the participant was asked to add his own suggestions. The interviewer checked every interview if new themes emerged and asked further about these themes until saturation was achieved and no new information was obtained. The interviewer (LWS) and a member of the research team (JWA) reviewed and coded all transcripts independently. Relevant fragments were first categorized into the main concepts of TAM and were further categorized into subthemes, using inductive analysis. Results were discussed on several occasions and differences were discussed until consensus was reached.

Results

Participants

Thirty-eight eligible patients received an information letter and informed consent. Patients (n=19) who returned a signed informed consent were included in the study. No information is available from the other 19 patients who did not respond to the invitation to participate in the study. Six patients dropped out after giving their informed consent, with reasons of exacerbation of illness, vacation, and too busy with school. Finally, 13 participants received the URL address of the website and a log-in code for the portal.

The mean age of the sample was 20 years (range: 17-22 years) and consisted of 12 women and 1 man. Most of the participants (n=12) were being treated by a rheumatologist. The mean duration of illness was 8years (range: 2-20 years). Of the 13 participants, 11 were in high school, and two participants were gainfully employed. They all used the Internet on a daily basis, most participants (n=10) with an average of over two hours a day.

Informative Website

Of the 13 patients, 12 indicated having visited the website several times. One participant visited the website only once. During their visits, all participants had read at least a part of the written information. Most (n=11) had seen one or more videos and read written life stories. The primary reason for (re)visiting the website was curiosity. Other reasons included searching for specific information or for experiences of other patients.

Perceived Ease of Use

Participants did not experience barriers visiting the website. Two participants had issues with loading a video, in retrospect due to their own computer and Internet connection.

Perceived Usefulness

Participants appreciated the website and graded it with a 7.6 (min 6.5, max 9.5) on a scale from 1 to 10. They found the design of the website appealing and the information practical, clear, easy to read, and well-targeted to young adults.

> *This really is for younger people. I sometimes look at the SLE site but that is mostly for people who are 40, 50 and 60 years of age and their problems. That is not really my cup of tea. This really reveals itself to be more for younger ones.* [Female, 21 years]

Of all the elements, the videos and life stories were thought to be the best. They enabled recognition and showed new ways to deal with solving problems related to the condition. Patients experienced support and recognition in these stories.

I sometimes think that I am the only one with arthritis. There aren't many with the same problems. Other people don't understand this; they don't see anything on the outside. It is nice to hear people of the same age talking about this problem. That is what I have too! You won't have to say it yourself; somebody else says it for you and I feel the same things. [Female, 21 years]

It really helped me, especially how to cope with fatigue and pain and how to solve it. [Female, 20 years]

You can hear and read the experiences from others, things they had to cope with, how they dealt with them. Often you can learn from their experiences, because you recognize them. [Female, 20 years]

All five themes (in Table 1) on the website were appreciated positively. The participants thought nonmedical themes such as dealing with pain, fatigue, and emotions, physical exercise, holidays, alcohol and drugs, sexuality, study and work, were most appealing.

Some young adults missed detailed information on new developments in medication. Others missed a forum. They thought a link to an existing Dutch discussion board for young adults with JIA and to detailed information about medication on other reliable websites would be valuable supplements.

All participants, except for the youngest, indicated that no or only little new information was added to their knowledge and skills by their visit to the website. Nevertheless, the website was considered useful as a confirmation of what they already knew.

I read that it is important to structure your medication. You have to learn that this is important. Also that before visiting a doctor it's important to make a list with questions. All things you know but important to read again. [Female, 21 years]

I think I am beyond that age. I was 15 when I got arthritis. I think I would have had more benefit from this between my 15th and 18th. I'm beyond that now. I know what it is; I know how it influences my lifestyle, my alcohol use during the holidays. So I recognize all the subjects but I already have my own opinion about these. It doesn't add anything for me. [Female, 22 years]

The youngest participant felt she found new and relevant information on the website.

In the hospital, they always talked about JIA. I asked myself: what does that mean? I felt really stupid. I didn't dare to ask. I read on the website that it was Juvenile Arthritis, my disease. [Female, 17 years]

Finally, participants indicated that the website might be useful for questions of their relatives:

It is very convenient for yourself and your surroundings. My friend sometimes wants to know more and for him it is also a good site to refer to. It is clearly explained what the disease is and how to cope with it. [Female, 21 years]

In summary, the website was considered useful for three reasons: (1) to find or re-read information (mostly already known), (2) to help in explaining the disease and its consequences to others, but most importantly, (3) to find recognition, and to see that other young people struggle with similar problems.

Intention to Use

Half of the participants intended to revisit the website; the other participants however indicated that they would only revisit the website if new information were added, if news was added or if their personal situation changed. They all recommended the website to other young people with a rheumatic disease.

Online Portal

All participants (n=13) used the portal for a period of two to three months.

Within this relatively short time, access to medical records was used most often, whilst fewer participants used the tools for e-consult (n=4) and four other participants used self-monitoring (n=4).

Most of the participants logged in just after a visit to the hospital. "Curiosity about what the doctor or nurse had written" was the main reason to check their medical record. One participant logged in just before her visit. She wanted to prepare herself and read what was discussed during her last consultation.

Perceived Ease of Use

The only problem participants reported (n=5) was the log-in code being too long and complex to be remembered, whereas the code could not be changed. Consequently, they used the portal less often than they wanted.

Perceived Usefulness

Participants graded the portal with a mean grade of 7.8 (min 7.5, max 8.0) on a scale from 1 to 10, and mentioned several advantages (see Table 3).

Table 3. Usefulness of the different parts of the portal, as mentioned by the participants.

Mentioned effects, advantages	Example quote
Access to medical record	
Feeling more in control	*"It's very functional to be able to check your appointment, to check the blood values and what was said during a consult. Being able to control your own treatment." [Female, 22 years]*
Keeping pace with illness activity	*"You have the most recent values and you are able to compare them with the latest values. I once had a liver condition and could see that on the values, it was obvious." [Female, 20 years]*
Reminder tool	*"Recently I wondered what we agree on as treatment and medication and now I was able to look it up. Also when I had an appointment I found out that the appointment was half an hour earlier than I thought." [Female, 20 years]*
Being able to share data with others (parents)	*"My parents never accompany me and now I am able to show them the summary of the consult." [Female, 21 years]*
e-Consult	
Easier communication with the hospital	*"To send a notice is easier than phoning to the hospital. I send a message and it doesn't matter if it's inconvenient. If I call, it might be inconvenient." [Female, 22 years]*
Better communication with doctor/nurse	*"You're able to think things through and to explain it better." [Female, 18 years]*
Self-monitoring	
Facilitates communication with physician	*"If things become worse suddenly, it is handy because you know when it went wrong. The doctor is also able to see when it went wrong. Because sometimes I'm ill and when he asks I don't know when I was ill." [Female, 19 years]*
Provides insight into (the course of) the disease	*"Yes, especially when I thought I'm in pain and very tired, it immediately asks what have you done to prevent it and every time you're not able to answer this question you know that you should have been less active." [Female, 20 years]*

Four participants used e-consult, and they considered e-consult helpful because of easier and better communication with the hospital. It enabled the participants to think more about the questions and to explain it better.

Most participants could not think of any disadvantages of the portal; although one participant suggested other people might think access to medical data is not safe. One participant indicated that too much information about her health had sometimes overwhelmed her:

> *The first time I thought I wish I hadn't read it. That also applies to the website. However it is good to read things about it. It is about you and therefore scary. On the website it is about different people. The portal is very personal.* [Female, 17 years]

Participants mentioned various aspects of usefulness which are summarized in Table 3.

The access to their medical records was considered the best feature of the portal, because it enabled participants to check their appointment, to see all laboratory results, to re-read treatment plans, feeling more in control of their own treatment, but also keeping track of the progression of the illness was expressed. The portal also facilitated sharing these data with their parents.

The opinions on the usefulness of the self-monitoring tools were more diverse. Some participants indicated them as useful to discover why they experience more symptoms at certain times. Others stated that it provides insight into the course of their problems like having pain or being tired.

A few young adults stated that they did not like filling in diaries or monitoring tools and did not want to be too occupied with their condition.

Intention to Use

All participants intended to use the portal again, especially for access to their medical records and using e-consult. Some participants were certain they would not use the diaries and monitoring tools; other participants would use these in case of exacerbation of their JIA. Some thought they would use the tools only if their physician asked for it, or their physician would use the information during the consultations.

Participants suggested the portal might be even more attractive if elements were added, including a facility for online appointments, access to x-rays, printing forms for blood collection before the consult, and an overview of physicians and clinical nurse specialists and their consulting hours.

Discussion

Principal Findings

In this study, the first users of an informative website and an online portal with opportunities for e-consult, access to medical records, and tools for self-monitoring were asked to evaluate the feasibility of these applications on ease of use, perceived usefulness and intention to (re)use. Both eHealth applications were found easy-to-use, and the young adults considered them as "clear and understandable" and useful.

Informative Website

On the website, the videos were considered as visually appealing and interactive and as a more pleasant way to learn compared to written information. This appreciation of videos as a source of information was also shown in similar studies in patients with JIA of the same age [6,14]. After seeing other young adults with JIA talking about their lives, some participants felt able to deal/cope with their own condition more adequately. This might indicate effects of modeling and persuasive information, which in fact are methods for enhancing self-efficacy and self-management behavior [23,24]. Most participants indicated they did not encounter information on the website which was new to them, which might be explained because they were relatively experienced patients, as indicated by mean disease duration. The website might be especially helpful for the relatively inexperienced patients, which would be a valid reason for developing these tools preferably for younger patients and for patients recently diagnosed with JIA. These results are in line with data concluding that patients who feel insecure, concerned or inexperienced are more in need of health related information [25,26]. Otherwise, participants from this study indicated that changes in their personal situation and new information might encourage the patient to visit the website again. Based on these results, the website is now actively used at the transition outpatient department as the main source to provide and support health information. The young adult is stimulated by all members of the team to use the site for adequate, additional information. Also, a section with news and events is added to the website in order to stimulate re-visiting the website. In these sections, new information on "being young and having a rheumatic disease" is regularly posted. For this purpose, we created links to the website of the Dutch Youth Network on Rheumatology [27] and the Dutch Arthritis Foundation.

Online Portal

Participants indicated that access to their medical record was the most useful tool of the portal, increasing their feelings of being in control and helping them to monitor their symptoms and disease activity. Similar results are also found in a large study on access and usage of Web-based communication among adult patients with a chronic disease [28,29]. In our study, young adults "felt more in control" because they could check their appointments, blood values, and "what was said during a consult". Feeling more in control as part of perceived usefulness in relation to access to a patient portal was also positively rated and recognized by adults with type 2 diabetes [30], and adults with rheumatoid arthritis [31].

Participants in our study expressed the thought that e-consult may lead to easier and better communication with physicians. This result is also reported in other studies on use and acceptance of electronic communication among patients with cancer [32], where email or e-consult were preferred over telephone contact. The finding that most of our participants did not use the e-consult or self-monitoring tools might be attributed to the short period of time between receiving the log-in code and the interview (two to three months). Our finding that participants were only moderately enthusiastic about self-monitoring tools

is in concordance with qualitative data on the development of a health information technology mode: the uptake of self-monitoring tools and also e-consult is stimulated if both have a linkage to treatment and to feedback from physicians [25,33]. Consequently, in the implementation phase, the multidisciplinary team will stimulate the young adult to use the tools. Also, the team will address active responses.

Limitations of the Study

Limitations for this study include participation of only a small group of first users of the applications. Although the sample seems to be representative as to age and illness duration [34], given its small size along with the aim of this study, generalization to the whole population of young adults with JIA is limited. Because it was a convenience sample, no effort was made to recruit the same amount of men and women, which resulted in a high percentage of women in this study. Although JIA is more prevalent in women [2], because of the small groups we cannot make a useful comparison. More research on the results within another group of young adults with JIA or another chronic disease is needed. The participants had a limited amount of time to use the applications; so only their first experiences with the website and portal were collected. No information is available on the patients who did not respond to the invitation to participate in this study. Data collection was performed by rather time consuming semistructured interviews. Within the context of this study, we chose this method to meet the young adults, ask their opinions, and to have the opportunity to encourage them to elaborate on issues of feasibility. In case of a larger sample size, other methods including an online focus group might have been suitable. Focus groups also used to discover perceptions of the participants, often on a limited number of issues, may facilitate the interaction between participants. A recent study on testing feasibility of an eHealth intervention for binge drinking among young people used an online focus group to explore acceptability among 110 adolescents and young adults [34]. For practical reasons, to avoid extra travel time or time lost at school, we chose to plan the interviews before or after a consult. Because this choice might influence our results, the interviews were set up in a separate room, by a young independent interviewer who was not involved in care. Because of their duration of disease, participants were well-accustomed to usual care in our hospital.

Feasibility Testing

With this study we highlighted the importance of conducting feasibility testing prior to implementation of eHealth applications in daily practice. In information science, the involvement of the end-user in the development process of eHealth applications is considered to be a crucial factor for the actual uptake of the applications in daily life [35,36]. A review of social media in adolescent and young adult health care underpinned our results that targeting health information, based on the needs of the specific group, could stimulate the actual use of an eHealth tool [37].

In this study, we focused on feasibility testing but in the actual development of website and online portal, we collaborated actively with young adults as well. They decided to a large extent the content, layout and structure of both applications,

based on their needs and preferences. The positive outcomes of our study may be attributed to this earlier collaboration. The TAM model, used in this study [17], has already evolved towards a Health Information Technology Acceptance Model (HITAM) [25] adding (behavioral) factors such as HIT self-efficacy and health beliefs/concerns.

Based on the results of this study and the high use and acceptance within the group of young adults, we can conclude that the Internet can be a promising tool to provide health information and improve self-management among young adults with rheumatic diseases. This point is also recognized in other studies of young adults with a chronic disease like HIV [38] or Spina Bifida [39] on use and preferences regarding eHealth. Also Stinson's study [14] of young adults with JIA showed similar outcomes. Young adults with JIA believe that *"Web-based interventions are a promising avenue to improve the accessibility and availability of JIA management strategies"* [14].

Also mentioned in the HITAM is the "subjective norm", indicating that when a HIT (eg, website or portal) is imbedded in social networks, consumers are more likely to have a positive attitude towards acceptance. Based on these assumptions and the results of our study, we linked the website to a discussion board and social media. However, here some concerns have to be expressed. Several studies show that most young adults primarily use the Internet and social media for contact with peers, for home work or for leisure activities [37,39-41]. Little is known about the actual use of these media in relation to this group and health care. Future research is needed to gain insight into the use and acceptance of these media in relation to health.

Further, website and portals are increasingly used in health care, most in addition to usual care. Further research into the consequences of replacing parts of usual face-to-face care by eHealth interventions, including cost-effectiveness, will be needed.

Conclusion

The young adults appreciated both website and online portal as feasible but they also had valuable suggestions to improve accessibility and use. Based on these findings, a news and event section was added on the website and a direct link was made to a discussion board and social media. To provide and support health information, the website is actively used in daily care. As concerns the online portal, the use of self-monitoring tools and e-consult can be stimulated if there is a direct linkage to treatment and feedback from the multidisciplinary team. Feasibility testing, before implementing the website and online portal in daily practice, has proven to be valuable. Results led to improvements in terms of integration in usual care and topics for further research.

Conflicts of Interest

None declared.

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Abbreviations

JIA: juvenile idiopathic arthritis
HITAM: health information technology acceptance model
TAM: technology acceptance model

Original Paper

An Interactive Website to Reduce Sexual Risk Behavior: Process Evaluation of TeensTalkHealth

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Abstract

Background: Different theoretical frameworks support the use of interactive websites to promote sexual health. Although several Web-based interventions have been developed to address sexual risk taking among young people, no evaluated interventions have attempted to foster behavior change through moderated interaction among a virtual network of adolescents (who remain anonymous to one another) and health professionals.

Objective: The objective was to conduct a summative process evaluation of TeensTalkHealth, an interactive sexual health website designed to promote condom use and other healthy decision making in the context of romantic and sexual relationships.

Methods: Evaluation data were obtained from 147 adolescents who participated in a feasibility and acceptability study. Video vignettes, teen-friendly articles, and other content served as conversation catalysts between adolescents and health educators on message boards.

Results: Adolescents' perceptions that the website encouraged condom use across a variety of relationship situations were very high. Almost 60% (54/92, 59%) of intervention participants completed two-thirds or more of requested tasks across the 4-month intervention. Adolescents reported high levels of comfort, perceived privacy, ease of website access and use, and perceived credibility of health educators. Potential strategies to enhance engagement and completion of intervention tasks during future implementations of TeensTalkHealth are discussed, including tailoring of content, periodic website chats with health educators and anonymous peers, and greater incorporation of features from popular social networking websites.

Conclusions: TeensTalkHealth is a feasible, acceptable, and promising approach to complement and enhance existing services for youth.

KEYWORDS

Introduction

Young people account for approximately half of unintended pregnancies [1] and contracted sexually transmitted infections (STIs) [2] in the United States each year. Interventions that provide complete and accurate information to adolescents, as well as motivation and behavioral skills to negotiate condom use with partners, have demonstrated success with respect to increasing consistency of condom use [3-11]. Such interventions explicitly or implicitly target constructs from the Information-Motivation-Behavioral skills (IMB) model of human immunodeficiency virus (HIV) risk reduction, which posits that risk-reduction information, motivation, and behavioral skills are fundamental determinants of risk behavior change [12]. Information relevant to STI prevention and motivation to reduce risk are posited to exert direct effects on condom use and to exert indirect effects through activation of risk-reduction behavioral skills. Motivation to engage in condom use is thought to be a function of several cognitions, including attitudes toward condoms, perceived social norms, and perceived personal vulnerability to STIs. Behavioral skills include sexual communication and negotiation skills. Although IMB-based sexual health interventions have succeeded in promoting condom use, sizable percentages of youth who receive interventions subsequently engage in inconsistent condom use and contract STIs [5-8]. This highlights the need for novel interventions that build on the IMB model.

Interventions that aim to increase and sustain consistency of condom use among youth appear to be fighting an uphill battle. It is normative for condom use to decline within and across successive relationships [13-15]. Motivation to use condoms may be undermined by a variety of factors, including equation of condom use with lack of intimacy and trust in one's partner [16-20]; perceptions that it is only the man's responsibility to obtain and carry condoms [21] and that possession of condoms is evidence of promiscuity [18,19,22]; greater concern for prevention of pregnancy than STIs [13,20,21,23-25]; reliance on hormonal contraceptives versus dual forms of contraceptives that include condom use [24,26]; involvement in a physically or emotionally abusive relationship, which may lead to inequities in power with respect to sexual decision making [27]; and sexual behavior in the context of substance use, which may lead to other forms of risk taking, including inconsistent condom use [28,29]. Regardless of the pathway by which motivation to use condoms wanes, inconsistent condom use can become habitual. It is thus important for adolescents to establish consistent patterns of condom use and other healthy behaviors early in their relationships and to challenge thoughts that may lead to normative declines in condom use.

Highly interactive, moderated websites are an ideal setting to foster health protective thoughts and behaviors. Adolescents feel comfortable using the Internet to obtain health information [30,31] and to express concerns to peers [32] and health professionals [33]. Across a variety of age groups, peer-based interventions to promote health commonly use websites as a forum to interact [34,35]. In the United States, an estimated 84% of youth aged 8 to 18 years have Internet access in their homes (78% among African American youth; 75% among Hispanic youth) [36]. Approximately 70% of youth go online daily and nearly 75% have created a social networking site profile [36]. Although it is difficult to predict changes in technology and youth culture [37], it is likely that websites will remain highly accessible to youth (eg, websites can be made mobile-compatible using a microbrowser). Private interactive websites can be designed to mimic the most appealing aspects of public social media websites, while also maximizing privacy and confidentiality for users. Intervening with youth on a public social media website may preclude discussion about sensitive personal information because privacy and security settings are owned and controlled by someone other than the health provider's or researcher's institution [38].

Different theoretical frameworks support the use of interactive websites to promote sexual health. Although behavior change theories—such as the IMB model of HIV risk reduction [12]—are useful in targeting areas for intervention, an individual's adoption of recommended behavior change may depend on the successful application of communication theory [39]. An intervention must not only be instructive, but persuasive [39-41]. Health communications must promote attention by being engaging and interesting, while also balancing arousal with comfort, promote understanding by being clear, and promote acceptance by appearing relevant and credible and by appealing to cognitions that influence motivation [41,42]. The Internet allows users to provide immediate feedback on whether different types of health communications are attended to, understood, and accepted. To be effective, health communications must also lead to little counterarguing (thoughts that inhibit agreement with an advocated position) [39]. Some adolescents are skeptical of information provided by authority figures [43]. In addition, adults are unlikely to guess the factors that will increase adolescents' attention to, understanding of, and acceptance of messages promoting health protective behavior [44]. Thus, it is critical to adopt methodology in which adolescents can provide guidance on the content and delivery of health communications [44]. Design-based research—a systematic, but flexible, methodology aimed to improve educational practices and outcomes—is particularly well suited to the development of technology-enhanced learning environments [45]. It involves iterative analysis, design, development, and implementation of an educational product. A fundamental feature is ongoing collaboration between researchers and recipients of the intervention to ensure that inquiry and practice are responsive to a group's needs [45]. The Internet can facilitate ongoing interaction between adolescents and health educators and allow for interventions that are responsive to the potentially changing needs of individual adolescents over time.

Although several Web-based interventions have been developed to address sexual risk taking among young people [46-52], no evaluated interventions have attempted to foster behavior change through moderated interaction between a virtual network of adolescents, who remain anonymous to one another, and health professionals. TeensTalkHealth is an interactive Web-based intervention designed to promote condom use and other healthy decision making in the context of romantic and sexual relationships. As depicted in Figure 1, the TeensTalkHealth

intervention aims to increase condom use and other health behaviors through targeting constructs of the IMB model of HIV risk reduction [12]. TeensTalkHealth provides information, motivation, and behavioral skills to decline risk behaviors, negotiate health protective behaviors, and build healthy relationships. Constructs of communication theory and principles of design-based research guide the TeensTalkHealth approach with respect to behavior change. Video vignettes, teen-friendly articles, and other content are designed to promote attention to, understanding of, and acceptance of health-promoting messages. These standardized components of the TeensTalkHealth intervention serve as conversation catalysts between adolescent website users and health educators, who have the opportunity to interact with one another via message board discussions, a key feature of the website intervention. Health educators and adolescent peers can read and respond to comments and questions posted by individual adolescents, which may serve to enhance the perceived credibility and personal relevance of health-promoting messages. Consistent with principles of design-based research, adolescents are consulted in the initial design of the website and planning of intervention content. Importantly, adolescent participants are able to shape website content as the intervention unfolds. Adolescent website users can interact with one another and with health professionals to shape the content of message board discussions and, potentially,

the order in which health professionals decide to feature predeveloped content on the website. This may enhance attention to, understanding of, and acceptance of health-promoting messages. The TeensTalkHealth intervention approach has 3 primary advantages: (1) support—interaction with peers and health educators as part of a virtual community can provide opportunities for learning and support; (2) convenience—access to content and interaction with others can occur on an ongoing basis, including times of greatest convenience and/or need; and (3) anonymity—individuals who are anonymous to one another may be more comfortable, which may increase candor, relevance of website content, and participant engagement.

This research examines the feasibility and acceptability of delivering a confidential, peer-based sexual health intervention through the Internet, which may lead to the expansion of treatments and services for youth. This paper describes a summative process evaluation [53] of the TeensTalkHealth website intervention. Evaluation data were obtained from 147 adolescents who participated in a study to determine the feasibility and acceptability of the website intervention and assessment methods. Data were collected across a 4-month intervention period and 2-month follow-up period. Findings can be used to guide further development of the TeensTalkHealth intervention and other interactive websites that aim to promote healthy decision making among adolescents.

Figure 1. Mechanisms of behavior change with respect to condom use and other health behaviors.
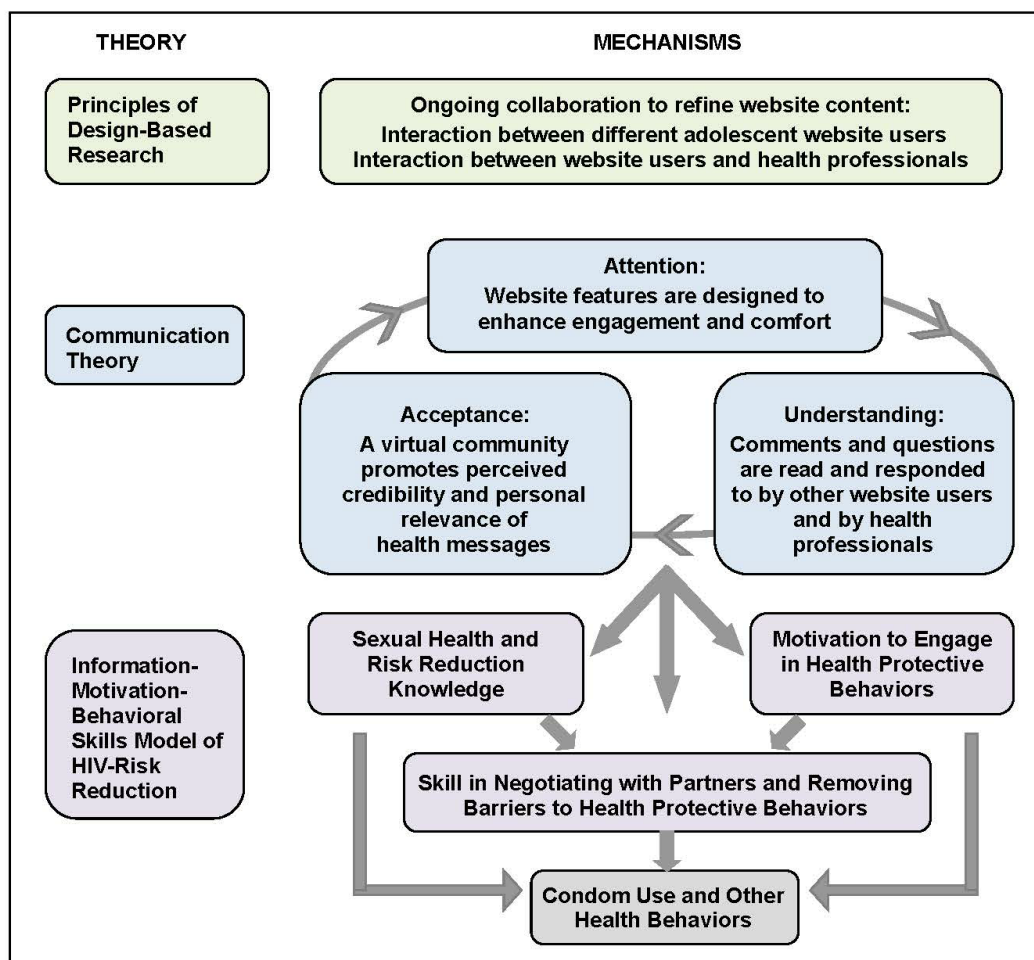
Methods

Study Procedure and Participants

The University of Minnesota Institutional Review Board approved this research. A federal certificate of confidentiality was obtained to protect sensitive data obtained from adolescents.

The principal investigator (first author) faxed letters and/or sent emails of introduction to executive directors of community-based teen clinics and principals of public and charter schools, followed initial modes of contact by one voicemail message if necessary, and met with interested staff to explain the purpose of the study and answer questions. Three of 5 approached community clinics became recruitment partners; 1 of the remaining 2 clinics planned to become a partner, but closed before recruitment began. Three of 17 approached schools became recruitment partners.

Recruitment took place between January and October 2011. Clinic staff were asked to distribute and collect recruitment flyers from all adolescents aged 14 to 18 years seeking services. At 2 school sites, research staff gave presentations about healthy relationships or sexual health during class, briefly described the study, and distributed and collected flyers immediately afterwards. The third school site distributed flyers to age-eligible students through email. Flyers contained a brief description of the study, including the potential to earn up to US $140 across a 6-month period. Adolescents were asked to fill out nonidentifying demographic information on flyers (age, sex, race/ethnicity). Those who were interested in the study were asked to add contact information.

Figure 2 depicts numbers of adolescents at different stages of recruitment, screening, and enrollment, as well as study inclusion and exclusion criteria. A total of 1226 flyers were collected across the period of recruitment. Of collected flyers, 682 indicated that an adolescent had interest in the study; 438 of the 682 adolescents were fully screened by telephone and 313 were determined to be eligible. Inclusion criteria were as follows: aged 14 to 18 years, engaged in vaginal or anal sex at least once during the past 3 months, and spent at least 2 days using the Internet independently during a typical week for a total of at least 2 hours. Adolescents who graduated from high school before spring 2011 or who were pregnant at the time of screening were ineligible. At the end of screening, adolescents aged 14 to 17 years were told that parental consent was required for participation. Study staff offered to speak directly with parents and guardians or to send a letter of introduction if the adolescent desired. Both the telephone script and letter of introduction contained an explanation that the TeensTalkHealth website was developed to "promote healthy decision making about relationships and sexual health" and that the website would feature "information and discussions about things like

saying no to sex, preventing pregnancy and STIs, using condoms and other birth control methods, and signs of healthy and unhealthy dating relationships." Enrollment meetings were scheduled with 194 adolescents who remained interested in the study and their parents if adolescents were aged 14 to 17 years; of this number, 37 adolescents were eventually not enrolled due to missed appointments, cancellations, and/or a decision not to participate.

Enrollment meetings were held in public places. Staff described the study in detail and answered questions, obtained assent and/or consent, revealed the adolescent's study condition, provided handouts to parents and/or adolescents about Internet safety and privacy, showed sample pages from the TeensTalkHealth website (tailored to study condition), and requested privacy if a parent or legal guardian was present so that the adolescent could select a nonidentifying username, a password that met University of Minnesota Office of Information Technology requirements, and answers to password recovery questions. At the end of the meeting, staff reviewed activities that were required for reimbursement and how to contact the study team with questions. From this point forward, research staff only interacted with adolescents via the TeensTalkHealth website and private channels of communication (eg, cell phone, email, letter).

Seven successive cohorts were screened, enrolled, and introduced to the website at the beginning of a given month. Across the first 6 cohorts, 127 participants were enrolled and assigned to the intervention or control condition (Figure 2). To augment the amount of data available to evaluate intervention content, 30 additional participants were enrolled and assigned to the intervention condition as part of a seventh cohort. Ten of 157 enrolled participants failed to complete a baseline survey. Data from 92 participants assigned to the intervention condition and 55 participants assigned to the control condition are presented in this paper.

A cohort's study involvement consisted of a preintervention period (ie, time between enrollment and the start of the next month), a 4-month intervention period, and a 2-month follow-up. All study participants were asked to complete 7 private monthly surveys online, including a baseline survey. Participants were reimbursed US $10 per survey and received a US $30 bonus if they completed all 7 surveys. As an engagement tool, control group participants who completed the first and/or second 3 surveys were additionally entered into 1 to 2 raffles for a US $20 bonus; chances of winning were 1 in 3. For the intervention group, 15 assigned intervention tasks were due on the final day of months 1 to 4. Participants who completed all tasks during a given month were reimbursed US $10; US $5 was provided for completion of 8 to 14 tasks. Thus, both intervention and control group participants could earn a maximum of US $140 across the study period.

Figure 2. Numbers of adolescents at different stages of recruitment, screening, and enrollment.
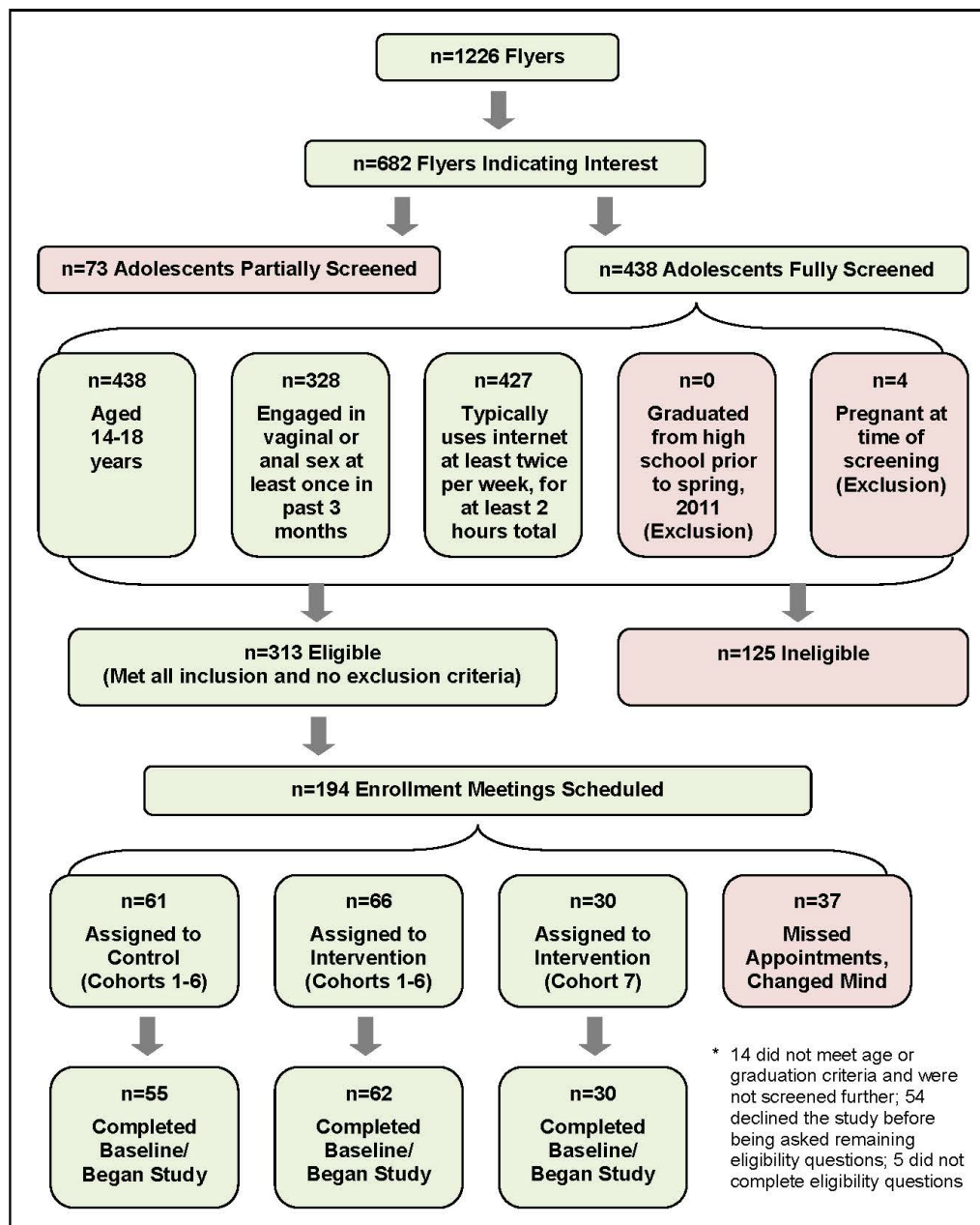
Website Development

Textbox 1 summarizes the website development goals. Before the pilot study, the research team consulted with youth advisors: adolescents aged 14 to 18 years and college undergraduates hired through community and university organizations focused on sexual health. Video vignettes, teen-friendly articles, and other website content were initially developed by 2 of the authors (SSB and AJK); content was iteratively refined by the research team and youth advisors during 14 group meetings held across a 5-month period. During group meetings, advisors provided suggestions on the website name, topics for website content, messages that may motivate adolescents to use condoms and engage in other health protective behaviors, moderation of website comments by health professionals, editing of video vignette screenplays, content of discussion questions, recruitment strategies, and criteria for reimbursement of participants' engagement in study activities. Separate from group meetings, advisors were asked to complete the baseline survey (without handing back their responses to questions), provide their completion time and thoughts on the overall length and breadth of the survey, and critique the wording of survey questions and responses.

Textbox 1. Website development goals.

Dose received (exposure)

1. Promote a high level of engagement on the website.

2. Encourage condom use through website content.

3. Promote a culture in which condom use is perceived as normative within different types of sexual relationships.

4. Be responsive to perceived barriers to condom use and other sexual health/relationship concerns.

Dose received (satisfaction)

1. Maximize the comfort of adolescents using the website.

2. Protect the privacy of adolescents using the website.

3. Design features that enhance the accessibility and ease of use of different sections of the website.

4. Enhance the perceived personal relevance of health communications on the website.

5. Enhance the perceived credibility of individuals delivering health communications.

6. Demonstrate respect for adolescents' autonomy.

TeensTalkHealth Intervention

TeensTalkHealth adopted several broad strategies to achieve website development goals. First, the website intervention featured moderated discussion between adolescent website users, whose identities were protected through nonidentifying usernames, and health educators on the research team. Website discussion on message boards evolved in response to relationship concerns and barriers to condom use identified by adolescents over time.

Second, the website featured different types of content that served as conversation catalysts between adolescents and health educators. Twenty video vignettes of young role models provided sexual health and risk-reduction information, motivation to engage in health protective behavior, and behavioral skills to negotiate condom use with partners or to address other barriers to healthy relationships. Multimedia Appendix 1 contains titles, synopses, learning objectives (not shown to participants), and discussion questions for vignettes. Ten videos addressed condom use, including planning for condom-protected sex, advocating for condom-protected sex, and handling consequences of unprotected sex. Six videos addressed setting sexual boundaries; 4 addressed coping with difficult relationship situations. Multimedia Appendices 2 and 3 contain sample video vignettes. Content was diverse to engage adolescents and address an array of factors that may affect condom use and other healthy decision making. In addition to video vignettes, teen-friendly articles and brief discussion topics also served as conversation catalysts.

A third feature of the website was easily navigable archives of video and text. The home page of the TeensTalkHealth website included Highlighted Topics, Recent Comments, and Replies to My Content boxes, and a Create New Discussion button and a featured poll. Separate pages of the website listed all titles of video topics, article topics, and other discussion topics, along with a corresponding synopsis of the topic or extract from discussion content. Adolescents could click on a specific topic to access message board discussion related to that topic. Indentation and placement of comments on message boards allowed website users to understand when a comment was made in direct response to another user, which facilitated the tracking of different conversations under a single topic. Other pages displayed all recent topics and comments, a list of resources (including emergency contact information), and a Contact Us form. Under the My Account page, website users could change their password and review currently assigned tasks, all comments and discussion topics they had submitted to that point, and replies to their content. Tabs at the top of the TeensTalkHealth website allowed users to navigate between different pages. A search bar was also present at the top of every page.

Adolescents in the intervention condition accessed website content for a 4-month period. Although users were free to access any content that was available from the time they joined, health educators assigned standard weekly content through a section of the website, My Required Tasks. Adolescents were asked to complete a total of 60 tasks across the 4-month intervention. Adolescents completed a brief private survey and public comment for each of 20 video vignettes, resulting in 40 video-related tasks. Similarly, adolescents completed a brief private survey and public comment for each of 4 teen-friendly articles, resulting in 8 article-related tasks. Finally, adolescents were asked to provide a public comment on 12 message boards with no associated video vignette or article. These "discussion-only" message boards typically began with thought-provoking information and questions posed by health educators.

To promote task and monthly survey completion, 3 to 13 reminders were sent to each participant per month through texting, voicemails, emails, and mailed letters. Targeted communications were made to those adolescents who had not yet completed tasks and/or responded to previous communications by staff. Of note, none of the adolescents complained about the frequency with which they interacted with staff.

Moderation of Website Comments

The manner in which health educators engage adolescents is critical to the success of TeensTalkHealth and similar interventions. Key principles of TeensTalkHealth moderation included (1) demonstrating that it is possible to protect health while also establishing, maintaining, and strengthening relationships and (2) developing a climate in which adolescents feel comfortable disclosing their own experiences, sharing what they have learned, and providing guidance to others. By adding comments to video, article, and discussion topics, adolescents are able to clarify their values and beliefs. Health educators attempt to reinforce health-promoting attitudes and behaviors and respectfully challenge risk-promoting attitudes and behaviors.

During the intervention period, all submitted comments by adolescents were read at least daily and approved by health educators before they appeared publicly. When enrolled, adolescents were told that identifying information and abusive language directed toward other website users would be removed. Identifying information was rarely submitted; abusive language was never submitted. No other censorship of adolescents' comments was made. Health educators identified and presented challenging website comments at weekly moderation meetings. Possible responses were considered by the team, which included the first author (SSB), a clinical psychologist. Moderation meetings yielded several guidelines for responding to comments:

1. Offer thought-provoking, yet specific, prompts to continue discussion.
2. Highlight adolescents' personal strengths.
3. Praise self-awareness and, when applicable, ask for additional information about thoughts and feelings that drive decision making and behavior.
4. Provide motivation (explicit rationales for engagement in health protective behavior) and cognitive-behavioral skills (explicit strategies to engage in health protective behavior) whenever possible.
5. Reframe and challenge risk-promoting statements—try to acknowledge or validate the essence of what has been said so that adolescents will be open to "hearing" a caution against risk.
6. Empathize with stressors (acknowledge difficulty) and, when applicable, provide cognitive-behavioral skills for coping.
7. Emphasize adolescents' autonomy and choice with respect to behavior—foster a sense of agency.
8. Challenge the idea that it is possible to completely avoid negative experiences when choosing to engage in risk.
9. Encourage adolescents to think about how past negative experiences can inform healthy decision making in the future.
10. Encourage adolescents to plan ahead—foster a sense of intentionality.

The following exchanges illustrate how health educators used moderation guidelines to address the challenge of negotiating condom use with a male partner when it is known that the female partner is using a hormonal contraceptive to prevent pregnancy.

Comments have not been edited for spelling or grammar; clarifying information has been added within brackets.

I started BC [birth control] a couple of months ago. The guy I was dating at the time was super excited that he didn't have to use a condom anymore. I mean, I wasn't as worried about not using one [referring to a character in Video 4, see Multimedia Appendix 1], but after I always freaked out a little. As much as I know it's bad, I didn't make him use a condom because it made him happy. I know he would have if I had asked, but I never did. Looking back, I wish I had made him. I regret not using one, even though I didn't get pregnant. [Multimedia Appendix 1] [Teen 1]

In relationships, there is a lot of give and take and most good relationships need compromise. On the other hand, condom use and pregnancy/STI prevention is one of those places I personally think it's okay to take a stand when your intent is to be as safe as possible. Teen 1, have you thought about how you'll do things differently in your next relationship? What might you say to a new partner? Does anyone have suggestions about what's worked for them? [Health Educator 1]

Actually, things with that guy didn't work out and I have a new partner. We've already talked about sex and condoms and all that, even though he's abstinent. We've come to the conclusion that if we ever do, condoms will always be used. We both have our whole lives ahead of us, and as much as we both want kids some day, not before we can figure out our place in life. It's nice actually, not having to stress about sex and if the condom/pill worked. [Teen 1]

I completely relate to this situation [referring to Video 4, see Multimedia Appendix 1], i just wish i had enough confidence to speak to my partners like this. Its so hard to change things once theyve been happening that way for so long. Its unfortunate but i dont know how to really change it sometimes. [Multimedia Appendix 1] [Teen 2]

Hey Teen 2, building your confidence can be a challenge. Some people might find it helpful to practice in front of a mirror or with a friend. Practicing saying the words out loud and many times is a really helpful way to prepare for talking about a difficult subject with a partner. Another helpful exercise to build your confidence is to make a list of reasons why what you are proposing is reasonable and desirable. If you really believe that what you want IS important for both of you, you will have an easier time staying confident in a tough conversation. [Health Educator 2]

The following exchanges illustrate how health educators used moderation guidelines to address sexual behavior in the context of substance use:

i have no problem having sex with my boyfriend if hes under the influance. i think it just makes things more interesting and exciting. [Teen 3]

It's true that having sex under the influence can make the experience more unpredictable. For some people that's exciting, but it can also be risky. Drinking or using drugs affects decision making, and can make it difficult to communicate clearly about what you want or don't want. What are some things that people can do to make situations like this less risky? Are there other ways to make sex exciting? [Health Educator 1]

i think having sex with a bofriend that has been drinking is discusting because for one their breath stinks & for two the person is not in its right state of mind, and its not ok to take advantage of them that way! [Teen 4]

I agree even in a relationship where i'm comfortable having sex i have always told my boyfriend that if either one of us or both of us have been drinking sex is not an option. [Teen 5]

Way to set a boundary, Teen 5! Sometimes setting up expectations and boundaries about sex before the situation happens makes it easier and less stressful in the moment. [Health Educator 2]

Lastly, the following exchanges illustrate how health educators used moderation guidelines to address potentially unhealthy relationships and encourage adolescents to clarify their boundaries with respect to the acceptability of a partner's behavior:

Can jealousy and anger be signs of love? Why or why not? If you're not sure, what are some reasons that it is hard to decide? [Health Educator 1]

I think there is a thin line, because jealousy can mean someone really cares about you, but it can also mean there over protective, it all depend on the circumstances. [Teen 6]

Could you say more about what circumstances you think jealousy shows caring, and what circumstances you think jealousy crosses the line? How would a person know when to be worried about their relationship? [Health Educator 1]

its sort of hard to explain, but i did read in a Cosmo magazine one time that a little bit of jealousy shown from your partner is okay. But i think it crosses the line if you're hangingout with your friends and your partner gets jealous and angry because they see you having a good time without them. you need to keep in mind that we are all human and we all need social needs, and if we're with the same people for ever then it gets boring, pllus you might lose a lot of friends if you're not hangingout with them. And your friends won't call you or invite you to things because they think you're always with your partner. –Trust me i've been there and it sucks. [Teen 7]

i agree with you. A little jealousy is good but it starts beccoming a problem when your partner gets mad at you when your with friends and maybe not texting him/her back right away. thats too far. but at the same time, that means that the trust isnt there either. Why else would he/she be constantly asking what your doing? [Teen 8]

Categorizing the TeensTalkHealth Intervention According to Behavior Change Techniques

Michie and colleagues [54] have defined behavior change techniques—or "active ingredients"—as observable, replicable, and irreducible components of an intervention designed to alter or redirect causal processes that regulate behavior. They highlight several benefits of using a standardized taxonomy to classify the active ingredients of behavior change interventions: (1) contribution toward a comprehensive list of behavior change techniques, which can serve as a resource to others; (2) faithful implementation of interventions found to be effective; (3) accurate replication of interventions in comparative effectiveness research; (4) facilitation of systematic literature reviews and meta-analyses testing the contribution of different behavior change techniques; and (5) greater ability to link behavior change techniques to theories of behavior change and to gain insight into mechanisms of action. TeensTalkHealth uses the following behavior change techniques in Michie et al's [54] taxonomy: considering the consequences of behavior (eg, health, social, emotional), shaping of knowledge (eg, identifying the antecedents of behavior, rehearsing how to perform a behavior), identifying goals and planning (eg, problem solving and other forms of coping, action planning, including formation of implementation intentions), providing social support (eg, emotional, informational, appraisal), comparing one's own behavior to others through modeling (eg, video vignettes) and social comparisons (eg, teen comments on message boards), and examining one's identity (eg, identification of the self as a role model, self-affirmation, visualization of oneself with changed behavior, reframing, addressing cognitive dissonance).

Measurement of Process Evaluation Components

Overview

Sources of process evaluation data included adolescents' responses on monthly surveys, staff experience, and automated tracking of website activity, including task and monthly survey completion.

Dose Received/Exposure

Different domains of intervention exposure were evaluated. First, automated tracking of website activity included (1) number of completed assigned tasks, (2) number of played and completed videos, (3) number of assigned articles and discussion topics visited, (4) number of website visits, (5) cumulative hours spent on the website, and (6) number of comments made. Completion of assigned tasks is arguably the strongest index of exposure because participants had to reflect on intervention materials to complete a brief survey or add a comment.

Second, responses on monthly surveys yielded a perceived engagement composite, the mean of 7 items: "Over the last

month when you visited the website, how much interest (0=no interest, 1=a little, 2=a lot) did you have in (1) watching new videos; (2) taking private surveys about videos; (3) reading articles; (4) posting new discussion topics; (5) reading what other teens have to say about videos, articles, and discussion topics; (6) reading what health educators have to say about videos, articles, and discussion topics; and (7) responding to comments from other people to continue a discussion?"

Third, monthly surveys were used to assess participants' perceptions of 3 website goals indicative of exposure: (1) encouragement of condom use, (2) normativeness of condom use, and (3) responsiveness to relationship concerns and barriers to condom use. Perceived encouragement of condom use was determined by calculating the mean of 5 items: "How much (1=not at all, 5=very) was the website trying to encourage consistent condom use (1) with new partners, (2) with long-term partners, (3) with casual partners, (4) with serious partners, and (5) even if someone is using hormonal contraceptives (eg, birth control pills, the patch, the shot)?" Perceived normativeness of condom use, assessed at the end of months 2 and 4 only, was determined by calculating the mean of 6 items: "How many teens on this website (1=almost nobody, 5=almost everybody) seemed to use condoms when (1) they had sex with new partners, (2) they had sex with long-term partners, (3) they had sex with someone they thought of as casual, (4) they had sex with someone they thought of as serious, (5) they were already using a hormonal contraceptive (eg, birth control pills, the patch, the shot) to keep from getting pregnant, and (6) they were using no other form of birth control?" Perceived responsiveness was determined separately for other adolescents on the website and for health educators. Perceived responsiveness was determined by calculating the mean of 3 items: "When I talked about something that keeps me from using condoms, other teens (health educators) on this website (1) said things to try to help me use condoms" and "When I talked about a problem I was having with a relationship, other teens (health educators) on this website (2) showed they cared and (3) tried to help solve the problem." Participants rated perceived responsiveness on a 5-point Likert scale (1=not at all true, 5=very true).

Dose Received/Satisfaction

Monthly surveys were used to assess participants' perceptions of 6 website goals related to satisfaction: (1) comfort, (2) privacy, (3) accessibility/ease of use, (4) personal relevance of health communications, (5) credibility of individuals delivering health communications, and (6) respect for autonomy by health educators.

Perceived comfort was determined by calculating the mean of 2 items: "When you were on the website, how comfortable (1=not at all, 5=very) have you felt (1) asking questions and (2) sharing your experiences?" Perceived privacy, assessed at the end of months 1 and 3 only, was determined through a single

item (subsequently reverse-scored): "How worried (1=not at all, 5=very) are you that people not connected to this study will find out personal information you have shared on the website?" Perceived accessibility/ease of use, assessed at the end of months 1 and 3 only, was determined by calculating the mean of 6 items: "How easy (0=not at all, 1=a little, 2=very) was it to use different parts of the website: (1) watching videos, (2) taking private surveys about videos, (3) posting a new discussion topic, (4) searching the discussions for a specific topic, (5) moving from 1 part of the website to another, and (6) using the website to take monthly sexual health surveys?"

Perceived personal relevance of health communications was determined by calculating the mean of 3 items: "How much (1=not at all, 5=very) did (1) people in the videos talk about things that matter to you, (2) teens on the website talk about things that matter to you, and (3) health educators on the website talk about things that matter to you. Perceived credibility, assessed at the end of months 2 and 4 only, was determined separately for adolescents on the website, models in videos, and health educators. Perceived credibility of adolescents and models were each determined through a single item: (1) "How much (1=not at all, 5=very) did adolescents on the website (the people in videos) know what they were talking about?" This item was also assessed for health educators. In addition to this item, 3 other items [55] were assessed to calculate a 4-item mean for perceived credibility of health educators: (2) "How believable was the information from health educators?" (3) "How accurate was the information from health educators? and (4) "How trustworthy were health educators?" Perceived respect for autonomy by health educators, assessed at the end of months 2 and 4 only, was determined by separately examining 3 items: "How much (1=not at all, 5=very) were health educators (1) trying to get you to do what they want, (2) trying to help you do what you want, and (3) leaving out information to get you to do what they want?"

The internal consistency (alpha) of each multi-item measure was calculated as an index of reliability.

Results

Recruitment

Demographic characteristics for adolescents who returned flyers, completed the baseline survey, and completed the final (2-month follow-up) survey are shown in Table 1. In comparison to adolescents who completed recruitment flyers, the final study sample was less likely to be aged 14 to 17 years than 18 years and more likely to be female than male; ethnic diversity was similar. Nearly 42% (61/147, 41.5%) of study participants reported consistent condom use during the 3 months before screening. No differences in age, sex, ethnicity, and condom use consistency at screening were observed by study condition among the first 6 cohorts (data available on request).

Table 1. Demographic characteristics of adolescents who returned flyers, completed the baseline survey, and completed the 2-month follow-up survey (N=1226).[a]

Demographic characteristic	Adolescents, n (%)		
	Returned flyers (N=1226)	Completed baseline (n=147)	Completed 2-month follow-up (n=111)
Age at baseline			
14-17 years	805 (72.1)	89 (60.5)	65 (58.6)
18 years	312 (27.9)	58 (39.5)	46 (41.4)
Sex			
Female	905 (80.7)	132 (89.8)	105 (94.6)
Male	216 (19.3)	15 (10.2)	6 (5.4)
Race/ethnicity			
Non-Hispanic white	729 (65.6)	92 (62.6)	70 (63.1)
>1 race/ ethnicity	129 (11.6)	24 (16.3)	22 (19.8)
Black/African American	133 (12.0)	16 (10.9)	10 (9.0)
Asian or Pacific Islander	58 (5.2)	8 (5.4)	5 (4.5)
Hispanic or Latino	50 (4.5)	5 (3.4)	3 (2.7)
Other race/ethnicity	13 (1.2)	2 (1.4)	1 (0.9)
Consistency of condom use in past 3 months at screening [b]			
100%	n/a	61 (41.5)	49 (44.1)
Less than 100%	n/a	86 (58.5)	62 (55.9)

[a] Percentages are shown for those adolescents who provided data for a particular demographic characteristic on the recruitment flyer.

[b] Consistency of condom use was not assessed until screening.

Dose Received/Exposure

On average, intervention participants logged on 20 times, spent a cumulative 6.2 hours on the website, and submitted 24.8 comments (Table 2). The mean number of videos participants initiated and completed playing was 12.4 and 10.3, respectively. On average, intervention participants visited 2.7 assigned articles and 8.2 assigned discussion topics. Approximately one-quarter of intervention participants completed all 60 assigned tasks during the 4-month intervention period (24/92, 26%). An additional third completed 40 to 59 tasks (30/92, 33%). Less than 10% completed no tasks (8/92, 9%). Rates of task completion declined over the course of the intervention period.

Table 2. Distributions of website activity variables.[a]

Index of website activity	Intervention participants (n=92)	Control participants (n=55)
Task completion, n (%)		
All months		
0	8 (8.7)	
1-19	15 (16.3)	
20-39	15 (16.3)	
40-59	30 (32.6)	
60	24 (26.1)	
Month 1		
0	13 (14.1)	
1-4	4 (4.3)	
5-9	10 (10.9)	
10-14	4 (4.3)	
15	61 (66.3)	
Month 2		
0	16 (17.8)	
1-4	7 (7.8)	
5-9	10 (11.1)	
10-14	7 (7.8)	
15	50 (55.6)	
Month 3		
0	21 (23.6)	
1-4	9 (10.1)	
5-9	6 (6.7)	
10-14	8 (9.0)	
15	45 (50.6)	
Month 4		
0	27 (30.7)	
1-4	8 (9.1)	
5-9	9 (10.2)	
10-14	5 (5.7)	
15	39 (44.3)	
Website interaction, mean (SD)		
Number of website visits[b]	20.0 (12.2)	10.1 (3.2)
Cumulative hours spent on website[b]	6.2 (3.6)	1.7 (0.6)
Number of comments made on website[c]	24.8 (15.3)	
Videos with initiated play (of 20)	12.4 (7.0)	
Videos with completed play (of 20)	10.3 (6.5)	
Assigned articles visited (of 4)	2.7 (1.5)	
Assigned discussion topics visited (of 12)	8.2 (4.3)	
Monthly surveys, n (%)		
Month 1	75 (83.3)	53 (96.4)

Index of website activity	Intervention participants (n=92)	Control participants (n=55)
Month 2	72 (80.9)	50 (90.9)
Month 3	66 (75.0)	53 (96.4)
Month 4	57 (65.5)	51 (94.4)

[a]An enrolled adolescent had to complete a baseline survey to become a participant. Across the tasks shown within all months or a given month, numbers tally to the total number of participants assigned to the intervention condition (minus any withdrawn participants for months 2-4) and percentages tally to 100%.

[b] A session "timed out" if participants did not navigate to or refresh a webpage within 15 minutes, necessitating a new visit if the participant still wanted to use the website. If participants did not log out, the timestamp for the last visited webpage was used to calculate the amount of time spent on the website during a given visit. Three outliers were not included when calculating the mean and standard deviation for cumulative hours spent on the website: 1 control group participant whose time amounted to 26.9 hours and 2 intervention group participants whose time amounted to 29.4 and 74.7 hours, respectively.

[c] A total 36 comments were requested as part of assigned tasks.

Adolescents reported moderate levels of perceived engagement (interest) in various website activities on average (Table 3). When individual items in the perceived engagement composite were examined, 40% to 50% of participants reported high levels of interest in reading what health educators and other adolescents had to say about videos, articles, and discussion topics. On average, participants perceived that the website was strongly encouraging condom use across a variety of situations. Most participants perceived condom use to be normative among at least half of adolescents on the website. Health educators were perceived to be more responsive to adolescents' relationship concerns than were other adolescents on the website.

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Table 3. Participant responses to monthly survey items designed to evaluate website development goals and internal consistency (alpha) of composite measures.[a]

Construct	Month 1		Month 2		Month 3		Month 4	
	α	Mean (SD)	α	Mean (SD)	α	Mean (SD)	α	Mean (SD)
Dose received (exposure)								
Perceived engagement (scale 0-2)[b]	.55	1.18 (0.30)	.67	1.17 (0.36)	.74	1.03 (0.39)	.57	1.14 (0.31)
Encouragement of condom use	.93	4.52 (0.83)	.88	4.63 (0.56)	.85	4.59 (0.58)	.92	4.39 (0.85)
Condom use normative[c]	—	—	.75	3.51 (0.57)	—	—	.83	3.61 (0.74)
Responsiveness to barriers								
Teens on website	.77	2.56 (1.09)	.80	2.67 (1.15)	.75	2.62 (1.09)	.79	2.79 (1.12)
Health educators	.80	3.16 (1.20)	.82	3.35 (1.10)	.71	3.30 (1.07)	.76	3.46 (1.05)
Dose received (satisfaction)								
Comfort on website[d]	.65	4.21 (0.86)	.66	4.24 (0.81)	.67	4.08 (0.89)	.61	4.01 (0.94)
Perceived privacy	n/a	4.81 (0.51)	—	—	n/a	4.83 (0.63)	—	—
Accessibility/ease of use (scale 0-2)[b]	.59	1.75 (0.28)	—	—	.70	1.77 (0.30)	—	—
Personal relevance of content	.71	3.37 (0.72)	.73	3.35 (0.72)	.82	3.37 (0.89)	.77	3.42 (0.77)
Credibility of teens on website[c]	—	—	n/a	3.50 (0.80)	—	—	n/a	3.49 (0.81)
Credibility of people in videos[c]	—	—	n/a	4.24 (0.81)	—	—	n/a	4.15 (0.85)
Credibility of health educators[c]	—	—	.85	4.52 (0.67)	—	—	.77	4.53 (0.64)
Respect for autonomy by health educators[c]								
How much were health educators...								
Leaving out information to get you to do what they want?	—	—	n/a	1.64 (1.26)	—	—	n/a	1.70 (1.19)
Trying to get you to do what they want?	—	—	n/a	2.93 (1.12)	—	—	n/a	2.85 (1.24)
Trying to help you do what you want?	—	—	n/a	3.76 (0.94)	—	—	n/a	3.79 (0.87)

[a] Responses are presented by end-of-month survey, collapsing across cohort. Dashes indicate that a construct was not assessed as part of a particular survey. When a single item was used to assess a construct, n/a (for not applicable) is indicated in lieu of the internal consistency (alpha).

[b] Perceived engagement and accessibility/ease of use were assessed using a 3-point Likert scale (0-2). Other constructs were assessed using a 5-point Likert scale (1-5).

[c] Participants were asked to think across the past 2 months.

[d] The correlation between these 2 items is presented instead of the internal consistency (alpha).

Dose Received/Satisfaction

Table 3 shows that participants felt a high level of comfort and perceived very high levels of privacy on the website. Mean ratings of accessibility/ease of website use approached "very easy." Personal relevance of content and perceived credibility of other adolescents on the website were normally distributed around mean values slighter greater than these scales' midpoints. Participants perceived high credibility of health educators and the models in video vignettes. Perceived respect for autonomy by health educators was assessed with 3 items. The perception that health educators were deliberately leaving out information was rare. Perceptions that health educators were trying to "get you to do what they want" and trying to "help you do what you want" were more common, with mean responses slightly less than and somewhat greater than the midpoints of the respective scales.

Retention

Retention rate, assessed by monthly survey completion, varied by study condition (Table 2). More than 80% (75/90, 83%) of intervention group participants completed their month 1 survey, whereas 66% (57/87) completed their month 4 survey. Corresponding percentages among control group participants were 96% (53/55) and 94% (51/54). (Note: 5 intervention group participants and 1 control group participant had withdrawn by the time of the month 4 survey.)

Discussion

This work demonstrates the feasibility and acceptability of TeensTalkHealth, a Web-based intervention designed to promote condom use and other healthy decision making in the context of romantic and sexual relationships. Key findings involving process evaluation components, primary challenges encountered by staff, and proposed solutions are discussed subsequently.

Adolescents' perceptions that the website encouraged condom use across a variety of relationship situations were very high. Thus, TeensTalkHealth succeeded in its first and foremost website development goal. Most participants also perceived that condoms were used by at least half of adolescents on the website. Mean values for personal relevance of website content, including message board discussion, were greater than the scale midpoint. Adolescents' perceptions of engagement (interest) and health educators' responsiveness were at these scales' midpoints, on average, whereas perceptions of peer responsiveness were less than the scale midpoint. Different strategies could be used in future applications of TeensTalkHealth to enhance engagement and perceived responsiveness. For example, tailoring may increase perceived personal relevance of intervention content, which may serve to enhance engagement, perceived responsiveness to concerns, and receptivity toward persuasion [56,57]. Assigned or recommended content could be tailored based on a small number of target areas identified through adolescents' responses to a baseline survey and issues of concern that emerge across the intervention period. During the TeensTalkHealth intervention, health educators addressed a variety of issues that could be applied toward the tailoring of content (eg, perceived norms that stigmatize possession of condoms by girls, perceived incompatibility between condom use and trust/intimacy in relationships, greater concern for pregnancy prevention than STI prevention, lack of sexual agency, use of substances to allay sexual anxieties or to generate excitement). Allowing adolescents to schedule a one-on-one website chat with health educators, if desired, may further enhance perceived responsiveness. Similarly, holding regular live website chats between adolescents and health educators (with a slight time delay to remove any identifying information) may cultivate a greater sense of community and support among adolescents. Features of popular social networking websites could be incorporated to a greater degree within the context of TeensTalkHealth. For example, adolescents could be allowed to build their own "identity" pages, with moderation of submitted material to preserve anonymity. In addition to implementing one or more of these strategies, future applications of TeensTalkHealth should examine the extent to which responsiveness may be a function of degree of interactivity among adolescent website users and between individual adolescents and health professionals.

Almost 60% of intervention group participants completed two-thirds or more of assigned tasks across the 4-month intervention period, suggesting a reasonable level of exposure for this feasibility study. Although interest in the website and perceived responsiveness of health educators and peers may account for differences in the degree of participation, demands

of the study protocol may also have been responsible. Among the intervention group, rates of task and monthly survey completion waned over time; the combination of 15 tasks and a lengthy assessment each month may have been too demanding for some adolescents. Monthly survey completion among control group participants, who had no other assigned tasks and could earn bonuses in raffles, remained greater than 90% across the intervention period. For this reason, it is recommended that assessments be conducted before and after, but not during, the intervention period. As Table 3 demonstrates, mean values for TeensTalkHealth evaluated constructs were consistent across the 4 months of intervention. Thus, assessment of constructs just after intervention completion appears reasonable and may increase participation in intervention activities. Another strategy that may enhance task completion is the incorporation of gaming features into the website [58]. For example, points could be awarded for completion of activities and messages posted in response to other adolescents; the points adolescents have accumulated could be prominently displayed on the home page with peers' accumulated points. If desired, periodic raffles could be held; points accumulated could correspond to number of raffle entries. Raffles may be an economically feasible approach to incentivizing participation among adolescents. Most incentives in this study were for completion of lengthy monthly assessments.

The TeensTalkHealth protocol yielded high indexes of satisfaction with respect to comfort on the website, perceived privacy, website accessibility/ease of use, and perceived credibility of health educators and models in video vignettes. Mean values for perceived credibility of other adolescents were greater than the scale midpoint at both assessed time points, suggesting that adolescents could identify with and potentially learn from the life experiences of selected peers. Mean values were also greater than the scale midpoint for a key respect for autonomy item ("How much were health educators trying to help you do what you want?"). The amount of time health educators can spend developing responsive content and engaging adolescents in conversation is critical to further enhancing these indexes of satisfaction. When moderating website content, professionals could attempt to elicit healthy relationship goals from individual adolescents and provide information, motivation, and behavioral skills that will help individuals achieve articulated goals. This may further increase adolescents' perceptions of personal relevance and respect for autonomy by health educators, which may in turn increase participation and retention.

Limitations of the present feasibility and acceptability study include underrepresentation of younger adolescents and males in the study sample. Requirement of parental consent may have been a barrier to participation for younger adolescents. If TeensTalkHealth and similar interventions are shown to reduce adolescent health risk behavior, waivers of parental consent may be considered by Institutional Review Boards of academic institutions. Similarly, health service organizations may consider website access to be an extension of services protected by privacy. Targeted recruitment (eg, through social networking sites or male-oriented organizations) may be necessary to reach higher numbers of male participants.

It is difficult to estimate the degree to which the present set of findings may be generalized to applications of TeensTalkHealth among general populations of adolescents and in contexts in which reimbursement for study activities or other incentives cannot be provided. Our convenience sample was likely comprised of adolescents who found the idea of anonymously interacting with others on a sexual health website to be particularly appealing. Additionally, adolescents may have been attracted by reimbursements for study participation. Both of these features limit generalizability of the present findings to general populations and contexts in which incentives cannot be given. It is possible that rates of participation would have been lower than that observed in the present study if incentives had not been given. The best way to determine the degree to which incentives may influence participation is to conduct future randomized controlled trials in which incentives vary across study conditions (eg, no incentives, modest raffle prizes where entries in the raffle are linked to degree of website participation, fixed reimbursement for completion of assessments and other study activities). Further, random assignment to tailored versus nontailored content across conditions of no incentives, modest incentives, and robust incentives may address the question of how to foster website engagement and participation in contexts where financial resources are limited. An additional consideration is the degree to which design-based research practices have been implemented [45]. Greater collaboration with adolescent website users and shaping of intervention content in response to adolescents' stated needs should result in greater engagement and participation on the part of adolescents.

The TeensTalkHealth approach to health promotion is a feasible and acceptable strategy for community health practitioners and other health professionals to engage adolescents. A primary advantage of this approach is that adolescents can privately, comfortably, and candidly disclose thoughts and feelings that drive decision making. Interactive technology allows health professionals to receive immediate feedback on the helpfulness of communications, respond to potentially changing needs of adolescents over time, and continually encourage health protective behavior. As the evidence base for the effectiveness of interactive health promotion websites is being established, practitioners may use websites as a complement to existing services. TeensTalkHealth and similar interventions require an investment of time by health professionals to build relationships with individual adolescents and among adolescent website users. With the present process evaluation as an aid, practitioners in diverse settings can consider the resources needed to implement and evaluate technology-based interventions that involve moderated interaction between adolescents and health professionals.

Conflicts of Interest

None declared.

Multimedia Appendix 1

Description of video vignettes designed to provide information, motivation, and behavioral skills.

[PDF File (Adobe PDF File), 149KB - resprot_v4i3e106_app1.pdf]

Multimedia Appendix 2

Sample video vignette: No Worries.

[MOV File, 98MB - resprot_v4i3e106_app2.mov]

Multimedia Appendix 3

Sample video vignette: Party Pressure.

[MOV File, 102MB - resprot_v4i3e106_app3.mov]

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Abbreviations

HIV: human immunodeficiency virus
IMB: Information-Motivation-Behavioral skills
STI: sexually transmitted infections

Original Paper

Development of a Website Providing Evidence-Based Information About Nutrition and Cancer: Fighting Fiction and Supporting Facts Online

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Abstract

Background: Although widely available, the general public, cancer patients, and cancer survivors have difficulties accessing evidence-based information on nutrition and cancer. It is challenging to distinguish myths from facts, and sometimes conflicting information can be found in different places. The public and patients would benefit from evidence-based, correct, and clear information from an easily recognizable source.

Objective: The aim of this project is to make scientific information available for the general public, cancer patients, and cancer survivors through a website. The aim of this paper is to describe and evaluate the development of the website as well as related statistics 1st year after its launch.

Methods: To develop the initial content for the website, the website was filled with answers to frequently asked questions provided by cancer organizations and the Dutch Dietetic Oncology Group, and by responding to various fiction and facts published in the media. The website was organized into 3 parts, namely, nutrition before (prevention), during, and after cancer therapy; an opportunity for visitors to submit specific questions regarding nutrition and cancer was included. The website was pretested by patients, health care professionals, and communication experts. After launching the website, visitors' questions were answered by nutritional scientists and dieticians with evidence- or eminence-based information on nutrition and cancer. Once the website was live, question categories and website statistics were recorded.

Results: Before launch, the key areas for improvement, such as navigation, categorization, and missing information, were identified and adjusted. In the 1st year after the launch, 90,111 individuals visited the website, and 404 questions were submitted on nutrition and cancer. Most of the questions were on cancer prevention and nutrition during the treatment of cancer.

Conclusions: The website provides access to evidence- and eminence-based information on nutrition and cancer. As can be concluded from the number of visitors and the number of questions submitted to the website, the website fills a gap.

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Introduction

Background

With more than 10,000 epidemiological studies, and several animal and in vitro experiments, the major diet- and nutrition-related factors in the etiology of cancer are now well-known to researchers. Numerous reports and guidelines have been written on cancers, which are widely available both online and in print [1-6]. However, one of the most consistent findings in health services research is that scientific knowledge often does not reach the general public.

Although several studies have shown that adhering to the guidelines concerning a healthy weight, a healthy diet, and sufficient physical activity does reduce cancer risk [7,8], approximately one half to two thirds of people think these factors do not contribute to their cancer risk [9,10], despite the fact that these guidelines are actively addressed by both national and international organizations in their campaigns for the general public [2,11].

Not only are the guidelines to reduce the risk of cancer not well-known, but also cancer patients are not well informed about the guidelines regarding nutrition during and after cancer treatment. Because these guidelines are not sufficiently implemented in daily practice [12], this can result in inefficient, inappropriate, or even harmful care [13]. Furthermore, information about nutrition and cancer is often provided on request and is not routinely discussed during consultation [14]. The literature shows that there is a high demand for nutritional information among cancer patients [15], and that 30-66% of cancer patients have unmet nutritional information needs [15-20]. As a result, cancer patients and survivors try to fulfill these needs by finding information. In a survey conducted among 217 young adult cancer patients, almost 90% reported the need for nutritional information, and 95% of the respondents have used websites to search for information [15]. In a study involving around 2000 breast, prostate, and colon cancer patients, approximately 25% of patients reported searching for information online [21]. The monitoring of Internet use in The Netherlands in 2014 showed that 50% of health care users searched the Internet for information on nutrition and exercise [22].

The actual information on nutrition and cancer available online is overwhelming, with numerous websites from individuals, foundations, and industry and health care organizations providing information [2,11,23-28]. However, for the visitors of these websites, it may be hard to distinguish evidence-based websites from those that are not and to separate myths from facts. This may lead to misconceptions resulting in unnecessary or worse changes in dietary habits with a negative effect on nutritional status and response to treatment [29]. Furthermore, conflicting information leads to confusion and uncertainty, which may negatively influence the quality of life of cancer patients. The provision of appropriate information can result in an improved health competence, a better sense of control over cancer, better symptom management, lower levels of distress, and higher levels of health-related quality of life [30].

A recent study shows that active information seeking about cancer from nonclinical sources may lead to improved dietary habits among cancer patients [31]. Furthermore, an evidence-based website may lead to a better sense of control over cancer. A recently launched website for lung cancer patients was used by patients to better understand the information given by their own specialist. An evaluation of the site showed that access to this information helped them to better cope with their disease [32].

Objective

Thus, cancer patients, both during and after treatment, as well as the general public, would benefit from correct, clear, and evidence-based information from an easily recognizable and evidence-based source. Therefore, the aim of this project is to make scientific information available to all people who have to deal with cancer. Because of the aforementioned positive effects, a website is used to provide people with nutritional advice to prevent cancer, nutritional advice during cancer treatment, and advice about what to do once their treatment is finished. The aim of this paper is to describe and evaluate the development of the website and to describe the experiences of the 1st year after the launch.

Methods

Prelaunch

The first content of the website Voeding en Kanker Info (Nutrition and Cancer Info) [33] was composed by collecting (1) items from oncology dieticians in daily practice (members of the Dutch Dietetic Oncology Group); (2) questions received by the helplines of various cancer organizations (eg, the Dutch Cancer Society and the World Cancer Research Fund); and (3) various fiction and facts published in the media.

Answering Questions

Questions were answered by registered dieticians specializing in oncology and nutritional scientists and were reviewed by members of the Dutch Dietetic Oncology Group. Evidence from meta-analyses of observational studies, reviews, and randomized controlled trials (RCTs), in combination with evidence from animal and in vitro studies, was used to formulate those answers. All questions and answers were used as content for the website.

Design

The website was designed with a home page where the questions were displayed. The editorial board, including the authors of the website, was fully shown on the home page. The 5 most prevalent tumor types (lung, breast, prostate, colorectal, and skin tumors) were described on separate pages; questions were categorized by tumor type and by the following categories: prevention, during treatment, or after treatment/tertiary prevention.

Pretest

Before the official launch, a pretest was performed, and the website was evaluated by cancer survivors, health care professionals, and communication experts. Survivors were recruited from the Online Cancer Patient Panel of the

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Netherlands Comprehensive Cancer Organization and from the oncology day-care center of a peripheral hospital where the questionnaire was filled out while the patients received chemotherapy. The professionals were communication specialists, registered dieticians, nutritional scientists, the staff of the World Cancer Research Fund and the Dutch Cancer Society, and patient advocates. Those who tested the website filled out a questionnaire on site design and layout, content, readability, and comprehensiveness of the texts. The questionnaire contained both open-ended and closed questions. The questions asked in the questionnaire for professionals can be found in Multimedia Appendix 1, and the questions in the questionnaire for patients can be found in Multimedia Appendix 2.

After the Launch

Public Relation

Immediately after the official launch, media attention was sought. One of the authors (EK) had interviews on regional and national radio stations, and articles were published in both regional and national newspapers and in magazines from patient organizations, health professionals, and the university. In addition, many websites (eg, Voeding Nu [34], Gezondheid [35], Foodlog [36], Onderzoekers [37]) paid attention to the launch of the website on nutrition and cancer. Each time a question was answered on the website, a notice was sent out via Twitter.

Submitted Questions

After the launch, visitors of the website could submit questions. After submitting the question, the person received a standard email explaining the answering procedure: a literature search is performed, the answer is read by a team of experts, and then it is sent to the submitter of the question. The questions were answered by nutritional scientists and dieticians and reviewed by members of the Dutch Dietetic Oncology Group. When necessary, advice was sought from other experts. Questions about specific personal and unique situations received a direct and personal answer. If the patient needed more personal feedback or additional guidance, referral to a dietician or to the treating physician was made. Questions or opinions from people with strong beliefs regarding nutrition and cancer were directly answered by the nutritional scientists and registered dieticians and were not placed on the website. In these answers, an explanation was given that only scientific evidence from sufficient observational studies, meta-analyses, reviews, and RCTs was used to formulate answers, in combination with animal, in vitro, and case studies. General questions on cancer were redirected to other sources of information, such as to the website of the Dutch Cancer Society [11]. General questions about nutrition were redirected to The Netherlands Nutrition Centre [38]. Questions and answers on nutrition and cancer were placed on our website.

Categorization of Questions

Visitors of the website who asked a question did not have to sign in or make a profile. Instead, they had to submit a form in which their name, email address, and some questions had to be filled in. To gain insight into the information needs of the visitors of the website, the questions were analyzed. Each form and question, with its matching answer, were read and imported to a Microsoft Access database (Microsoft, Redmond, WA, USA). Questions were categorized and ordered independently by 3 of the authors (MRV, SB, and AMAA). The categories were "products promoting health" and "products harming health/increasing cancer risk." In addition, 3 periods were defined, namely, "prevention of cancer," "nutrition during treatment," and "nutrition after treatment." Information on the number of question submitters and the number of questions per submitter was recorded and calculated.

User Statistics

Google Analytics was used to collect information about the number of page views, the number of visitors, and the length of stay.

Results

Prelaunch

Overview

Feedback was provided on content and site design; in addition, improvements were also suggested. Based on the results of the pretest, improvements in design, content, and navigation were made before the official launch of the website.

Feedback From Patients

Fifty-six patients started the questionnaire, and 38 patients (68%) filled in the complete questionnaire. As can be seen in Table 1, 15 respondents (27%) had visited a website on nutrition and cancer before the launch of our website or a general search on Google. Ten (24%, 10/41) patients did not find the information in our website to be completely clear. Their reactions were "I can't find which diet is important for my sort of cancer", and "I do not understand the relationship between apricot kernels and nausea." Twenty-five patients (45%) thought the website was not complete: "There are only 5 types of cancer", "What types of food should I avoid?", "Information is missing", "it is not completely clear how many nutrients I need to keep my body healthy and fit", and "You can see the website is not finished yet". Of all of the patients who completed the questionnaire, 28 (74%) would recommend the website to others. The reasons for not recommending the website were "There is not enough new information on this website", "I do not see the difference between the website of the Dutch Cancer Society and this website", and "I hope there will be referrals from other websites, as I do not think you will find this website without a referral".

Table 1. Results of pretest by cancer patients

Question number	Question	Yes	%	No	%	Other	%	Total
Q2	Did you visit other websites on nutrition and cancer?	15	27	41	73			56
Q6	Is it clear in a glimpse what the website is about?	31	76	10	24			41
Q7	Is it clear in a glimpse who the owner of the website is?	17	40	26	60			43
Q9	Does the website meet your expectations?	26	65	14	35			40
Q12	What do you think of the chosen font? Is it clear?	36	92	3	8			39
Q13	What do you think of the colors used? Are they pleasant?	34	87	5	13			39
Q14	What is your opinion of the selection of the pictures? Are they pleasant?	34	87	5	13			39
Q16	Is the layout clear?	34	87	5	13			39
Q17	Can you easily find what you are looking for?	34	87	5	13			39
Q20	Do you think the texts on the website are comprehensible?	37	95	2	5			39
Q23	Do you think the website is complete?	20	53	1	3	17	45	38
Q24	Is it clear where you can ask questions?	29	76	9	24			38
Q27	Does the website look reliable?	33	87	5	13			38
Q28	Would you visit this website?	32	84	6	16			38
Q29	Would you recommend the website to others?	28	74	3	8	7	18	38

For most respondents, the first impression of the website was a positive experience: "clear", "fresh", and "looks reliable". Improvements were suggested as follows: "smaller images", "not only young and healthy individuals on the images", "Such a website suggests that you can alter your disease with nutrition, while it actually is about altering your diet to cope with your cancer", and "Always mention the source, where did you find the answer to the question?". Suggestions on the structure of the website were also given: one suggestion was "More links", while another respondent suggested "More scrolling options instead of links".

Feedback From Health Care Professionals and Communication Experts

Fifty professionals from 5 groups (communication specialists, dieticians, nutritional scientists, staff of the World Cancer Research Fund and the Dutch Cancer Society, and patient advocates) were contacted; 23 professionals (46%) provided feedback on the website. They provided comments about its layout, which were similar to the feedback of the patients: "the images are too large", "the front page is not clear", and "I do not understand the navigational options of the website". In addition, comments were made on the question form: "I cannot find your question form". Other comments included positive remarks on the total look of the website: "I like the vibrant colors and the positive feel of the website", and "the texts are easily accessible and comprehensible".

Their general comments on content were as follows: "Why do you only mention the 5 most common types of cancer?", "Where can I find a full reference list?", and "I was looking for information for professionals, a pity it is not there". Opinions differed on the difficulty level of the texts. Some respondents said the level of the texts was appropriate, whereas others commented that the texts were too difficult for the general public.

As a result of all the feedback, a clear distinction was made between the different phases: before treatment (primary prevention), during treatment, and after treatment. Nondiet-related information on tumor types was deleted, because this can be found on other websites [11]. Categorization by the 5 major tumor types was no longer used. Alterations were made to the logo, the font size of the website, the pictures used, and the navigation options. Additional information on nutrition and cancer was uploaded to the website before the launch. The comprehensiveness of the texts was tested [39] and adjusted in such way that all texts matched the B1 level of the Common European Framework [40]. A preview of the home page of the website just before the launch is shown in Figure 1.

Figure 1. Home page of the website (May 2014).

After the Launch

Public Relation

The results of the public relation activities were reflected in the number of views of the website. Right after the launch in May 2014, the level of media attention was high, and this is reflected in the large number of website views seen in Figure 2. The peaks in May reflect the media attention in the national newspaper Metro and radio interviews, and the peak in July reflects a Facebook post of the National Cancer Institute promoting the website. From December onward, business cards were handed out by dieticians and oncology nurses, and the website was actively promoted at several large conferences, which is reflected by a steady rise in website views and users.

Figure 2. Website views per month.
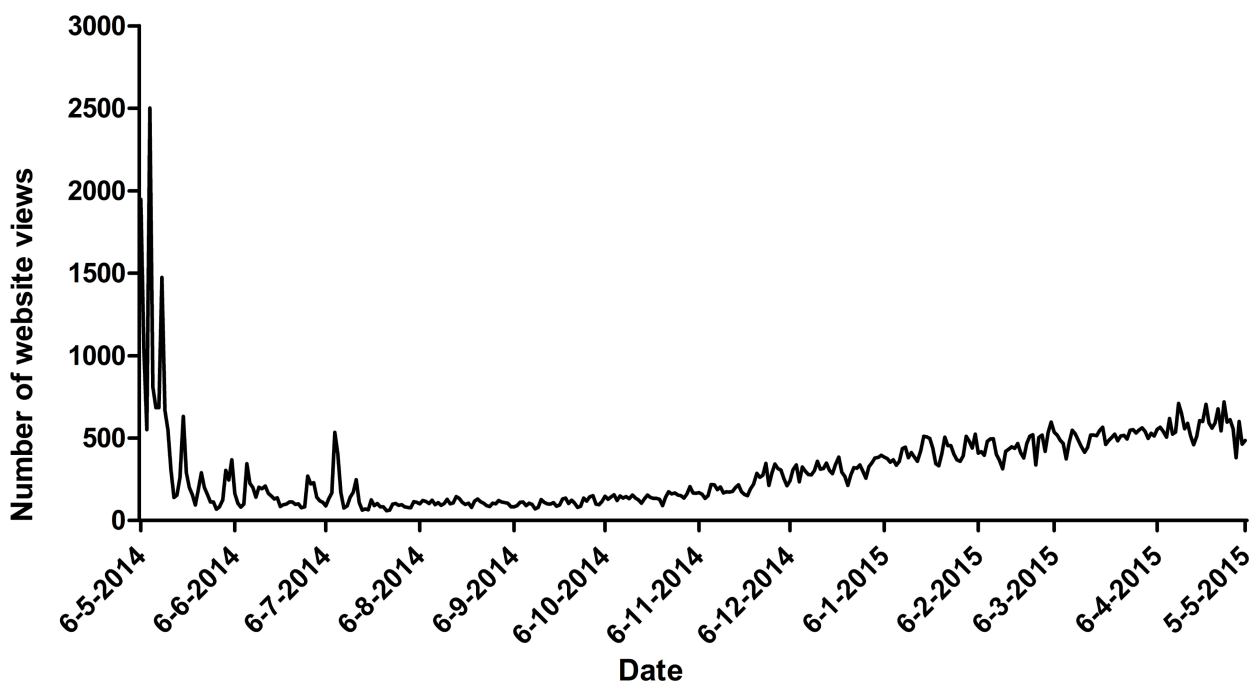
User Statistics

Between May 6, 2014, and May 5, 2015, 322,627 page views, 2.9 pages per visit, 90,111 visitors, a length of stay of 2.17 minutes per visit, and 109,596 website views were registered; there was an average of 7509 visitors, 26,885 page views, and 9133 website views per month. An increase can be seen in the number of website views, as shown in Figure 3. As much as 88.33% (n=96,817) of website views were from The Netherlands, 6.74% (n=7391) came from Belgium, and the remaining (4.91%; n=5388) came from non-Dutch speaking countries.

Figure 3. Comparison of website views in June 2014 and April 2015.
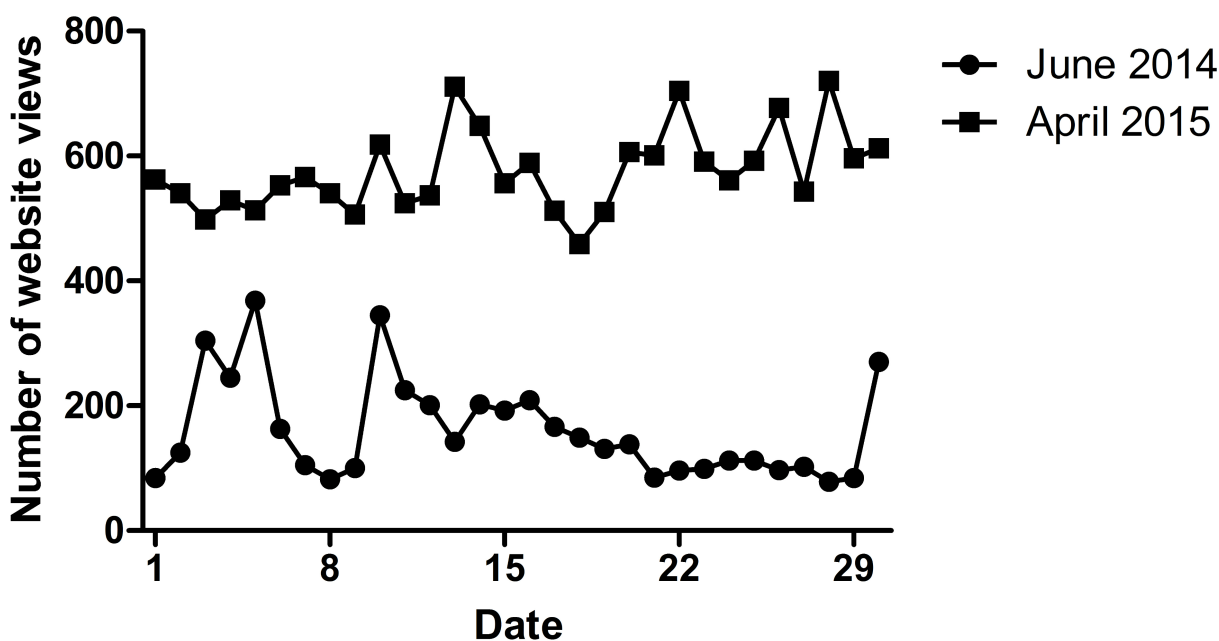
Information on Question Submitters

In total, 338 people submitted 404 individual questions. A majority of people sent in 1 question (n=299, 88.4%). Thirty-nine people (12%) who submitted questions asked more than 1 question: 25 submitters asked 2 questions, 9 submitters asked 3 questions, 3 people asked 4 questions, 1 person asked 7 questions, and 1 person submitted 9 questions. Question submitters were not asked for feedback on the website, because we had not informed the visitors of the website that they could be contacted. Therefore, to make sure the privacy of the question submitters was preserved, no user satisfaction survey was performed.

Submitted Questions

In the 1st year of the website launch, 404 questions were submitted via the contact form. Detailed information on these questions can be found in Table 2.

Table 2. Categorized questions submitted to the website in the first year after the launch.

	Prevention	During treatment	After treatment	Other questions	Total
Products promoting health	64	135	9		208
Products harming health/increasing cancer risk	31	53	5		89
Other topics				107	107
Total	95	188	14	107	404

As can be seen in Table 2, most of the questions were on factors promoting health, both to prevent cancer and during the treatment of cancer.

Representative examples of questions on nutritional factors to prevent cancer, possibly promoting health were "Is biological fruit better?", "Does the intake of dairy products affect my cancer risk?", "Can a product such as chia seeds prevent cancer?", and "What do you think of the use of curcuma to prevent cancer?". Examples of questions on nutritional factors to prevent cancer, possibly harming health were "Does drinking coffee increase my cancer risk?", "Is it true that people with a low cholesterol level have an increased cancer risk?", "Does omega 6 increase cancer risk?", and "Do artificial sweeteners increase my risk of getting cancer?".

Questions on nutritional factors during cancer treatment, possibly promoting health were "Can you advise me how to season my foods, to improve taste?", "Is it known whether broccoli helps to treat my cancer?", "Can I use probiotics during my cancer treatment?", and "Are red fruits good to use for breast cancer patients?".

Questions on nutritional factors during cancer treatment, possibly harming health were "Is it true that sugar feeds my tumor?", "Is it harmful to eat soy products during my breast cancer treatment?", and "Is it true that green tea interferes with my antitumor treatment?".

The questions on nutritional factors after cancer treatment, possibly promoting health were "What can I eat now that my stoma is removed to prevent the recurrence of my cancer?", "Will eating soy products along with my tamoxifen use help to prevent the recurrence of my breast cancer?", and "What nutrition can you advise to prevent the recurrence of prostate cancer?". Questions on nutritional factors after cancer treatment, possibly harming health were "Does cheese harm you when you had breast cancer?", "Can you drink wine if you are using tamoxifen after breast cancer?", "Can using curcuma after melanoma treatment harm my health?", "Does consuming sugar increase my risk of cancer recurrence?", and "Can I use fruit and yoghurt together after being cured of colorectal cancer?".

The majority of submitted questions were on specific foods or food components, not on complaints. However, when looking at the questions visited at the website, the top 10 were mostly filled with questions regarding complaints related to their disease, such as nausea, dry mouth, or diarrhea. In addition, 61 questions were requests for business cards.

After 1 year, 121 articles could be found on the website. In these 121 articles, 238 questions could be answered. In total, 372 questions (N=404; 92.0%) were answered. Expert advice was sought on the topics of diabetes/sugar and cancer, vitamin D and cancer, the interaction of foods and nutrients, and pharmaceuticals. The response time to questions was 1 day for the standard response, and the median response time was 3 days (range 0-280 days) for a detailed answer.

Discussion

Principal Findings

Before the official launch, the website was designed (based on feedback and suggestions), pretested, and adjusted according to the provided feedback: extra questions and answers were added, the subdivision by tumor type was removed, and alterations were made to the logo, the font size, the pictures used, and the navigation options. In the 1st year after the launch, a total of 404 questions were submitted on nutrition and cancer. Most of the questions were on food products promoting health, both in the prevention of cancer and during the treatment of cancer. A total of 90,111 people visited the website during this period.

When investigating the submitted questions, it was noticed that there are a lot of opinions on nutrition and cancer, which are not completely evidence based. These beliefs often arise from the results of in vitro and animal studies, but are not confirmed in human studies. Therefore, most of the answers to commonly asked questions on the website start with "No, there is no

scientific evidence." This is due to the fact that only studies in humans were used as evidence, because research only conducted in animals and in in vitro studies cannot be directly translated into humans. Besides the evidence-based answers, some answers are based on best practice-based evidence. Questions on complaints are mostly answered according to best practice-based evidence, whereas questions on specific nutrients are provided with evidence-based answers.

The very limited results from in vitro or animal studies sometimes lead to hypes in the media. Some examples are specific foods that people believe could prevent cancer, support cancer treatment, or promote general health (curcuma, chia seeds, etc). A large number of people follow this hype, which is reflected in the number of questions on these food products that were posted on the website. The question arises regarding why a large number of people use these products to prevent cancer or to support cancer treatment, despite the fact that their use is not evidence based. It might be possible that people do not want to put much effort into following healthy lifestyle advice, and therefore, they look for supplements or specific foods that can support their treatment. Indeed, a high number of questions about dietary supplements that might support cancer treatment or might decrease cancer risk were posted on the website.

There was a discrepancy between the topics of the submitted questions and the top 10 questions visited on the website. Therefore, it is likely that the questions on complaints were already answered by the content of the website, and fewer questions had to be asked on this topic.

Limitations

In the prelaunch test, the nonresponse might have been due to the fact that patients were asked to fill out the questionnaire while receiving their chemotherapy. Furthermore, open questions lead to the highest number of dropouts: "What is your first impression of this website?" and "Is it clear at first sight what information can be found on this website?"

The visitors were not asked for feedback after the launch of the website. However, in a focus group, the patients were asked for their opinions of the website. These patients were glad the website was launched, and they were able to find the information that they were looking for. In their opinion, the website was clear, informative, and complementary to the online information available at that point.

As mentioned earlier, to preserve privacy, no information on the sex and age of visitors was recorded. Therefore, no conclusions can be drawn on the characteristics of the visitors. Because the average time spent on the website was 2.17 minutes, and the visitors visited 2.9 pages on average, we assume that the visitors really searched for information on nutrition and cancer and did not visit the website by accident. However, it is unknown whether these visitors are cancer patients, relatives, health care professionals, or members of the general public. When looking at the type of questions submitted to the website, most of the questions were on the prevention of cancer and nutrition during treatment. This might suggest that both the general public and cancer patients visit the website. The lack

of questions on nutrition after treatment could be due to the fact that once people are cured from cancer, they do not want to read about cancer anymore, so these people will not visit the website. Another reason could be that cancer survivors do not think about cancer in relation to tertiary prevention, or that the submitter of the question makes no distinction between primary or tertiary prevention.

The response time in answering questions varied widely for different questions. This was due to the vast number of questions submitted following the launch, and the fact that there were so many questions that needed extensive research. Therefore, the response time was much longer than anticipated. Because it is not appropriate to make people wait for so long, especially in palliative settings, this needed to be resolved. Extra personnel were hired, and the answering methods were optimized: standard answers were formulated that could be adjusted for specific personal situations. The response time has decreased since these measures were taken: most questions are answered within 2 weeks. In addition, questions were submitted that already could be found on the website; these readers were referred to the specific question and answer on the website. This also decreased the response time.

To reach a larger number of potential users of the website, beginning in December 1, 2014, business cards were distributed via oncology nurses, dieticians, and oncologists to inform patients about the existence of the website. This led to an increased number of visitors to the website and eventually to more questions.

Comparison With Prior Work

Globally, there are more websites on nutrition and cancer; however, our website is the only Dutch website solely on nutrition and cancer where people can ask questions. Internationally, there are other websites, such as that of The Cancer Nutrition Center [41] and the American Society of Clinical Oncology [42]. However, the focus of these websites is exclusively on practical information for the patient, and no scientific evidence is presented. Therefore, our website has a unique concept.

In The Netherlands, there are no other websites on the full scope of cancer and nutrition to prevent cancer, or during treatment and after treatment. Therefore, our website was compared with the nutritional part of The Dutch Cancer Society website [11] and with the Dutch Lung Cancer Information Center website [43].

When comparing the user statistics of our website with the user statistics of the nutritional part of The Dutch Cancer Society [11], we noted some differences. Our website had 7500 visitors per month versus 1250 visitors per month on the nutritional section of the other website. However, the length of stay on our website was substantially shorter: 2.19 minutes on our website, compared with 7.63 minutes on the nutritional part of The Dutch Cancer Society website. The country of origin of the visitors was comparable for both websites. The Dutch Cancer Society website has not seen a change in the number of visitors since the launch of our website [44]. A reason for this might be that our website attracts different people than those visiting the

nutritional part of The Dutch Cancer Society website or that people visit both websites. It might also be that people are looking for information on The Dutch Cancer Society website and accidentally visited the part about nutritional information, instead of specifically searching for information on nutrition and cancer. In the past, people might have used other, less reliable websites in addition to their potential use of The Dutch Cancer Society website. Since the launch of our website, they have access to evidence-based information on nutrition and cancer and the opportunity to ask questions about nutrition and cancer.

Some differences were also noted when comparing the results of our website with the results of the website of the Dutch Lung Cancer Information Center [43]. First, the number of questions was substantially higher for the lung cancer website (57 versus 34 questions/month). The relative difference in the number of questions may be due to the topic of both websites. The Lung Cancer website focused on medical questions, which were answered by medical specialists. In comparison, a smaller number of questions could be expected for our website, because it only focuses on nutrition and cancer, thereby targeting only a smaller group of people. Another difference between the 2 websites is that the Lung Cancer website was able to register the identity and sex of its visitors. This information was not recorded on our website. A similarity between both websites is that most visitors only asked 1 question.

Recommendations for Future Website Developers

Based on the experience from developing this website, the following recommendations are provided to future website developers:

- Start with an assessment of the information needs within the target group. For instance, a patient panel or patient focus groups can be used to explore wishes and demands regarding the future website.
- Before launching the website, test for its readability, usability, completeness, etc. Ask potential users/target group (ie, patients, health care professionals) and communication experts for feedback.
- Make it possible to register user information of the website visitors using cookies, to be able to further tailor the website to your visitors' demands.
- Do not underestimate the man power needed to maintain a website driven by visitors' questions. Be sure that there is enough man power to respond quickly to patients' questions.
- Make use of printed press and social media channels to promote your website to the target group, so your website is used to its full potential.

Conclusions

The Voeding en Kanker website provides access to evidence-based, best practice-based, and eminence-based information on nutrition and cancer. As can be concluded from the number of questions submitted and the number of visitors to the website, in comparison with the number of visitors to the nutritional part page of The Dutch Cancer Society website and the Dutch Lung Cancer Information Center website, our website fills a gap in the provision of information about nutrition and cancer. Future work includes ongoing improvement of the website by answering questions and responding to current events more quickly. The website will be used to respond to actual news events; additionally, a section with recipes for cancer patients suffering from alterations in their taste and a section especially focused on health care professionals will be developed.

Authors' Contributions

MRV was responsible for answering questions on the website and for collecting questions, the prelaunch test, the analyses, promoting the website, and writing the manuscript. SB was responsible for answering questions on the website, collecting questions, the prelaunch test, promoting the website, and reviewing the manuscript. AMAA was responsible for answering questions on the website, promoting the website, and reviewing the manuscript. JV-B and EK were responsible for answering questions on the website, collecting questions, promoting the website, and reviewing the manuscript.

Conflicts of Interest

None declared.

Multimedia Appendix 1

The questions asked in the questionnaire for professionals.

[PDF File (Adobe PDF File), 2KB - resprot_v4i3e110_app1.pdf]

Multimedia Appendix 2

The questions in the questionnaire for patients.

[PDF File (Adobe PDF File), 5KB - resprot_v4i3e110_app2.pdf]

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Abbreviations

RCT: randomized controlled trial

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<u>Original Paper</u>

A Mobile Internet Service for Self-Management of Physical Activity in People With Rheumatoid Arthritis: Challenges in Advancing the Co-Design Process During the Requirements Specification Phase

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Abstract

Background: User involvement in the development of health care services is important for the viability, usability, and effectiveness of services. This study reports on the second step of the co-design process.

Objective: The aim was to explore the significant challenges in advancing the co-design process during the requirements specification phase of a mobile Internet service for the self-management of physical activity (PA) in rheumatoid arthritis (RA).

Methods: A participatory action research design was used to involve lead users and stakeholders as co-designers. Lead users (n=5), a clinical physiotherapist (n=1), researchers (n=2) with knowledge in PA in RA and behavioral learning theories, an eHealth strategist (n=1), and an officer from the patient organization (n=1) collaborated in 4 workshops. Data-collection methods included video recordings and naturalistic observations.

Results: The inductive qualitative video-based analysis resulted in 1 overarching theme, merging perspectives, and 2 subthemes reflecting different aspects of merging: (1) finding a common starting point and (2) deciding on design solutions. Seven categories illustrated the specific challenges: reaching shared understanding of goals, clarifying and handling the complexity of participants' roles, clarifying terminology related to system development, establishing the rationale for features, negotiating features, transforming ideas into concrete features, and participants' alignment with the agreed goal and task.

Conclusions: Co-designing the system requirements of a mobile Internet service including multiple stakeholders was a complex and extensive collaborative decision-making process. Considering, valuing, counterbalancing, and integrating different perspectives into agreements and solutions (ie, the merging of participants' perspectives) were crucial for moving the process forward and were considered the core challenges of co-design. Further research is needed to replicate the results and to increase knowledge on key factors for a successful co-design of health care services.

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KEYWORDS

XSL•FO
RenderX

Introduction

Background

User involvement in the development of health care services is important for the viability, usability, and effectiveness of services [1-3]. However, even when the users are involved, the development process may be unsuccessful, and the service may not be accepted and used. Previous research has reported diverse results regarding both benefits and drawbacks of user involvement [1,2]. One explanation for the drawbacks may be that little is known about the various aspects of collaboration associated with the development of a successful service [4,5].

Co-design implies active involvement of lead users (ie, potential users of the future service) to incorporate their experiences and knowledge into the new service [6]. "User-centered design" [7] and "participatory design" [1] are umbrella terms for design strategies. Experience-based design (EBD) [6] is a subform of participatory design that involves including lead users as co-designers. EBD uses principles from design science including architecture, product, and computer design to make the service or product safe, effective, and enjoyable for the user. Because the users' experiences are essential to providing optimal care, they have been used to improve health care services [8]. EBD is also complementary with personalized care, which focuses on the individuals' experiences, preferences, and goals in the provision of optimal care [9,10].

Co-design also denotes a collaboration between the stakeholders and system developers. Collaboration can be defined as the interaction between the stakeholders and system developers with the aim of achieving a shared goal [11]. Successful collaborations may be a key factor in the outcome of a project [12,13]. However, previous research related to co-design has primarily described the process on a macro level, for example, the benefits and drawbacks regarding money, time, and how user participation informs the new service [2,14]. Empirical studies describing the collaboration between co-design participants are scarce [2,4,5]. We were able to identify only 1 previous study that used video recordings to describe the collaboration during co-design meetings [15]. Therefore, research describing the collaboration during co-design is needed to extend our knowledge on effective collaborations to move the process forward.

Study Objective and Overview

This study will provide a description of the challenges observed during co-design meetings. During the first step of the ongoing project, lead users presented ideas on core features that are to be included in the future service [16]. During the second step of the co-design, lead users, a clinical physiotherapist, researchers with knowledge in physical activity (PA) in rheumatoid arthritis (RA) and behavioral learning theory, an eHealth strategist, and an officer from the patient organization collaborated to provide data for the system requirements and specification of the future service [17]. The aim of this study was to explore the challenges in advancing the co-design process during the requirements specification phase of a mobile Internet service for the self-management of PA in RA.

Methods

Design

To explore the challenges in advancing the co-design process, an inductive, qualitative, participatory-action research design was applied [18]. The co-design process was performed during 4 workshops in February and March, 2013, at Uppsala University, Sweden.

Data collection included video recordings [19] and naturalistic observations [20]. The purpose was to capture situations and events in which the co-design participants discussed issues deemed important for advancing the co-design process. This study was approved by the regional ethical review board in Stockholm (D nr 2010/1101-31/5).

Selection and Recruitment of Participants

The co-design group (n=10) was formed to create a feasible workgroup and to capture different perspectives (ie, experiential and theoretical knowledge). Potential co-design participants were identified through our research and clinical networks and were invited by email by the first author. The inclusion criteria were adequate Swedish communication skills and access to the Internet with confidence in using the Internet. Furthermore, the participants were chosen to include different perspectives, including experiential knowledge in living with RA, clinical experience in supporting individuals with RA to be physically active, theoretical knowledge on behavioral learning theory, evidence for PA in RA, and/or service design.

Potential co-design participants who provided preliminary consent were informed about the study by the first author. Written information and a questionnaire on background characteristics, expertise, PA behavior, and Internet habits were provided by mail or email. Participants provided their final consent for participation by attending the first workshop. All but 1 of the participants agreed to attend all 4 workshops.

The participants included 5 lead users, including a patient research partner, 2 researchers with knowledge in behavioral learning theories and PA in RA, 1 clinical physiotherapist, 1 officer from the Swedish Rheumatism Association, and 1 eHealth strategist. Three of the participants were men, and the median age was 55 years (age range 34-73 years). All but one of the participants possessed a university degree. The lead users were chosen to reflect diversity regarding age, sex, years since diagnosis, and PA habits. A few of the participants reported experiential and/or theoretical knowledge in more than 1 of the perspectives (ie, experiential knowledge in living with RA, knowledge of behavioral learning theories and evidence for PA in RA, clinical experience in supporting individuals with RA to adopt and maintain PA, and/or service design).

Planning and Arranging the Co-Design Workshops

A pilot workshop was held before the start of the study to test the data-collection procedures; for example, technical solutions for the video recordings and the feasibility of an observation protocol used by the observers. This resulted in decisions on how to arrange the participants' seating and where to place the microphone and camera. In addition, it was decided that a

technician was needed to set up the camera before each workshop to integrate the video recordings with the interactive.

The positioning of the camera can have a significant impact on the captured data and was carefully considered [19]. The camera was placed on a tripod and was positioned to capture the collaboration between participants, their faces and nonverbal actions, and references to the mediational means used (ie, interactive boards, an online notice board (Trello), and plastic sheets with an outlined mobile phone) (Figure 1). The interactive board and plastic sheet facilitated visualization of the future mobile Internet service during the discussion. They were also used to collect data on the system requirements and specification of the future service. These data were analyzed and presented elsewhere [17].

To facilitate and collect data during the co-design workshops, 1 moderator and 3 researchers were present. The moderator, who had substantial experience with moderation, programming, and designing of digital devices, directed the workshops. The last author (PÅ, experienced in qualitative research and research on physiotherapy integrated with behavioral medicine) was responsible for alignment of the process. The camera operator (CM, experienced in qualitative research and video-based research) and 2 observers (ÅR, experienced in qualitative research and behavioral medicine; CK, experienced in qualitative research, naturalistic observations, and health informatics) collected data during the workshops. The observers only watched and took notes and did not participate in the workshops (Figure 2).

The 4 co-design workshops were performed at intervals of 1-4 weeks in university lecture rooms and lasted between 3½ and 5½ hours. The aim of the workshops was to provide basic data on the system requirements and specifications for the mobile Internet service. The first workshop started from the results of the first step of the co-design process: core features of a future Internet service as proposed by lead users participating in focus group interviews [16]. Thereafter, the first and last authors (ÅR and PÅ), the eHealth strategist, and the moderator planned the workshops iteratively; that is, each co-design workshop was built on the results and experiences from the previous workshop. Textbox 1 presents an overview of the major content and participants at each co-design workshop.

Textbox 1. Overview, major content, and attending participants at the co-design workshops.

Workshop 1: Brainstorming

- Introduction
- Warm-up session
- Brainstorming on needs and proposed features

Attending participants: 3 lead users, 2 researchers, 1 physiotherapist (PT), 1 eHealth strategist, and 1 Swedish Rheumatism Association (SRA) officer

Workshop 2: Focusing

- Warm-up session
- Transforming needs to features
- Creation of the first prototype

Attending participants: 5 lead users, 2 researchers, 1 PT, 1 eHealth strategist, and 1 SRA officer

Workshop 3: Requirements specification

- Presentation of available physical activity apps
- Presentation of the first mobile phone prototype
- Creation of the second prototype

Attending participants: 4 lead users, 1 researcher, 1 PT, 1 eHealth strategist, and 1 SRA officer

Workshop 4: Requirements specification

- Presentation of the second mobile phone prototype
- Continuous specification of features

Attending participants: 4 lead users, 1 researcher, 1 PT, 1 eHealth strategist, and 1 SRA officer

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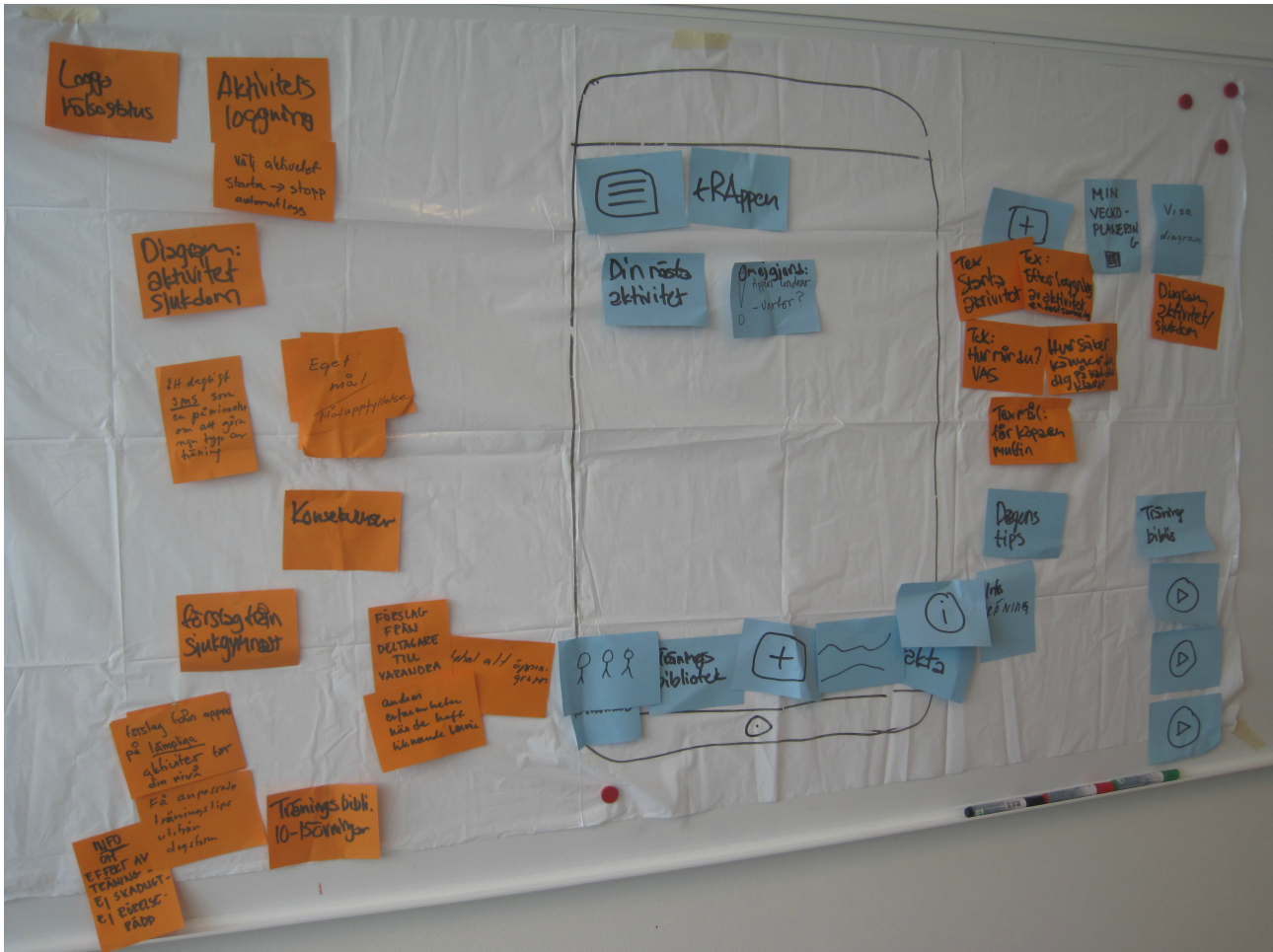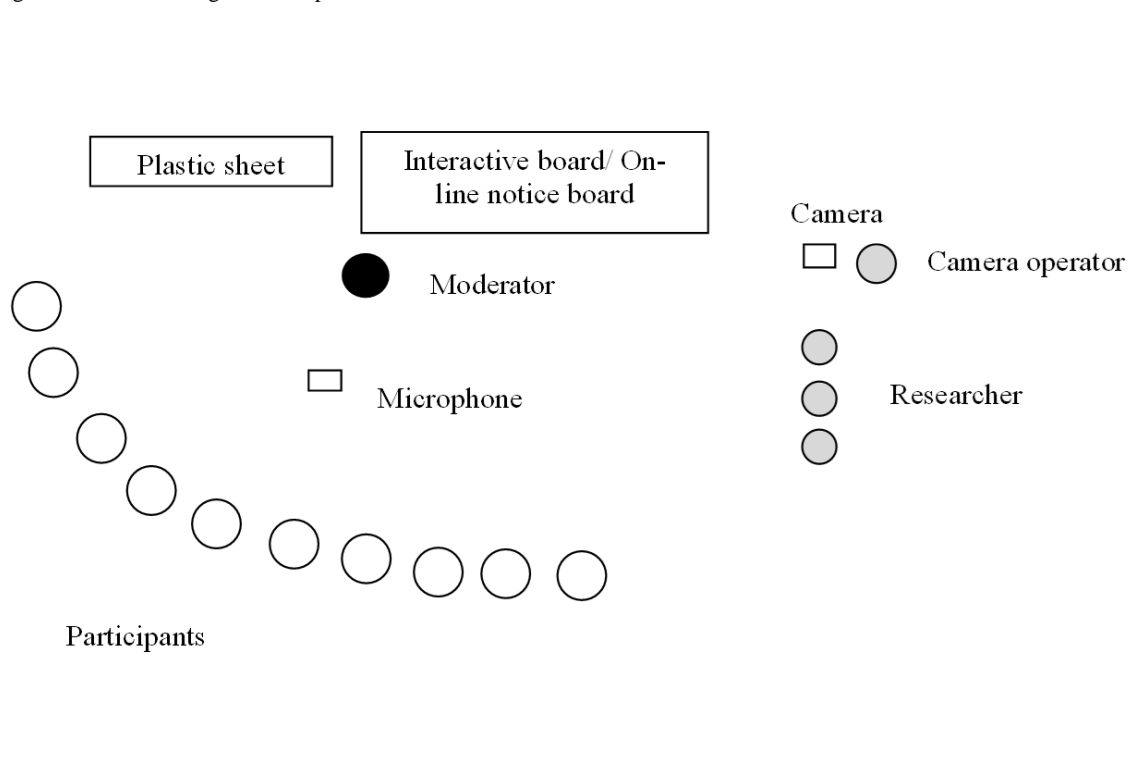**Figure 1.** Plastic sheet with an outlined mobile phone.

Figure 2. Arrangement of the co-design workshops.

Data Collection

Data were collected by video recordings [19] and an observation protocol [20].

Video Recordings

A video camera (Sony PD170) was used to record the workshops. The camera was connected to a computer. The Wirecast program enabled integration of data from the camera and the interactive board. A conference microphone was used to assure good quality sound. The camera operator taped each workshop and saved the recordings on the computer every 20 minutes.

Observation Protocol

The 2 observers used an observation protocol, developed for this study, to take notes on contextual factors, the collaboration between participants, interesting situations and events, and the observers' own reflections (ie, the atmosphere and feelings expressed during the workshops). These data were used as a complement to the video recordings and for identification of potential challenging events.

Data Management and Analysis

The data consisted of approximately 16 hours of video recordings along with the observation protocols. The video recordings enabled repeated viewings of the relevant sequences where the challenges occurred. It also gave the other researchers the opportunity to discuss, confirm, reject, or adjust the analysis presented.

The inductive video-based analysis [19] was performed (ÅR) in 8 major steps (Textbox 2). The transfer of video data into text data resulted in a more thorough understanding of the challenges. A description of the transcript symbols and abbreviations used for participants are provided in Tables 1 and 2, respectively [21]. In addition, repetition of speech was reduced, and all the participants are referred to as female and the moderator as male.

Textbox 2. The 8 steps of the qualitative inductive video-based analysis.

Step 1: Mapping of the co-design workshops

Between each workshop, the video recordings were described and classified according to the content in the workshops. During this preliminary viewing, notes were taken on situations that could be of interest after further analysis [19]. The 2 observation protocols were also compiled to obtain an overview of the observers' notes.

Step 2: Familiarization

After the last workshop, the video recordings were viewed several times, and 107 sequences of interest were collected. The compiled observation protocols and the notes from the first step of analysis helped in identifying these situations.

Step 3: Building and rebuilding analytic collections

The identified sequences were viewed, compared, and labeled according to the participants' actions. This step was iterative and involved labeling and relabeling of the sequences. The research questions were specified, which guided the viewing and resulted in modification and narrowing of the number of sequences. New sequences were added, and several sequences were lengthened, that is, 2 or more sequences became 1, were removed, or shortened. A total of 68 sequences remained.

Step 4: Categorization

Patterns began to emerge. Categories and subcategories were created and labeled. Selected sequences were further modified, and some were combined with other sequences.

Step 5: Representation

The sequences within each subcategory were viewed and prioritized according to how well they illustrated the challenge. In each subcategory, 1 or 2 sequences that were considered most illustrative were transcribed by the first author and finally translated into English.

Step 6: Formulating representation

During this stage, categories and subcategories were described in text, and the essence of each category was formulated. This resulted in further revision of the labeling and succession of the categories and subcategories. Themes were shaped.

Step 7: Validation

The notes from mapping and the observation protocols were checked again against the identified categories to make sure that no issues had been missed that could further answer the research questions. This resulted in the creation of 1 complementary category and modification of one of the subcategories.

Step 8: Refinement of results

The final step consisted of adjusting the theme, subthemes, categories, subcategories, and illustrations, and refining the labeling to enhance the text presentation of the challenges.

Table 1. Transcription symbols.[a]

Transcription symbol	Definition
[	Separate left double-row brackets indicate a point of overlapping onset
Bold letters	Words written in bold letters indicate some sort of stress or emphasis
Capital letters	Words written in capital letters indicate shouting
((M looks at RA))	Italic words or sentences in double parentheses are used to mark the transcriber's descriptions of nonverbal signs and events
//	Two parallel lines indicate that the transcript has been shortened, that is, lines have been removed
=	Equal signs are used in pairs and indicate where a sentence stops and where it continues

[a]Modified according to Ten Have (1999) [21].

Table 2. Abbreviations used for the participants.

| Abbreviation	Definition
RA	Lead users
RE	Researchers
PT	Physiotherapist
SRA	Officer from the Swedish Rheumatism Association
E	eHealth strategist
M	Moderator

Researcher triangulation was used to ensure trustworthiness during the analytic process. The first author participated in regular meetings with the second author, who guided the first author in the video-based analysis. Discussions involved deciphering what occurred during the selected sequences, including the challenges and their consequences for the process. Furthermore, labeling the theme, subthemes, categories, and subcategories evolved. The categorization and illustration of issues were discussed with the last author 3 times during the analysis process, which resulted in a consensus of the categorization and further refinement of the aim.

Results

Themes and Subthemes Identified

The analysis resulted in 1 overarching theme and 2 subthemes. A total of 7 categories and 12 subcategories illustrated the challenges deemed important for advancing the co-design process toward the goal (Figure 3 and Table 3). The results will be outlined by descriptions of the content of the categories and subcategories. To further illustrate the challenges, excerpts of the transcripts will also be presented.

Figure 3. Overview of the overarching theme, subthemes, and categories describing the challenges in co-design.
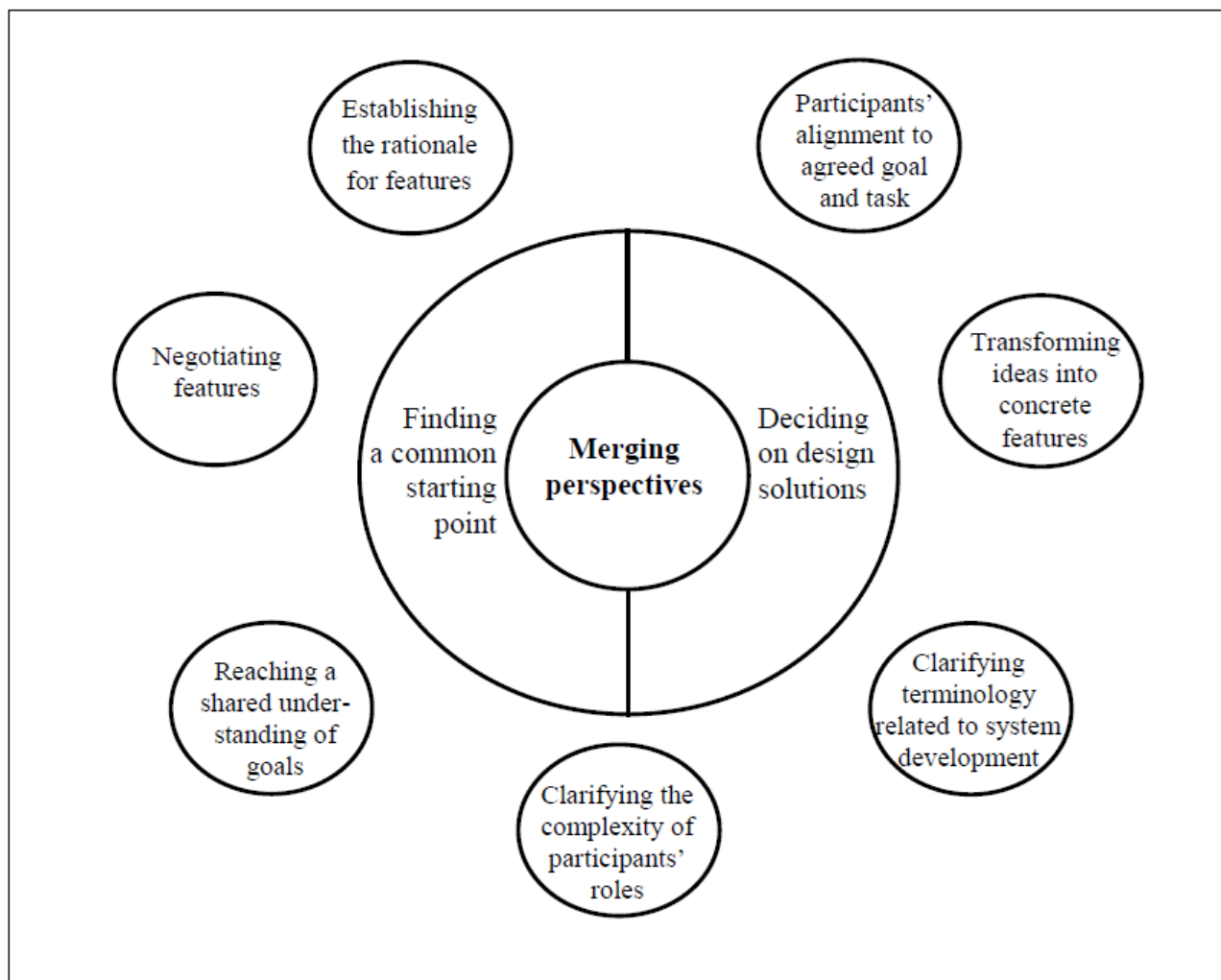
Theme: Merging of Perspectives

The participants struggled to merge their individual perspectives during all phases of the co-design process. The participants shared, argued, and considered their different viewpoints, and integrated and counterbalanced these differences to find mutual agreements and solutions. In addition, 2 essential areas of merging were identified: "Finding a common starting point" and "Deciding on design solutions" (Figure 3).

Table 3. Overview of categories, subcategories, and specific illustrations of challenges in co-design.

Categories	Subcategories	Illustrations of challenges
Establishing the rationale for features	Combining different points of view	• To imagine what feedback on personal progression means to the users; feedback on behavior goal achievement (physical activity, PA) or feedback on physical outcomes (eg, improved strength or mobility).
		• To convey that exercise peers are important not only for inspiration and advice on new exercises but also for maintenance of PA.
		• To acknowledge that home exercises for flexibility, as well as PA according to the recommendations, are health enhancing.
		• To acknowledge both short-term symptom relief and long-term sustained health as a goal of PA.
		• To acknowledge the importance of a personal, realistic PA maintenance goal, as well as one for pain relief.
	Identifying the significance of condition-specific characteristics on feature design	• To choose how to provide feedback on health outcomes and what outcome measures to use.
		• To understand whether it is possible to experience 100% health with rheumatoid arthritis (RA) and the consequences of designing graphs to monitor health reported using visual analog scales.
		• To agree on how to present information on the negative consequences of sedentary life versus the positive consequences of a physically active life style.
		• To decide on a feature to adjust PA goals to facilitate maintenance during exacerbation of RA.
Negotiating features	Consensus solutions emanating from different points of view	• To decide on the scope of PA monitoring in the future service; should perform PA only according to established recommendations.
		• To agree on the relationship between health and PA behavior and whether or not this is relevant to present in monitoring graphs.
	Finding necessary solutions for features despite remaining disagreements	• To agree on whether or not to provide individualized advice, and if so, how? From the system, physiotherapist, or peers.
		• To decide whether to include a video library with general exercise programs or not.
Reaching a shared understanding of goals of future service	Agree on overall aim of the mobile Internet service	• To agree on a type of service to develop: a question-answer service or a service for PA behavioral change and maintenance.
	Agree on profile of target users	• To choose whom to focus on: adopters or maintainers of PA, those wanting inspiration, or those in need of specific exercise advice.
		• To agree on whether the target users should be described as just being curious about PA or already having an established interest in PA.
		• To choose if the target users should have established contacts with health care or not.
Clarifying and handling the complexity of participants' roles	Handling multiple roles	• To imagine the users' needs and consider those needs as well as their own needs as an academic or a professional need.
		• To clarify what opinion to express; my personal opinion or the evidence-based opinion.
	Ensure all perspectives are voiced	• To know when and how to synthesize arguments or solutions based on the perspectives of absent participants.

Categories	Subcategories	Illustrations of challenges
Clarifying terminology related to system development	Make sense of the terminology	• To conceptualize and distinguish between needs and features. • To make sense of the concept "target user group"; does it mean that some individuals are excluded or not?
Transforming ideas into concrete features	Recognizing needs and their corresponding features	• To identify which features can encourage PA during periods with less motivation. • To identify how users can get access to information when in need of encouragement. • To identify features indicating when exercise has not been performed as planned.
	Visualizing the features on the mobile Internet service	• To arrange the feature on a dummy. • To imagine the experience of the welcome screen depending on preferred focus; peer group or self-monitoring.
Participants' alignment to the agreed goal and task	Optimizing the mobile Internet service	• To prioritize the most important features out of all suggested. • To avoid a too complex service by restricting the number of features. • To determine the correspondence between suggested features and the overall goal of the future service.

Category: Establishing the Rationale for Features

Overview

The participants needed to combine their different points of view on issues related to PA in RA to be able to agree on appropriate features. They also needed to identify specific disease characteristics. The participants argued for their points of view, listened, and asked each other questions.

Combining Different Points of Views

Participants struggled to merge their different perspectives: for example, on feedback on personal progression and the role of peers in facilitating PA.

The participants also had different views on the aim of PA itself, which affected discussions about which features to include in the future service. Was short-term symptom relief to be expected, or was the overall goal of PA general health enhancement? During the second workshop, one of the researchers raised these diverse perspectives (Excerpt 1; Figure 4).

The discussion ended with agreement on 2 main features of the future service: (1) peer support for specific advice and inspiration and (2) self-monitoring for personal goal setting, activity planning, and feedback on performance to support maintenance of PA.

Figure 4. Excerpt 1. Different point of views.


```
        ((RE leans forward as if listening intensively))

RE:    I can see a difference between us who work with
       physical activity and you who live with the disease.

RA:    Yes, yes

RE:    You are focused on how physical activity should
       decrease symptoms that you experience right now
       whereas we have the perspective on physical activity
       as a life-style ⌐change =
SRA:                    └ Mmm

RE:    =that should support maintenance of health in general in the long term.

RA:    Yes

RA:    Mmm ((nods)) ((RA1, E, SRA also nod))

RE:    So I think this is important for us to discuss

M:     ⌐Mmm
SRA:   └Mmm

RE:    So that we share the same perspective. Otherwise I think it will be difficult for us
       to move forward in this process.

PT:    I think so too.
```

Identifying the Significance of Condition-Specific Characteristics on Feature Design

One challenge was to agree on how specific characteristics connected to RA would impact feature design. For instance, whether it is possible for a person with RA to feel 100% healthy should be considered in the design of the anchors of graphs that monitor health. The disease course in RA was also considered because it is characterized by episodes of flares and remissions, which affect physical performance. This concern influenced the decision on whether to include a feature to easily review personal goals.

Category: Negotiating Features

Overview

A salient challenge for the co-design participants was negotiation. The negotiations were observed as a continuous process between participants' arguments before final solutions were agreed upon. Two different methods of reaching agreements were observed: consensus solutions emanating from different points of view and necessary solutions to features despite remaining disagreements.

Consensus Solutions Emanating From Different Points of View

The co-design process required participants to create solutions regarding which features to include in the future mobile Internet service even though they possessed different points of view. This way of negotiating was characterized by the participants' ability to reach a consensus solution. This occurred when participants discussed what physical activities should be monitored in the future service and the relevance of displaying PA performance and general health perception in graphs. During the discussion of the latter, the moderator reflected over what he heard, "It sounds as if quite a lot of you with RA want to use graphs to monitor health as an excuse for NOT exercising. Is that not exactly the opposite of what we want the mobile Internet service to do?" The participants laughed and agreed.

Finding Necessary Solutions for Features Despite Remaining Disagreements

Even more challenging was the need to find a solution without consensus. The negotiation then ended with one of the participants giving up her opinion in favor of the opinion of the majority of the group. For example, this occurred when the participants agreed on a solution regarding if and how individualized advice should be provided in the future service and whether a video library should be included. This is illustrated by a discussion during Workshop 3 in Excerpt 2 (Figure 5).

Figure 5. Excerpt 2. Finding necessary solutions for features despite remaining disagreements.

```
RA:    But wait. I'm thinking: How detailed does the exercise descriptions have to be? If we
       mean exercises such as walking or so//

SRA:   It does not have to be so specific or?

RE:    ((nods and makes thumbs up))

RA:    Quick walk, ┌ slow walk
RE:               └ Yes exactly-like that //

RE:    It could be like an exercise library in the App

E:     With more general exercise programs. ┌Not specific descriptions
RE:                                         └Yes,┌general ((nods at E))
RA:                                              └Yes, not specific ((nods and points towards E))

PT:    ┌((holds her hands on her chin and listens))
RE:    └((looks at PT a few times during discussion))
       PT you look concerned

PT:    Yes, a little ((puts her hand on her forehead
       and looks down on the floor, laughs and
       looks up again)) Yes, but I, I.....I will get
       used to the idea ((other participants laugh))
```

Category: Reaching a Shared Understanding of the Goals of the Future Service

Overview

A challenge faced in the initial stage of the co-design process was agreement of the participants on the overall aim of the future service and identification of the target users. The participants expressed frustration and uncertainty in not knowing which services to develop. The moderator repeatedly clarified that this was part of the process, and they all needed to agree to be able to specify the features in the future service.

Agree on Overall Aim of the Future Mobile Internet Service

The future service should be designed to facilitate and inspire PA in people with RA. Participants discussed whether the service should be a question-answer service or a self-management service for PA behavior change and maintenance. Should the future service focus on which exercises to perform or include measures to facilitate PA behavior? Excerpt 3 exemplifies one of the discussions during Workshop 2 (Figure 6).

The discussion finally ended with an agreement that the mobile Internet service should serve as a self-management tool for PA behavior change and maintenance.

Figure 6. Excerpt 3. Agree on overall aim of the future mobile Internet service.

```
PT:   I don't understand!

M:    No,┌but that

PT:      └I do not understand what kind of service
      to develope and I understand that it might
      not be an answer to that question.

M:    No, but that is ┌what

PT:                   └But that is two totally different
      Apps.If we provide a program for self-management of
      physical activity that processes data on physical activity and health
      or if we decide to provide a question-answer service.

M:    ┌That is what we are supposed to decide on during these workshops.

PT:   └Yes ((a clear and direct confirmation))

E:    We are not there yet ((PT and other participants look towards E))

M:    What do we want to recommend to persons with RA? Do we want to develop a new question-
      answer service with personnel that have knowledge about RA and training or do we want the
      future service to be an algorithmic program that processes data on performance and health?
```

Agree on the Profile of Target Users

Initially, there was a need to agree on the characteristics of the users of the future service. For example, should the target users be new adopters or maintainers of PA? Was it sufficient to be just curious about PA or already have an established interest and ambition to be physically active? Should it be necessary to have established contacts with health care to obtain access to the service?

During Workshop 1, the participants discussed the characteristics of the target users. Ideas written on notes from each participant were posted on the wall, discussed, and voted on. The discussion finally led to an agreement for the target user group to be adults with RA who had some experience with and were prepared to self-manage PA. They should also be experienced Internet users.

Category: Clarifying and Handling the Complexity of Participants' Roles

Overview

Another challenge was to clarify the roles of the participants: for example, who they represented and what responsibilities they had. The participants needed to attend to their roles during the co-design workshops and they were also uncertain whose opinion to express. The moderator helped clarify their roles and ensured that different perspectives were explored.

Handling Multiple Roles

The academics and professionals encountered a challenge in determining the needs of the target users of the future service while satisfying their own needs as researchers, clinical physiotherapists, or eHealth strategists and in providing knowledge in their various areas of expertise. During Workshop 2, the moderator explained the reason for the discussion: the participants should have the "I perspective." All the participants were present as experts who need to design a service that the expert group believed was optimal to inspire people with RA to live a physically active life. One of the researchers interrupted and requested further clarification on her roles (Excerpt 4; Figure 7).

The moderator continued and explained that all participants with an academic or professional role had to formulate what was important from their professional perspective. The moderator clarified the roles of the group members several times during the workshops.

Figure 7. Excerpt 4. Handling multiple roles.

```
RE:   Who am I? We are all "I" with different competences

M:    Yes ⌐that is=

E:    Hmm,⌐yes exactly

M:    =that is why we are here. We talked about hmm… the target users… ((shows the participants
      the list on the Trello on agreed target user characteristics))
      Actually, the future service will be targeting these users. So that is one "I".

RA:   Hmm ((Nods, leans forward and listens))

M:    But, your perspective as a researcher participating in these workshops will also be to
      try and formulate what you as a researcher wants to get out from the service, even if the
      interface looks and works in one particular way for the users.

RE:   Mmm ((Nods, straightens up))

M:    For instance, that the future service can provide you with statistics or something else
      that you need as a researcher//

RE:   It is good that this has been cleared up.
```

Ensure All Perspectives Are Voiced

The participants tried to voice others' perspectives if someone was absent but expressed difficulties in knowing when to do it and whose responsibility it was to ensure that all perspectives were heard. For instance, when one of the researchers was absent during one of the workshops due to illness, the other researcher suggested a feature that she believed would be important from a behavioral medicine perspective (a visual analog scale to measure a person's self-efficacy or confidence in performing physical activities).

Category: Clarifying Terminology Related to System Development

Overview

Because some of the participants had little or no experience in system development, it was challenging to conceptualize and understand the basic terminology used within this area. The moderator and participants with earlier experiences in system development repeatedly clarified and explained terms to enable discussions on how the future service should function.

Making Sense of Terminology

Participants had particular difficulties in distinguishing between the terms "needs" and "features." *Needs* were defined as something that is needed to reach your goal and a *feature* was defined as something that fulfilled that need, that is, something that would be accomplished by use of the mobile Internet service. These definitions were needed for the participants to visualize their needs for the future service.

Category: Transforming Ideas Into Concrete Features

Overview

The moderator had a difficult and strenuous task of helping participants recognize needs, transform those needs into features, and visualize the future service. He used prompts, such as scenarios and questions. He also used mediational means, such as a plastic sheet with notes, interactive boards, and programed

prototypes to visualize the future service. However, there was also extensive collaboration between the participants and the moderator to specify and visualize features.

Recognizing Needs and Their Corresponding Features

First, it was crucial to identify which needs could be satisfied by specific features in the future service. For example, when one of the lead users expressed the need for encouragement when she felt less motivated to be physically active, the moderator asked, "Have you got any suggestions for a feature that could satisfy that need?" The moderator also described the scenario, "You have a need for information and you need someone to tell you why you should exercise. What feature could that correspond to?" Sometimes, the participants identified and expressed needs and transformed the needs into features. For example, 1 participant expressed the need for a consequence when she did not perform an exercise as planned. Another participant suggested that this could be satisfied by receiving feedback on the percentage of performed exercises compared with planned exercises.

Visualizing the Features on the Mobile Internet Service

A part of the co-design process was to visualize the future service. The participants arranged notes illustrating the buttons on a mobile phone on a plastic sheet attached to the wall. The moderator also used the interactive board to draw buttons according to participants' suggestions. By changing the place and size of the outlined buttons, the participants could visualize how the design of the welcome screen influenced the first impression of the future service. In the later phases of the co-design process, prototypes of programmed mobile phone services were presented.

Category: Participants' Alignment to the Agreed Goal and Task

Overview

Another strenuous task for the moderator was to keep the participants aligned with a common goal during the co-design

process to optimize the future service. He used prompts, summarized the discussions, and asked questions to guide the participants toward the task and goal achievements. The participants, by contrast, sometimes had difficulties in understanding why they needed to prioritize.

Optimizing the Mobile Internet Service

The most important features of the service needed to be prioritized, which caused some frustration. The future service needed to include desirable features while maintaining simplicity. An alignment between suggested features and the

comprehensive goal of the service also needed to be secured. This was discussed during Workshop 3.

The moderator summarized the features included in the 2 proposed prototypes of the future service. One prototype focused on peer support (app 1), and 1 prototype focused on self-monitoring (app 2). Did these 2 prototypes correspond to the overall aim of the future service (ie, to support self-management of PA in RA)? (Excerpt 5; Figure 8).

The participants determined that both peer support and self-monitoring were important and should be included but might be too complex for 1 service.

Figure 8. Excerpt 5. Optimizing the mobile Internet service.

```
RE:    Ohhhh, I think it's a shame to only do one App. I think what's there ((points to App1 on
       the interactive board)) should be integrated into the group icon there ((points to App2
       on the plastic sheeet))

RA:    Absolutely. I think so too

RE:                                          Hmm

SRA:   Yes, I am more inclined to take the App1 ((points to the
       interactive board)) and put it into the middle there
       ((points to App2 on the plastic sheet))//

M:     So you believe that what we have done is actually a
       further development of App1 ((points to App1))

All:   YES!
```

Discussion

Principal Findings

In this study, we learned that co-design is a complex and demanding process that faces several challenges. The challenges observed were related to reaching agreements and making decisions necessary to advance the co-design process. The merging of participants' different perspectives was particularly challenging, yet it seemed to be the core activity in a successful co-design process.

The constant need to merge participants' respective perspectives placed extensive demands on collaboration. Merging of perspectives can be described as the participants' efforts to consider and value their different viewpoints and to integrate and counterbalance these into a mutual agreement to progress the co-design process toward the overall goal. The merging was built on individual perspectives, that is, experiential and theoretical knowledge and participants' ability to share these with others. Merging also included finding solutions. Data showed that the co-design group exhibited 2 methods of negotiating and finding solutions: consensus solutions or solutions despite remaining disagreements. This description of the co-design group's ability to merge is in accordance with what theoretically has been described as a "collectivity-of-practice" [22].

According to our results, the participants' different points of view caused the process to be difficult and time consuming, which may lead to conflicts between lead users and system

developers and negatively impact the process [23,24]. Relationship conflicts have a negative impact, whereas task conflicts improve group performance [25]. Our data indicated that the co-design group primarily experienced task conflicts. During these task conflicts, the participants presented, valued, and argued for their various perspectives, which widened the group's decision basis. High demands were placed on the participants' ability to merge their perspectives. Our assumption is that a health care service based on merged perspectives would be more feasible to both lead users and health care providers compared with services developed by more conventional means. However, this assumption must be studied further.

Challenges Faced

One of the goals for the co-design process was to determine what type of service to recommend for people with RA in order to self-manage PA. The frame, structure, and features to include in the future service were not predetermined, which was frustrating and difficult for the participants. Consistent with previous research, stating clear goals contribute to a more effective collaboration in this study [26]. To handle this challenge, the future target users, the scope, and the aims of the service should be clarified early in the process.

Another challenge in the initial stage of co-design concerned the participants' roles and responsibilities. The participants were unsure about their respective roles and expectations, which have previously been reported to negatively impact co-design performance [23,27]. Particularly, the academics and professionals had complex roles and were expected to contribute

using their unique expertise while considering how to use their competencies without dominating. They were also expected to imagine the needs of the future users. The complex roles for researchers were previously described as a substantial challenge in participatory action research projects [28]. Our study expands that challenge to include not only researchers, but also the other participants in the co-design group. However, the researchers still expressed more concerns regarding their roles and the risk of dominance compared with other participants.

Another challenge concerned the recognition and transformation of the participants' needs and ideas into concrete features to optimize the future service. The moderator, who had substantial experience with programming and designing digital devices, had a distinct role in this process. Needs and features were defined in terms that enabled the participants with no experience in this field to discuss the features on the future service. The moderator also programmed prototypes that allowed the participants to visualize the future service. The inclusion of engineers to help transform users' needs into technical applications has been reported previously [27]. Our study emphasizes the importance of including experts in programming and system design to help the co-design participants imagine, discuss, and visualize the features on the future service.

Limitations

The most important limitation to consider is the fact that the results are based on only 1 co-design process. By involving 4 researchers (ÅR, CM, PÅ, and CK) in the data collection, and 3 in the data analysis, the researchers' different preconceptions, viewpoints, and analytic skills were used to achieve high credibility of the results. Nevertheless, some important issues may not have been explored.

Another limitation concerned the data-collection methods. We used video recordings and observations to collect data on the co-design process. When planning the workshops, we discussed the possibility of using 2 cameras to enable simultaneous views of the participants, the interactive board, and the moderator, which is technically complicated. Instead, we connected the camera to a computer and used the Wirecast program to enable simultaneous views. As the workshops proceeded, the participants were clearly more active when using plastic sheets and notes compared with the interactive board. Consequently, we lost the possibility of simultaneous views and had to shift the camera focus between participants, the moderator, and the plastic sheets. The 2 naturalistic observers who were present at the workshops provided an additional overview of the process, which complemented the video recordings in a satisfactory way and contributed to data triangulation.

Strengths

A unique feature of this study was the use of video recordings and naturalistic observations of the co-design workshops to capture the challenges during the process. Previous empirical studies have used diverse methods to describe and explore the co-design process; for example, surveys [4,12,13], observations

and audio-recordings [5], and focus group interviews [27]. We have only been able to identify 1 earlier study that used video recordings to study collaboration during co-design meetings [15]. The use of video recordings provided access to detailed data on the interplay of talk, behavior, and context. It also enabled repeated viewings of the video recordings during analysis and gave the authors access to authentic data. The observation protocols facilitated the identification of the challenges and verified the results from the video-based analysis.

A strength was the use of multiple strategies to secure the credibility of the findings. We used multiple data sources, video recordings, observation protocols, and multiple observers. Researcher triangulation was performed during the different stages of data analysis. By providing a thorough description of the setting, scope of the workshops, methods used, and analysis performed, we intend to make it possible for the reader to assess the transferability of the challenges to similar co-design processes [29]. Our co-design process aimed specifically to develop a mobile Internet service for self-management of PA in RA and included multiple stakeholders in 1 co-design group. The transferability might be unique to processes similar in aim and scope. Nevertheless, the identified challenges at a general level may be valid for other co-design processes attempting to develop and improve health care services and should be evaluated in future services.

Ethical Considerations

Participatory action research and video-based analysis raises some ethical issues [19]. The use of video-based analysis revealed each participant's views, preferences, and actions. Therefore, it is of major concern to thoroughly consider how to present the data to retain confidentiality.

Conclusions

Co-designing the system requirements of a mobile Internet service with multiple stakeholders is a complex and extensive collaborative decision-making process. Considering, valuing, counterbalancing, and integrating different perspectives into agreements and solutions (ie, the merging of participants' perspectives) were crucial for advancing the process and considered the core challenges of co-design.

This new knowledge of crucial challenges is worth considering when planning and performing future co-design processes on eHealth services that include multiple stakeholders. This study emphasizes that the challenges are crucial for success and should not be omitted but carefully considered and prepared for. Further research is needed to replicate the results in similar and new contexts. Studies on how the participants' and group characteristics influence the process of merging would also contribute to the field in a significant way. Finally, the inclusion of multiple stakeholders within 1 co-design group is more beneficial than the formation of separate co-design groups for each of the stakeholders with respect to the development and improvement of health care services.

Conflicts of Interest

None declared.

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Abbreviations

EBD: experience-based design
PA: physical activity
RA: rheumatoid arthritis
SRA: Swedish Rheumatism Association

<u>Original Paper</u>

Informed Choice for Participation in Down Syndrome Screening: Development and Content of a Web-Based Decision Aid

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Abstract

Background: In Denmark, all pregnant women are offered screening in early pregnancy to estimate the risk of having a fetus with Down syndrome. Pregnant women participating in the screening program should be provided with information and support to allow them to make an informed choice. There is increasing interest in the use of Web-based technology to provide information and digital solutions for the delivery of health care.

Objective: The aim of this study was to develop an eHealth tool that contained accurate and relevant information to allow pregnant women to make an informed choice about whether to accept or reject participation in screening for Down syndrome.

Methods: The development of the eHealth tool involved the cooperation of researchers, technology experts, clinicians, and users. The underlying theoretical framework was based on participatory design, the International Patient Decision Aid Standards (IPDAS) Collaboration guide to develop a patient decision aid, and the roadmap for developing eHealth technologies from the Center for eHealth Research and Disease Management (CeHRes). The methods employed were a systematic literature search, focus group interviews with 3 care providers and 14 pregnant women, and 2 weeks of field observations. A qualitative descriptive approach was used in this study.

Results: Relevant themes from pregnant women and care providers with respect to information about Down syndrome screening were identified. Based on formalized processes for developing patient decision aids and eHealth technologies, an interactive website containing information about Down syndrome, methods of screening, and consequences of the test was developed. The intervention was based on user requests and needs, and reflected the current hospital practice and national guidelines.

Conclusions: This paper describes the development and content of an interactive website to support pregnant women in making informed choices about Down syndrome screening. To develop the website, we used a well-structured process based on scientific evidence and involved pregnant women, care providers, and technology experts as stakeholders. To our knowledge, there has been no research on the combination of IPDAS standards and the CeHRes roadmap to develop an eHealth tool to target information about screening for Down syndrome.

KEYWORDS

decision support intervention; decision making; informed choice; prenatal diagnosis; pregnancy; development; Web-based intervention; eHealth tool; telemedicine

Introduction

Interest in the use of information and communication technology in health care is increasing. Interventions based on eHealth have increased, but there is a lack of empirical evidence about the benefits, and greater awareness with respect to the development process, implementation, and evaluation is needed [1]. In obstetrics, digital solutions have been shown to be a useful form of health care delivery, but there is a need for further validation and evaluation [2].

Prenatal screening for Down syndrome (a genetic condition caused by the presence of an extra copy of chromosome 21) [3] is well established. In Denmark, all pregnant women are offered such screening in the first trimester, determined using a combination of maternal age, sonographic measurement of fetal nuchal translucency, and maternal serum concentrations of free beta-human chorionic gonadotropin and pregnancy-associated plasma protein-A. This screening offers a detection rate of approximately 90% for a false positive rate of 5% [4]. Pregnant women with a fetus considered to be at increased risk of Down syndrome are offered further invasive diagnostic tests such as chorionic villous sampling or amniocentesis, which carry a procedure-related risk of spontaneous miscarriage of about 0.5% to 1% [5]. The main purpose of screening for Down syndrome is to assist pregnant women in choosing whether to accept or reject participation based on informed choice [6,7]. Informed choice relies on information of a certain quality and reflection of patient values and is based on the principle that it is unethical for patients not to be informed of the consequences of health care interventions and an informed choice is associated with a better outcome [8]. Pregnant women need information about the condition for which the test is offered, the method by which the test is carried out, the consequences of the test results, and the fact that the test is optional [9]. Women of advanced maternal age tend to choose invasive tests because to their age and not their individual risk assessment [10]. Several studies have demonstrated the benefits of making an informed choice compared with an uninformed choice [11-15], yet not all pregnant women do so [16-18]. Accordingly, it is important to focus on ways to inform pregnant women about such options.

Pamphlets, audiotapes, workbooks, and videotapes are examples of interventions that prepare patients to decide on health care options [19]. Such aids have been shown to improve knowledge and support informed choice [20]. Care providers should be aware that patients use the Internet to search for information on health-related issues and should support this use [21]. In 2012 in Denmark, 99% of couples with children had access to a personal computer at home, and 86% of families had access to the Internet [22]. Accordingly, a large proportion of the Danish population has access to health-related websites which are among the most frequently used [23]. Web-based health information is unregulated and varies in quality and consistency [24]. Web-based interventions and eHealth technologies can change behavior, improve knowledge, and deliver health care information in a more flexible and time-efficient manner but this requires focus on development and implementation [25-27]. Patients are using the Internet in several ways with respect to health information: searching for health information, participating in support groups, and consulting with health professionals [28,29]. A Swedish study demonstrated that pregnant women often use the Internet to find information on topics related to pregnancy and concluded that antenatal care providers should be able to guide pregnant women to high-quality, Web-based information [30]. The aim of this study was to develop an eHealth tool that contained accurate and relevant information to improve pregnant women's ability to make an informed choice about whether to accept or reject participation in screening for Down syndrome. Elements of participatory design, an approach for developing technical solutions to real-world problems in cooperation with stakeholders, were used to define problems and create sustainable solutions [31].

Methods

Theoretical Framework

International Patient Decision Aid Standards Collaboration Guide

The IPDAS Collaboration is an international group of researchers, practitioners, and stakeholders that developed a checklist of approved criteria to ensure the quality of patient decision aids. The IPDAS guide was used to ensure the quality of the content and fulfill the aim of developing a useful and effective tool. The criteria are grouped into three main areas (content, development, and effectiveness) and consist of 12 quality dimensions (Textbox 1) [32].

Textbox 1. Quality dimensions outlined by the International Patient Decision Aid Standards (IPDAS) Collaboration.

Twelve quality dimensions:

- Using a systematic development process
- Providing information about options
- Presenting probabilities
- Clarifying and expression values
- Using patient stories
- Guiding or coaching in deliberation and communication
- Disclosing conflicts of interest
- Delivering patient decision aids via the Internet
- Balancing the presentation of options
- Using plain language
- Basing information on up-to-date scientific evidence
- Establishing effectiveness

Center for eHealth Research and Disease Management Roadmap

The CeHRes roadmap was designed to guide planning, coordination, and execution of the developmental process of eHealth technologies [27,33]. The roadmap was based on a holistic approach whereby individual elements in a complex system are interrelated and influence each other. The roadmap was used as guidance for the development of the eHealth tool to ensure a continuing process in accordance with the approach of participatory design. According to the roadmap, the development of an eHealth technology starts with multidisciplinary project management and undergoes 5 main steps: contextual inquiry, value specification, design, operationalization, and summative evaluation (Figure 1) [27,34]. Our study applied elements of participatory design, an approach for developing technical solutions to real-world problems in close cooperation with stakeholders and end users, to define problems and create sustainable solutions for practice [31].

Figure 1. CeHRes roadmap.
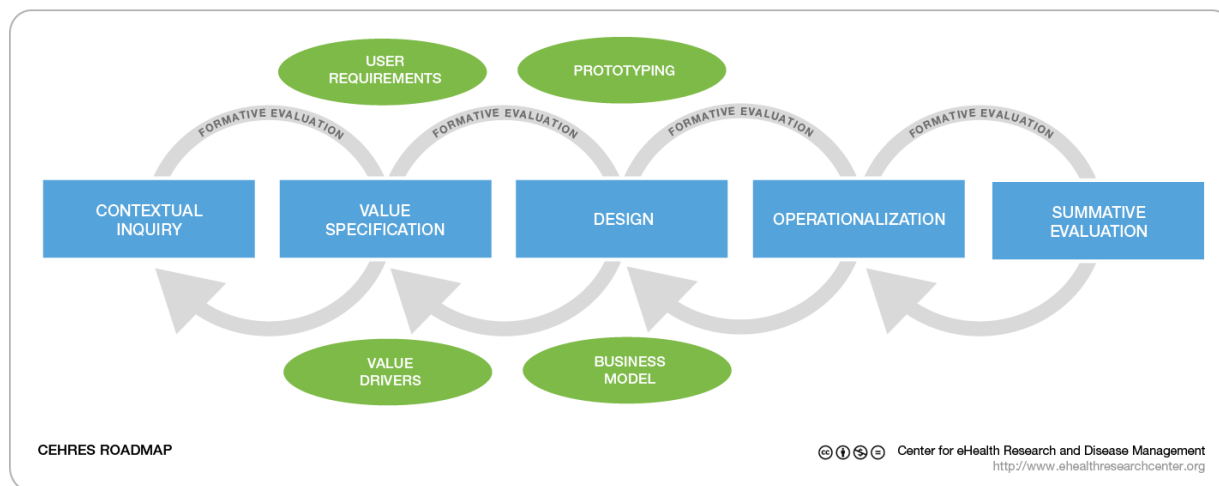
Steps 1 and 2: Contextual Inquiry and Value Specification

The Process of Development of the eHealth Tool

In this phase the project management and the approach of the system design were clarified to ensure an effective process. A research group was established to run the development process of the intervention. The first author (MMS) was the project manager responsible for the process, content, and design. As part of their higher education qualification project, three multimedia design students from Lillebaelt Academy of Professional Higher Education were engaged to design and build the intervention. To ensure a clinical approach, experts in maternal fetal medicine provided advice [27]. The research group, developers, and expert group worked in collaboration to develop the intervention, and pregnant women were regularly involved in the process [35].

Background Literature

The databases PubMed and Embase were searched systematically for studies that investigated the effects of

interventions compared to conventional care in pregnant women considering Down syndrome screening and generated the basis for a systematic review. The review was used as background information for this study and has been published elsewhere [36].

Design

A qualitatively descriptive method was used to assess pregnant women's needs for information about Down syndrome screening. Qualitative description is a useful method to obtain knowledge about an individual's experience in an area that is poorly understood and a target for an intervention [37-39]. The method was used throughout the study from data collection to analysis. The qualitatively descriptive method can help to focus on the experiences of the pregnant women and stay very close to the data obtained [37]. The goal of the method is descriptive and uses low inference interpretation to present findings in everyday language. Data collection in qualitatively descriptive studies is often directed at the *who*, *what*, and *where* of experiences and usually includes minimally to moderately structured open-ended individual and/or focus group interviews [39].

Setting

The study was performed at the Maternal Fetal Medicine Clinic at Odense University Hospital. About 4100 pregnant women are referred to the hospital every year, and the clinic performs about 18,000 ultrasound scans per year. In Denmark, Down syndrome screening incurs no cost to the pregnant women.

Data Collection

One interview with three care providers was held in the early stage of the study. The care providers were recruited from the Maternal Fetal Medicine Clinic at Odense University Hospital. Inclusion criterion was professional experience in maternal fetal medicine. Three care providers with different professional backgrounds were recruited: a consultant, a nurse, and a midwife. All three care providers were women with more than five years of experience in maternal fetal medicine. The interview with the care providers was established to elucidate the current clinical pathway for Down syndrome screening, the staff's perception of the pathway, and new ideas on how to inform pregnant women. While three care providers might be considered a relatively small number for a focus group interview, this provided the opportunity for in-depth questions and greater involvement of the participants.

Two focus group interviews with pregnant women who had formerly participated in Down syndrome screening at Odense University Hospital were held to identify the perceived information that was required, the source of the information, and the challenges with respect to Down syndrome screening. One interview with eight pregnant women was held in the early stage of the study, and one interview with six pregnant women was held in the middle of the study. The pregnant women were recruited from midwife consultations at the time of nuchal translucency scanning at Odense University Hospital. The inclusion criteria were: healthy (physically and mentally) pregnant women with uncomplicated pregnancies who spoke and understood Danish. All participants were informed about

the study and gave their informed content to participate. The women varied in age, parity, and education to ensure wide representation. The pregnant women's ages ranged from 21 to 39 years, and they were expecting their first, second or third child. Pregnant women in the first interview were included during the whole period of pregnancy, whereas women in the second interview were included during first or second trimester of pregnancy.

All focus group interviews were moderated by MMS and one other interviewer, and a semi-structured guide was used to elicit the participants' experiences. An interview guide, based on the literature search and field observations (only the third interview) was used to keep the conversation focused on the following themes: knowledge about Down syndrome screening, challenges in connection with the screening process, and possible improvements. All three interviews were digitally recorded.

Supplementary to the qualitative interviews, field observation was carried out to authenticate the challenges of providing information about Down syndrome screening. Field observations comprised direct observation in the Maternal Fetal Medicine Clinic at Odense University Hospital and were held after the two first interviews. Over a period of two weeks, MMS and one of the technical experts observed pregnant women, their partners, and care providers in the clinic. The participants were observed and interviewed at these consultations and at information meetings in the clinic. Their responses were noted by both observers. This method can help to overcome the discrepancy between what participants say and what they do and also may help to uncover behavior which the participants are not aware of [40]. In this study, field observations were carried out to qualify the meaningfulness and understanding of the first two interviews in order to prepare for the third interview (content and interview guide) rather than generating individual data.

Data Analysis

The qualitatively descriptive approach was also used for data analysis. All three focus group interviews were digitally recorded. The interviews were transcribed verbatim by a secretary to optimize the analysis. First, the transcribed material was read to obtain an overview and impression of the data. Furthermore, recurrent themes were identified. Second, the data were read again and relevant text sections were made. The data were coded into meaningful titles according to the themes identified in the first step. Third, all text sections with similar codes were categorized into general themes. The data were reread to reflect and identify common factors and differences. Finally, to ensure correct coding and categorization, the data were reviewed for coherence and reallocated if discrepancies were found [37,41]. Coding and categorization was done by hand and in Microsoft Word. Due to the relatively small amount of data, computer analysis programs were not required.

Field observations were carried out to qualify the meaningfulness and understanding of the first two interviews to prepare for the third interview (content and interview guide) rather that generating individual data. Hence, the notes from the field observations were used to support the findings of the

first two interviews and to prepare for the last interview and was not analyzed separately.

Steps 3 and 4: Design and Operationalization

These two phases refer to the design of prototypes that fit with the values and user requirements and concern the practical development and employment of the technology. Based on the themes identified, an interactive website with information about Down syndrome screening was developed. The website reflected accurately the process and information provided by the Maternal Fetal Medicine Clinic at Odense University Hospital in line with national and international standards. The website was developed with a focus on seven elements (Table 1).

Table 1. Important elements in the development of the eHealth tool.

Element	Action
Goals	Goals were established to ensure a clear direction for the development of the intervention. The goals were to ensure that knowledge was imparted to pregnant women about Down syndrome screening, to support them in making an informed choice, to present existing and new information in new ways to the pregnant women, to reflect a professional and friendly service from the hospital, and to provide all information with a neutral attitude with respect to the different options available to the pregnant women.
Design	The design of the website was based on user values and was simple in design, look, font, and colors. Other websites, both national and international, were searched for inspiration. The website was developed in WordPress, a content management system for setting up websites, and Google Analytics was used for user information and search engine optimization. Images used on the website were selected or created in cooperation with the expert group to ensure medical accuracy and realism.
Mock-up	A mock-up model of the website was used through the development process to oversee the direction of the work.
Clinical content	The clinical content of the website was based on national and international guidelines for Down syndrome screening, user requirements of pregnant women, and input and reviews from the expert group. The clinical content also took into consideration the needs of pregnant women to have informed choice about Down syndrome screening, the method of testing, interpretation of negative or positive results and the fact that the test was optional [9,42]. Furthermore, the eHealth tool allowed pregnant women to become actively engaged in the decision-making process [43].
Language	To ensure plain language, an expert in health communication reviewed and revised the text before it was used on the website.
Decisional conflict	Screening for Down syndrome was characterized by a decisional conflict with no single best choice. The eHealth tool aim was to provide information about the condition, the options, benefits and harms, probabilities, and interpretation [20].
Communication risks	Making an informed choice about Down syndrome screening involves dealing with risks and statistical issues. In accordance with recommendations for risk communication, the Web-based interventions were designed with special focus on presenting risk in alternative ways using graphics, plain language, and consideration of how statistics are presented [44]. Presenting information in frequency format is beneficial to convey statistical information [45].

Step 5: Evaluation

Finally, the user-friendliness of the eHealth tool was tested. The prototype version of the intervention was tested on six pregnant women and two experts who used the website and gave feedback and suggested improvements. The website was also evaluated using the IPDAS checklist for developing patient decision aids.

Results

Steps 1 and 2: Contextual Inquiry and Value Specification

Themes Identified by Care Providers

The professionals concluded that some of the pregnant women had based their choice on a predetermined decision rather than an informed choice. Faced with an increased risk of Down syndrome, the pregnant women were frustrated and had difficulty making a choice because of lack of knowledge. Furthermore, the professionals discovered that pregnant women found it difficult to deal with the meaning and significance of cut-off values. The importance of having enough information to make an informed choice was also evident. The professionals suggested developing Web-based material to supplement the existing means of providing information that would enable

pregnant women to continue to enjoy their pregnancy. Examples of themes identified by the care providers are shown in Textbox 2. The themes were selected based on relevance and frequency in the interviews.

Themes Identified by Pregnant Women

To make an informed choice, the majority of the pregnant women in the focus group stated that they needed more information, although this varied by degree. Some women reported that they expected a normal outcome and therefore did not require much information. Others reported that they wanted to know everything about the screening. Common to all was the expectation of obtaining a picture of their unborn child at the time of scan, and this caused some consternation among care providers who felt that their role was being trivialized. Several women reported doubt with respect to the interpretation and understanding of cut-off values and sought extra information. Some of the women stated that while they received a number of booklets, they had not read them and preferred to obtain information from the Internet and from friends and family. Only a few received information from their general practitioner. Using the Internet, the pregnant women sought the experiences of other pregnant women and used a number of different sites. Several of the women stated that they liked to use websites with a chat room. They did not necessarily want

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to chat with others, but they liked to follow other women's chats and to see that other women also had doubt with respect to the interpretation and understanding of cut-off values. Common to all was the need for reliable and helpful information available on a single website. Examples of themes identified by pregnant women are shown in Textbox 2. The themes were selected based on relevance and frequency in the interviews.

Textbox 2. Themes from interviews with pregnant women and care providers.

Examples of themes from interviews with care providers:

- Quality of the information
- Seeking confirmation for normality
- Lack of knowledge for pregnant women at increased risk
- Different agendas between the care providers and the pregnant women
- Doubts about the meaning of the cut-off values

Examples of themes from interviews with pregnant women:

- Difficulties in making an informed choice
- Need for knowledge/information and where to find it
- No understanding of cut-off values
- Assessment of available information

Steps 3 and 4: Design and Operationalization

Common to all pregnant women in the interviews was the need for reliable and helpful information available at a single Internet site. Based on the interviews it was decided to develop an interactive website [46] to support pregnant women in making an informed choice about Down syndrome screening. The content of the website was based upon the identified themes among care providers and pregnant women and guidelines for Down syndrome screening. The website reflected the clinical pathway at Odense University Hospital and was divided into subpages according to this (see Multimedia Appendix 1). The design of the website was based on user values and was simple in design, look, font, and colors. The majority of the topics on the website were described in written text supplemented by short videos of care providers explaining the topics and showing the screening methods. Both care providers and pregnant women reported doubt with respect to the interpretation and understanding of cut-off values. Hence, it was decided to use both static graphics and animated infographics to help visualize the text and give a better understanding of the statistical aspects of screening for Down syndrome. During the interviews with pregnant women it became clear that several of the women liked to use websites with chat forums and it was decided to include a chatroom on the website designed for pregnant women to share stories. Pictures were used on the website to reflect the present topic and to create a professional and accommodating atmosphere (see Multimedia Appendix 2). Images used on the website were selected or created in cooperation with the expert group to ensure medical accuracy and realism.

Step 5: Evaluation

The prototype version of the intervention was tested on six pregnant women and two clinical experts who used the website and gave feedback and suggested improvements. The website was also evaluated using the IPDAS checklist for developing patient decision aids. Based on the feedback and evaluation the website was adjusted with special focus on usability.

Discussion

Principal Findings

This paper describes the development of an eHealth tool as an intervention to improve pregnant women's ability to make an informed choice about Down syndrome screening. This was based on a theoretical framework to develop a patient decision aid and a roadmap to develop eHealth technologies in the form of an interactive website [46].

The development of the intervention was a complex and time-consuming process involving many people to support existing means of informing pregnant women in a more interactive manner using new information and communication techniques. Using the guide from the IPDAS standards for developing patient decision aids helped us to ensure the quality of the content and fulfill the aim of developing a useful and effective tool. The IPDAS standards are suitable for developing patient decision aid tools and have been used in the development of several patient decision-making tools [47-49]. By combining this with the CeHRes roadmap, a focused and structured collaborative developmental process was provided. The evolution of the process helped to ensure the development of an intervention that was based on the needs and wishes of pregnant women. The CeHRes roadmap has been used in several studies as guidance for the development of eHealth technologies [50,51] but to our knowledge, this is the first time that the combination of the IPDAS standards and CeHRes roadmap has been used to develop an eHealth tool specific to information about Down syndrome screening.

A qualitatively descriptive method was used to approach data. Qualitative description research closely reflects data and provides a comprehensive summary in simple language. In

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contrast to other qualitative research approaches, there is a sharper line between exploration and description of data [39]. Qualitative description has been criticized for being unclear and not sufficiently theory-based. However, when the approach is used for the right purpose, this criticism is unreasonable [37]. Qualitative description should be used when a description of a certain view is required, and using this method to focus on the experiences of the pregnant women has been useful for gaining information used to develop an eHealth tool. Employing a qualitatively descriptive method provided the opportunity to collaborate closely with the pregnant women in a timely and resource-effective way.

Focus group interviews helped to provide knowledge and understanding of the area of prenatal screening for Down syndrome and were an effective method in the process of developing the intervention. However, focus group interviews are less suitable for producing data on individuals, as there is less time for each individual to speak and social interaction in the group can prevent different views from being expressed. This might risk atypical views not being reported [52]. Two focus group interviews with eight and six pregnant women each were considered adequate for this study to provide background information for an intervention rather than an analysis of interaction. In addition, the topic was quite personal, which may not be ideal in a large group. Conversely, three staff members was a relatively little number for a focus group interview. However, this gave the opportunity for in-depth questions and greater involvement of the participants. Field observations provided the opportunity to authenticate the challenges of providing information about Down syndrome screening, and the pregnant women were very willing to share their thoughts and stories. It gave the opportunity to observe what questions were asked when the pregnant women had doubts and also what worked well and less well. Field observations are useful for understanding a certain phenomenon, but less so for causalities [53]; in addition, the observations are time-consuming and often unstructured. The researcher has a certain perspective and will focus on this, while other things may not be noticed. Furthermore, the researchers must be aware of their influence on the participants being observed. Working in pairs, observers can meet the challenges, share experiences, and support each other. Field observations were carried out to qualify the meaning and understanding of the first two interviews and guide the content of the third interview and were not analyzed separately. Field observations in combination with interviews were valuable in authenticating the challenges of providing information about Down syndrome screening. We gathered important data during the two weeks of field observations, and this experience should be included in future studies.

One of the strengths of our study was the involvement of technology experts, pregnant women, and care providers in the process. This resulted in the development of an intervention based on user needs that also reflected hospital practice. Patient decision aids increase knowledge and support informed choice [20]. When developing eHealth tools, it is important to prioritize the process, commit people, and invest time to make an effective and useful intervention. Goal setting affects performance and persistence and has an energizing effect [54]. All stakeholders involved in the process were familiar with the goals of the intervention and worked with common goals. The content of the website is reliable, current, and evidence-based in accordance with the recommendations of the Danish Health and Medicines Authority [6]. For sustainability, it is important to maintain and update the website. Another strength of our study is the openness of the website which can be used by all pregnant women regardless of risk. Many individuals have little understanding of statistical analysis so it is difficult for them to understand probabilities and risk [55]. We found that pregnant women had difficulty dealing with cut-off values.

Limitations

While an expert in health communication rewrote the website and videotext, there is still a risk that not all pregnant women will cope with such information. Accordingly, it is important to consider the website as a supplement to face-to-face consultations. The website contains a chat room designed for pregnant women to share stories, which is challenging to implement. It may be possible to supplement the website with video communication. Another limitation could be the exclusion of vulnerable and non-Danish speaking participants in the study.

Comparison With Prior Work

Other studies concerning the development of eHealth tools recognized the importance of a structured process to develop a successful intervention and used a theoretical framework for the process [48,50,56,57]. Women assigned to an interactive, computerized Prenatal Testing Decision Assisting Tool with information about prenatal testing had higher knowledge scores and less decisional uncertainty [15]. The increased use of information technology will affect health care, and more interventions in this area are likely to be seen. Pregnant women seek and care providers recommend the use of Web-based interventions to provide information. There is benefit in delivering decisions aids on the Internet, but few are developed for Web-based use [58]. Our findings indicate a need for Web-based information, and this current study shows that it is possible to develop Web-based decisions aids for patients.

Conclusions

This paper describes the development of an interactive website [46] to inform pregnant women about screening for Down syndrome in a highly specialised obstetric unit in Denmark. The development of an interactive website to support pregnant women in making informed choices about whether to accept or reject participation in Down syndrome screening relies on a well-structured process based on scientific evidence and involving stakeholders such as pregnant women, care providers, and technology experts. The study has demonstrated how different frameworks and methods must be used in a complementary manner to develop an eHealth tool. The website supports existing forms of educating pregnant woman and is designed to support pregnant women's ability to make an informed choice. Further research has been done to investigate whether this intervention improves pregnant women's ability to make an informed choice with respect to screening for Down syndrome, and the results will be published at a later date.

Acknowledgments

Conflicts of Interest

None declared.

Multimedia Appendix 1

Sitemap overview.

[PDF File (Adobe PDF File), 1KB - resprot_v4i3e113_app1.pdf]

Multimedia Appendix 2

Homepage of the Graviditets Portalen website.

[PDF File (Adobe PDF File), 141KB - resprot_v4i3e113_app2.pdf]

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Abbreviations

CeHRes: Center for eHealth Research and Disease Management
IPDAS: International Patient Decision Aid Standards

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Protocol

Cardiovascular Risk and Its Associated Factors in Health Care Workers in Colombia: A Study Protocol

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Abstract

Background: Cardiovascular diseases are the leading cause of mortality worldwide, for this reason, they are a public health problem. In Colombia, cardiovascular diseases are the main cause of mortality, having a death rate of 152 deaths per 100,000 population. There are 80% of these cardiovascular events that are considered avoidable.

Objective: The objective of the study is to determine the prevalence of the cardiovascular risk and its associated factors among the institution's workers in order to design and implement interventions in the work environment which may achieve a decrease in such risk.

Methods: An analytical cross-sectional study was designed to determine the cardiovascular risk and its associated factors among workers of a high complexity health care institution. A self-applied survey will be conducted considering sociodemographic aspects, physical activity, diet, alcohol consumption, smoking, level of perceived stress, and personal and family history. In a second appointment, a physical examination will be made, as well as anthropometric measurements and blood pressure determination. Also, blood samples for evaluating total and high density lipoprotein cholesterol, triglycerides, and fasting blood sugar will be taken. A ten-year global risk for cardiovascular disease will be determined using the Framingham score. A descriptive analysis of the population's characteristics and a stratified analysis by sex, age, and occupation will be made. Bivariate and multivariate analysis will be made using logistic regression models to evaluate the association between cardiovascular risk and the independent variables. The research protocol was approved by the Scientific and Technical Committee and the Ethics Committee on Research of the Fundación Cardiovascular de Colombia.

Results: The protocol has already received funding and the enrollment phase will begin in the coming months.

Conclusions: The results of this study will give the foundation for the design, implementation, and evaluation of a program based on promoting healthy lifestyles, such as performing regular physical activity and healthy food intake in order to avoid and/or control the cardiovascular risk in the workers of a high complexity health care institution.

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Introduction

Cardiovascular Risk Factors

Cardiovascular risk factors are biological or behavioral characteristics that increase the probabilities of developing a cardiovascular disease (CVD) or dying from this cause [1], in those who have them. According to the World Health Organization (WHO), risk factors are classified in behavioral (modifiable) and biological. Behavioral risk factors include smoking, alcohol consumption, unhealthy diet, and physical inactivity, while the biological risk factors include hypertension, overweight, obesity, diabetes mellitus, and hypercholesterolemia [2].

The high prevalence of these risk factors has led CVD to become the leading cause of mortality worldwide, and, therefore, a public health problem. According to the WHO in 2008, these diseases were responsible for 30% of the mortality worldwide, almost 17.3 million people [3], from which 7.3 million were caused by coronary disease and 6.2 million by cerebrovascular disease [4]. In accordance with the WHO projections, the number of deaths by CVD worldwide will increase from 17 million in 2004 to 23.4 million in 2030 [5].

CVD affect not only the global mortality rates, but also the life quality of the population. CVD are responsible for 151.377 million disability-adjusted life years, from which 41.34% are due to coronary disease and 31% due to cerebrovascular disease [5]. Additionally, 90% of all deaths by CVD occur in low and medium income countries [6]. In contrast, it is estimated that 80% of these cardiovascular events are avoidable [7].

In the Latin-American population, the age adjusted mortality rate due to potentially treatable conditions is 42.2 for diabetes mellitus, 60 for heart ischemic disease, and 45.4 for cerebrovascular diseases per 100,000 population [8]. Studies conducted in this population have found a higher prevalence of risk factors in women than in men, except for smoking, which is higher between men [9].

In Colombia, CVD are the leading cause of death, being responsible for 28% of all deaths, and having a mortality rate of 152 deaths per 100,000 population. The main risk factors are overweight (48%) and physical inactivity (43%) [6,10]. In a regional context, in Santander-Colombia, the most prevalent cardiovascular risk factors are: low fruit/vegetable intake (94%) (less than 5 portions/day), low level of physical activity (70.6%), and overweight or obesity (50.7%) [11].

Study of Health Care Workers in Bucaramanga, Santander

Otherwise, in a study conducted in health workers of a tertiary care institution in Bucaramanga, Santander, where the global cardiovascular risk and the prevalence of metabolic syndrome between workers were evaluated, a high prevalence of cardiovascular risk factors was determined, although the population was relatively young (median age was 44.3 years). In this study, the prevalence of hypertension was 54%, central obesity 40.3%, overweight 46.3%, obesity 21%, sedentary 82.4%, dyslipidemia 24%, smoking 10.4%, glucose intolerance

4.6%, and diabetes 1.6%. The ten-year global cardiovascular risk was 2.2% (5.2% in men and 1.4% in women). This study also established that male doctors were the population with the highest risk factors and the worst metabolic indices [12].

Fundación Cardiovascular de Colombia (FCV) is a high complexity health institution located in Floridablanca-Santander, Colombia. This institution is the biggest of the Colombian Northeast, and is specialized in the attention of CVD and their sequels. FCV's health team is highly qualified and is dedicated to the prevention, diagnosis, and treatment of high complexity diseases, especially the cardiovascular ones.

Given the importance of maintaining a healthy lifestyle, FCV proposes the development of this study, with the objective of determining the prevalence of the cardiovascular risk and its associated factors among the institution's workers in order to design and implement interventions in the work environment which may achieve a decrease in this risk.

Methods

Study Design

The design of the study is an analytical cross-sectional one.

Study Participants and Eligibility

Workers from clinical and administrative areas of a high complexity health care institution specialized in the attention of CVD, of Floridablanca, Colombia (Fundación Cardiovascular de Colombia) will be included. No exclusion criteria will be considered.

Sample Size

The institution has 1235 workers; 745 belong to the clinical area and 490 to the administrative area. All workers will be invited to participate in the study.

In order to increase the participation in the study, a sensitization strategy will be implemented by sending, through email, invitations and messages regarding the benefits of maintaining healthy lifestyles.

Data Collection

During 6 months, data collection will be held through two appointments. During the first appointment, a self-applied survey for sociodemographic aspects, physical activity, diet, alcohol consumption, smoking, level of perceived stress, and personal and family history of cardiovascular risk will be conducted with prior written informed consent. A second appointment will be made with the indication of wearing comfortable clothes and an 8-10 hours fasting, without having made intense physical activity or having consumed alcohol. Physical examinations will be made, and anthropometric measures and blood pressure will be recorded. Also, trained and qualified staff will take two blood samples; the first sample will assess total cholesterol levels, high density lipoprotein (HDL) cholesterol, triglycerides (TG), and blood glucose (Figure 1 shows this).

All personnel (nurses, physician, and nutritionist) involved in the research were previously trained on the procedures, tools,

and instructional design for the collection of information, as well as for the quality control of data.

A second sample will be taken and stored in the FCV biobank in order to perform future measures of new biomarkers related

to cardiovascular risk, such as homocysteine, tumor necrosis factor, and fibrinogen, which could be better predictors of cardiovascular risk than conventional markers [13].

Figure 1. Data collection. Total-C: total cholesterol; LDL: low density lipoprotein; HDL: high density lipoprotein; and TG: triglycerides.
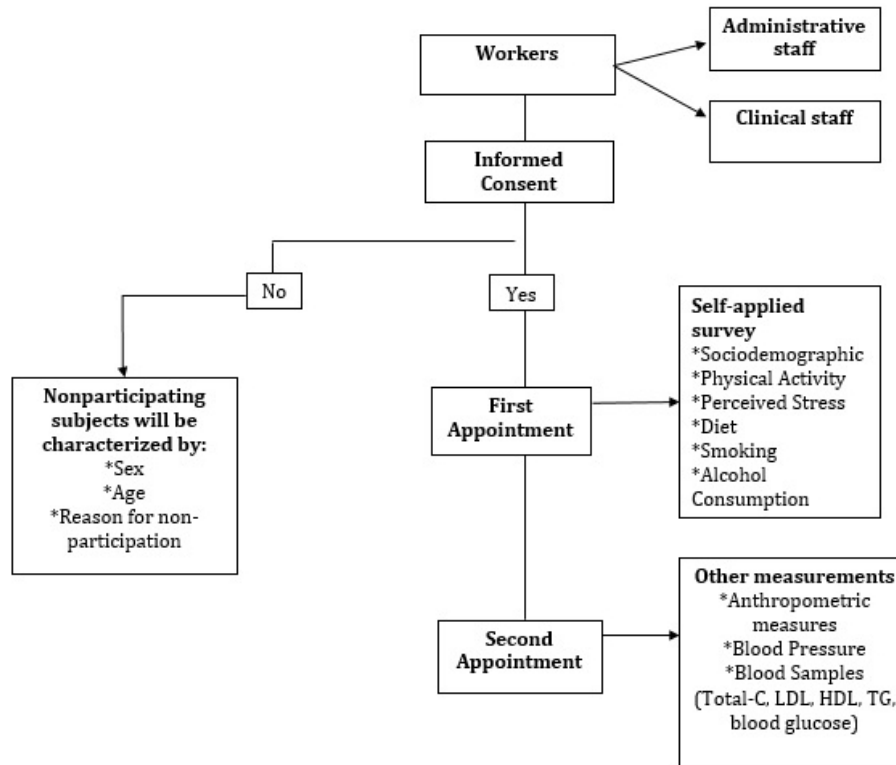
Study Variables

Sociodemographic Variables

Sociodemographic variables include age, sex, socioeconomic level, monthly income, level of education, marital status, social security, occupation, first-degree family history and personal history of cerebrovascular or CVD before age 60, reproductive history, cancer history, and whether or not the participant is receiving treatment for a chronic disease.

Smoking

A participant's smoking habit will be measured using the smoking index, which includes the daily smoked cigarettes, the number of years the person has smoked, and an estimation of the total amount of cigarettes. It is calculated by the formula, (average number of cigarettes smoked per day) x (number of years smoked)/20 [14].

Alcohol Consumption

Alcohol consumption will be measured by the alcohol intake frequency questionnaire, which has been validated in Colombia [15]. Through this questionnaire, the frequency of alcohol consumption by specific alcoholic drink (beer, brandy, rum, wine, whisky) during the last month will be investigated.

Physical Activity Measurement

Physical activity will be evaluated using the International Physical Activity Questionnaire, short version, which was adapted to the Colombian population, considering the urban social context of low and middle socioeconomic strata, since they represent the highest proportion of people in the country [16-18]. The questionnaire evaluates the intense physical activity, the moderated physical activity, the weekly walking time, and the sitting time. The following categories will be considered for the analysis,

Category 1, or low, is for those who do not meet the criteria of the categories 2 and 3. They are considered inactive.

Category 2, or moderate, is for any of the following: 3 or more days of vigorous physical activity at least for 20 minutes a day; or 5 or more days of moderate-intense activity or walking for at least 30 minutes a day; or 5 or more days of any combination of walking, moderate-intense activity, or vigorous-intense activity achieving at least 600 minutes per week (MET).

Category 3, or high, is for either of the following two criteria: vigorous-intense activity for at least 3 days and accumulation of 1500 MET; or 7 or more days of any combination of walking, moderate-intense activity, or vigorous-intense activity achieving at least 3000 MET.

Diet Measurement

A questionnaire of frequency of food consumption during the last month will be given. This questionnaire will inquire about the most common food groups of the Colombian population. Also, the survey will inquire about some dietary habits.

Level of Perceived Stress

This variable will be measured through the perceived stress scale. Stress is a physical and psychological adaptive response to the demands and threats of the environment. The Perceived Stress Scale was designed with the purpose of discovering how stressful people perceive everyday life events. This scale is comprised of two dimensions: coping with stressors, and perception of stress [19,20].

This scale is composed of 14 items that assess how stressful the daily events in the last month are for people. This is a validated scale in the Colombian population, it has 5 answer options as in the Likert scale, where 0=never, 1=almost never, 2=occasionally 3=often, and 4= very often. The total score of the scale is obtained by inverting the scores of the items 4, 5, 6, 7, 9, 10, and 13 (as it follows, 0=4, 1=3, 2=2, 3=1, 4=0), and adding the 14 items. At a higher score, the higher is the level of perceived stress [19-21].

Anthropometric Variables

Body Composition

The recommendations of the Manual of the International Society for the Advancement of Kinanth, the international standards for the anthropometric evaluation [22], will be applied.

Body Composition by Bioimpedance

The body composition analyzer Tanita TBF-300A will determine this. The scale will measure the following variables: weight, body fat percentage, fat body mass (kilogram, kg), lean body mass (kg), and total body water (kg).

Body Composition by Body Mass Index

This will be determined as the relation between the height and the body weight (kg/m2). The WHO defines a normal range of body mass index (BMI) as between 18.5 and 24.9; overweight is defined as a BMI >25, obesity is classified in 3 classes: class I with a BMI between 30-34.9; class II with a BMI between 35-39.9; and class III or morbid obesity with a BMI >40 [23,24].

Height

This will be measured in a 0.1 centimeter (cm) scale using a stadiometer. Subjects will be asked to remove their shoes and any head ornaments that may affect the measurement. The measurement will be read carefully, verifying that the squad of the stadiometer is stuck to the wall and horizontal to the plane of measurement. The reader's eyes will be on the same horizontal plane as the stadiometer, in order to register an accurate measurement.

Waist Circumference

The measuring tape will be positioned at the smallest circumference of the natural waist or in the midpoint between the inferior margin of the last rib and the iliac crest, with the reader standing in front of the subject in order to localize correctly the measurement zone. Subjects will be asked to breathe normally and the measurement will be taken during expiration with the arms alongside the body. The cutoff point will be the one established by the International Diabetes Federation (IDF) for Latin population, ≥90 cm for men and ≥80 cm for women [25].

Hip Circumference

Subjects will be asked to stand up with feet together and without contracting the buttocks. Positioning the measuring tape around the maximum circumference of the buttocks and checking that the tape's position is horizontal all around the body is how the perimeter will be measured.

Waist-Hip Ratio

This will be calculated by dividing the waist circumference (cm) by the hip circumference (cm). All the anthropometric variables will be measured twice, and the average of them will be taken for the analysis. The cutoff point will be, >0.90 for men and >0.85 for women and/or BMI >30 kg/m [26].

Blood Pressure

There are 3 readings that will be taken at intervals of at least two minutes, with a digital sphygmomanometer (Omron HEM-7114), having the following recommendations.

1. Subject's bladder must be empty, and they must have not smoked or drunk coffee 30 minutes before the measurement of the blood pressure (BP).
2. The patient should be seated comfortably for at least 5 minutes, with the back supported. The upper arm must be bared without constrictive clothing and supported at heart level. The legs should not be crossed and the feet must be on the floor.
3. The size of the cuff will be selected according to the circumference of the subject's arm (sizes S, M, L)
4. The brachial artery will be identified and the cuff bladder will be positioned 2 cm above the antecubital fossa.

BP ≥140 mmHg/90 mmHg [27] will be considered hypertension, as well as being in medical treatment for hypertension.

Biochemical Variables

Blood Samples

Peripheral blood samples through venous puncture will be taken with the Vacutainer system, using three tubes of 7 ml without anticoagulant and two tubes of 4 ml with anticoagulant (Becton, Dickinson, and Co USA; Ref #366431yRef #366437, respectively). The samples will be centrifuged during 10 minutes at 3000 revolutions per minute; the component's separation will be made in the laboratory within a biological safety cabinet. The vials will be labeled with the assigned code and stored at -80°C. Prior to storage, the date, number of vials, and person responsible for the procedure will be recorded.

Fasting Blood Glucose

Fasting prior to sample taking will be verified, as well as pharmacological treatment with hypoglycemic drugs or insulin. Prediabetes will be considered with fasting blood glucose values

between 100 milligrams per deciliter (mg/dl) and 125 mg/dl, and diabetes will be considered with fasting blood glucose ≥126 mg/dl (7.0 millimole per Liter, mmol/L), according to the American Diabetes Association [28].

Lipid Profile

Analysis of the lipid profile will be made by colorimetric techniques. The kits are in agreement with the ones referenced by the largest observational studies in CVD and include the following characteristics.

Total Cholesterol

The enzymatic method for quantitative determination of cholesterol was used. For analytic sensitivity, the method is linear up to 19.3 mmol/L (750 mg/dl); inferior limit of detection, 0.08 mmol/L (3 mg/dl). Hypercholesterolemia will be considered with cholesterol level >200 mg/dl [29].

Triacylglycerol

The colorimetric method was used to determine triacylglycerol levels. The analysis is linear up to 11.4 mmol/L (1000 mg/dl); inferior limit of detection, 0.05 mmol/L (4 mg/dl). Hypertriglyceridemia will be considered with values above 150 mg/dl [29].

High Density Lipoprotein Cholesterol

This was quantified by colorimetric assay (HDL-C plus) using esterase and cholesterol oxidase coupled to polyethylene glycol. The analytical sensitivity-inferior limit of detection: 0.08 mmol/L (3 mg/dl). Values will be considered abnormal if they are lower than 40 mg/dl for men and lower than 50 mg/dl for women [29].

Low Density Lipoprotein Cholesterol

This was calculated by the formula in Friedewald [30]. Low density lipoprotein (LDL) cholesterol (mg/dl)=total cholesterol-HDL cholesterol-triacylglycerol/5 or LDL cholesterol (mmol/L)=total cholesterol-HDL cholesterol-triacylglycerol/2.2. This formula will be applied when TG are ≤4.5 mmol/L. Abnormal values will be considered with LDL >130 mg/dl [29,31,32].

The methods were selected for being described, standardized, and analyzed according to the guidelines of the National Committee for Clinical Laboratory Standards manual EP5-T2 [33].

Metabolic syndrome will be defined by the Adult Treatment Panel III classification [29,33] and by the classification of the IDF [34,35].

Ten-Year Global Risk of Cardiovascular Disease

The risk (myocardial infarction, heart failure, angina, ischemic stroke, hemorrhagic stroke, transient ischemic attack, peripheral arterial disease) will be measured using the Framingham score, which contemplates the following variables: sex, age, systolic blood pressure, arterial hypertension in treatment, smoking, diabetes mellitus, HDL and total cholesterol, and determining four risk categories (low <15%, moderated 15%-20%, high 20%-30%, and very high >30%) [36].

Statistical Analysis

A descriptive analysis of the characteristics of the study population will be done. Continuous variables will be described with means and SD or median and interquartile range (25%-75%), according to their distribution assessed by the Shapiro-Wilk test. Categorical variables will be described as proportions with a 95% confidence interval.

Stratified analysis by sex, age, and occupation will be made. To identify the differences between comparison groups, Student t test will be used for continuous variables with normal distribution, and the Mann-Whitney test for continuous variables with skewed distribution. Categorical variables will be compared using the chi-square test or the Fisher´s exact test. For categorical variables, the comparison of proportions test will also be used. A stratified analysis by sex, age, and occupation will be made. Bivariate and multivariate analysis will be made using logistic regression models or lineal regression models, depending on the outcome variable, to evaluate the association between cardiovascular risk and the independent variables.

Additionally, an analysis of the basic data of the individuals who refuse to participate in the study (gender, age, reason for not participation) will be performed, and these data will be compared with those of the participants to minimize selection bias.

Ethics and Dissemination

Research will be conducted in agreement with the 1993 Number 08430 Resolution from the Health Ministry of Colombia, by which the scientific, technical, and administrative standards for health research are established (Republic of Colombia, 1993) [37]. The Scientific and Technical Committee and the Ethics Committee on Research of the Fundación Cardiovascular de Colombia approved the research protocol. Written informed consent will be asked of all the participants of the study. The findings about this project will be disseminated through peer-reviewed publication and conference presentations.

Results

Currently, this study is in the phase of training the personnel responsible for conducting the surveys and measurements. Data collection phase is expected to begin in two months. It is also expected that the data collection phase will end in a time lapse of sixth months given the total study population.

Discussion

Given the interest of different institutions worldwide [38-41], which have emphasized the promotion of health in the workplace, this study will contribute evidence to occupational health by the establishment of the cardiovascular profile of the workers of a high complexity health care institute.

Determining the prevalence of the cardiovascular risk and its related factors will allow the design and assessment of the effectiveness of interventions directed to decrease or avoid those factors, which will comply with the WHO Strategy of Diet, Physical Activity, and Health. This strategy, established in article 64, "Workplaces are important environments for health

promotion and disease prevention. People should be able to adopt health decisions in their workplace in order to reduce their exposure to risk. It is precise to ensure the opportunity of adopting healthy decisions in the workplace, as well as supporting and promoting physical activity" [42].

This study seeks to show the impact that generates an institutional program of promotion, prevention, and control of worker's risk factors. Thus, this will support the objectives of the 60th World Health Assembly, which highlights the global action plan on workers' health 2008-2017 [43], where workplace and primary prevention of risk factors are considered the central focus for the economic development and world productivity.

Conflicts of Interest

None declared.

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Abbreviations

BMI: body mass index
BP: blood pressure
cm: centimeter
COLCIENCIAS: Colombian Institute for the Development of Science and Technology
CVD: cardiovascular disease
FCV: Fundación Cardiovascular de Colombia
HDL: high density lipoprotein
IDF: International Diabetes Federation
kg: kilogram
LDL: low density lipoprotein
MET: minutes per week
mg/dl: milligrams per deciliter
mmol/L: millimole per liter
TG: triglycerides
WHO: World Health Organization

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Original Paper

Evaluating Comparative Effectiveness Research Priorities for Care Coordination in Chronic Obstructive Pulmonary Disease: A Community-Based eDelphi Study

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Abstract

Background: Despite research supporting the use of care coordination in chronic obstructive pulmonary disease (COPD), there is relatively little known about the comparative effectiveness of different strategies used to organize care for patients. To investigate the most important COPD care coordination strategies, community-based stakeholder input is needed, especially from medically underserved populations. Web-based platforms are electronic tools now being used to bring together individuals from underrepresented populations to share input and obtain clarification on comparative effectiveness research (CER) ideas, questions, and hypotheses.

Objective: Use low computer-literate, collaborative survey technology to evaluate stakeholder priorities for CER in COPD care coordination.

Methods: A mixed-method, concurrent triangulation design was used to collect survey data from a virtual advisory board of community-based stakeholders including medically underserved patients with COPD, informal caregivers, clinicians, and research scientists. The eDelphi method was used to conduct 3 iterative rounds of Web-based surveys. In the first 2 survey rounds, panelists viewed a series of "mini research prospectus" YouTube video presentations and rated their level of agreement with the importance of 10 COPD care coordination topics using 7-point Likert scales. In the final third-round survey, panelists ranked (1=most important, 8=least important) and commented on 8 remaining topics that panelists favored most throughout the first 2 survey rounds. Following the third-round survey, panelists were asked to provide feedback on the potential impact of a Web-based stakeholder engagement network dedicated to improving CER in COPD.

Results: Thirty-seven panelists rated the following care coordination topics as most important (lower means indicate greater importance): (1) measurement of quality of care (mean 2.73, SD 1.95); (2) management of COPD with other chronic health issues (mean 2.92, SD 1.67); (3) pulmonary rehabilitation as a model for care (mean 3.72; SD 1.93); (4) quality of care coordination (mean 4.12, SD 2.41); and (5) comprehensive COPD patient education (mean 4.27, SD 2.38). Stakeholder comments on the relative importance of these care coordination topics primarily addressed the importance of comparing strategies for COPD symptom management and evaluating new methods for patient-provider communication. Approximately one half of the virtual panel assembled indicated that a Web-based stakeholder engagement network could enable more online community meetings (n=19/37, 51%) and facilitate more opportunities to suggest, comment on, and vote for new CER ideas in COPD (n=18/37, 49%).

Conclusions: Members of this unique virtual advisory board engaged in a structured Web-based communication process that identified the most important community-specific COPD care coordination research topics and questions. Findings from this

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study support the need for more CER that evaluates quality of care measures used to assess the delivery of treatments and interventions among medically underserved patients with COPD.

KEYWORDS

Introduction

Background

Chronic obstructive pulmonary disease (COPD), a chronic lung condition characterized by progressive airflow limitation, shortness of breath, and productive cough, is the third leading cause of death in the United States [1]. Estimates indicate that approximately 15 million US adults are living with COPD [2]; however, the actual number of adults living with COPD is likely much higher, because COPD often goes undetected and undiagnosed [2]. In 2010, the economic burden of COPD in the United States was approximately US$ 50 billion, including US$ 30 billion in direct and US$ 20 billion in indirect health care costs [3]. The largest share of the cost burden was caused by poorly managed comorbidities (eg, hypertension, heart disease, and mental illness) experienced by patients [4]. Although different approaches to managing COPD and its complicating factors have been studied for decades [5], so far relatively little is known about the comparative benefits and harms of care coordination strategies used to help patients manage COPD in the presence of morbidity and comorbidity [6]. Care coordination has been defined as, "the deliberate organization of patient care activities between 2 or more participants (including the patient) involved in a patient's care to facilitate the appropriate delivery of health care services" [7]. Organizing care involves health care personnel and resources needed to carry out patient care, which is often governed by information exchange among participants responsible for different facets of care [8]. Participants in the care coordination process can include patients, family caregivers, physicians, nurses, pharmacists, social workers, and others [7].

Inadequate coordination between primary and specialist care and between community and medical settings may be the main reason for poorly managed symptoms observed in patients with long-term conditions such as COPD [9]. Therefore, there are a variety of care coordination strategies used to support self-management and treatment services for patients with COPD, such as smoking cessation, influenza and pneumonia vaccination, pulmonary rehabilitation, and symptomatic and maintenance pharmacotherapies. Effective care coordination in COPD through ongoing multifactorial management can not only reduce health care costs stemming from the effects of poorly managed COPD, such as dyspnea (ie, shortness of breath) exacerbations, but also improve a patient's health-related quality of life [10]. The most effective chronic care coordination strategies can be identified through comparative effectiveness research (CER), which explores the extent to which the organization of care and communication between health care providers is collaborative and productive [4,8,10,11,12]. In

CER, the benefits and harms of alternative treatments and interventions are directly compared to determine their efficacy to prevent, diagnose, treat, and monitor clinical conditions in real-world settings [13]. To ensure that care coordination strategies provide the most benefits to patients with the least potential for harm [14,15], it is recommended that key stakeholders remain engaged in all stages of health care decision-making processes [4,11,12,14,16]. In health care, a "stakeholder" is defined as anyone who can have a significant influence on an organization's ability to address a health-related issue of interest [14]. Often, health issues such as the presence or absence of a particular disease or condition bring stakeholders from different groups together. These different groups include health care providers, allied health care professionals, patients, and informal caregivers. "Stakeholder engagement" is defined as the process of working collaboratively with and through diverse groups of people to gather input from all those affected by the topic of interest, to help solve the health problem or improve health status of patients [14,17].

To date, there has been limited involvement from individuals most affected by care coordination processes (ie, patients and informal caregivers) in defining CER topics and evaluating COPD care coordination strategies [16,18]. Pickard and colleagues [19] first used 2 phases of in-person meetings with clinicians, researchers, and representatives from health care plans, patient advocacy groups, and professional health organizations to identify "the effectiveness of supplemental oxygen for COPD" as the highest priority CER topic in COPD. Krishnan and colleagues [20] later assembled 54 stakeholders representing government entities, research institutions, health plans, and patient advocacy organizations to develop an updated list of high-priority CER topics in COPD. A series of 2-year workshops sponsored by the COPD Outcomes-Based Network for Clinical Effectiveness and Research Translation explored priorities in the following 4 discrete areas: (1) chronic care; (2) care coordination; (3) acute care; and (4) transitions in care. Within the "care coordination" category, the topics, "management of COPD in the presence of comorbidity" and "pulmonary rehabilitation as a model for care coordination," were ranked as the 2 highest priorities; however, neither topic was rated as "most important" by participating stakeholders. Although both studies [19,20] identified COPD care coordination priorities for CER, there was limited involvement from actual patients with COPD or their informal caregivers (ie, family members and friends who aid and supervise the daily care of people living with an illness or disability). Stakeholders from these highly relevant groups can help identify important care coordination topics that clinical, administrative, and research-oriented stakeholders may overlook. Supporting frequent collaboration between researchers and key COPD

stakeholder groups is essential to sustaining patient-centered research targeted at improving the management and treatment of the disease [18]. Research teams that engage stakeholder groups from underrepresented patient and informal caregiver groups can establish patient-centered priorities for care coordination in COPD through meaningful and collaborative partnerships.

Current Barriers to Stakeholder Engagement

Current barriers to meaningful stakeholder engagement include lack of interest, limited stakeholder education about research topics and health issues, and human/fiscal resource constraints. These barriers can preclude researchers from identifying, engaging, and interacting with stakeholders; however, there are a number of innovative, technology-based methods that help overcome some of these obstacles [14]. For example, low-cost, Web-based collaborative platforms use convenient virtual spaces (eg, discussion boards, chat rooms, community forums) to decrease the geographical and temporal barriers to recruiting and retaining low socioeconomic status (SES) chronic disease patients. Moreover, diverse patients with ethnic and minority backgrounds are interested in adopting health information and communication technologies (ICTs) that were previously viewed as out of reach for these historically marginalized populations [21,22]. Patients with COPD use the Internet to locate information to self-manage their condition and communicate with others about their health [23]. To improve stakeholder engagement in CER related to COPD, a flexible research infrastructure must exist that is sensitive to sociotechnical changes in collaboration [24]. The flexibility and convenience of the Internet provides a platform to quickly disseminate surveys and anonymous responses to all panelists [25]. Web-based community building enables virtual advisory boards to grow quickly and inexpensively. On Web-based community platforms, stakeholders are given the freedom to securely share ideas, request feedback, and obtain clarification on research questions and hypotheses without having to attend panel meetings at fixed times in fixed locations. Increasing the adoption of Web-based collaborative platforms among low-income, medically underserved patients with COPD will likely improve stakeholder engagement during the research agenda-setting process, which, in turn, can enhance the overall relevance of CER for patients living with COPD [26].

Currently, more CER is needed to help better understand the relative benefits and harms of the many available strategies used to coordinate the delivery of care in COPD. Community-level input on the importance of different strategies can improve the design of CER studies of COPD care coordination approaches in different health care settings. As such, the primary objective of this stakeholder engagement study was to systematically prioritize CER topics related to COPD care coordination using electronic feedback provided by a diverse community-based panel of stakeholders. A secondary objective was to gather stakeholder input that could help inform the development of a Web-based stakeholder engagement network dedicated to evaluating, translating, and disseminating CER findings in COPD care coordination.

Methods

Research Design

A mixed-method concurrent triangulation design [27,28] was used to collect both quantitative and qualitative data on the relative importance of different approaches to COPD care coordination. This pragmatic design merged quantitative and qualitative data to generate a greater understanding about the highest priority COPD care coordination topics as perceived by a virtual advisory board of stakeholders living and working in the community. The eDelphi method, an electronic version of the Rand Corporation's Delphi method [29], was used obtain an informed consensus from stakeholders living and working in or near the university community. The eDelphi method is a group communication process that uses a series of surveys administered to an anonymous, informed panel to achieve convergence of opinions on a particular topic. During an eDelphi study, each panelist is encouraged to form an opinion, and independently reassess his/her opinion based on anonymous feedback from fellow panelists in successive survey rounds [30-32]. Researchers who use the eDelphi method for opinion pooling create a nonconfrontational environment where panelists can potentially modify their opinions with limited peer pressure [33,34]. Web-based survey iteration generally continues for a designated number of rounds until consensus (ie, when agreement exists among at least three fourths of panelists) is reached [33]. Research suggests that completing a structured series of 3 Web-based questionnaires is generally sufficient for reaching consensus [35-38]. Often, panelists are also provided the opportunity to submit qualitative feedback to clarify and expand upon their quantitative rankings of the topic(s) at hand. Researchers are able to corroborate and validate results from an eDelphi study by directly illustrating quantitative data with qualitative findings [39].

Compared with the traditional paper-based and snail mail Delphi, the eDelphi offers researchers several other advantages, including the following: (1) Web-based storage, processing, and transmission of secure data; (2) protection of respondent anonymity; (3) rapid feedback to panelists in the form of tables, charts, and statistics; and (4) fewer logistical challenges generally associated with bringing groups of people together for research-related purposes [25,40,41]. The eDelphi method is substantially different from in-person focus groups and online discussion forums. This consensus-building method provides the opportunity for panelists to provide independent feedback without being in direct communication with others. With anonymous feedback, there is little risk for panelists higher up on professional hierarchies to manipulate the opinions of other panelists [42].

Panelist Recruitment and Identification

Overview

The commitment of stakeholders to participate in eDelphi studies is often related to their level of interest with the topic [30]. In this study, a diverse panel of stakeholders with an interest in COPD care coordination was recruited through a collaboration with a community engagement and research

(CEnR) program operating at a large, research-intensive university in the Southeastern United States. The mission of the CEnR program is to reduce health care and research disparities by linking the medically underserved to research opportunities and medical and social services. Partnerships with community organizations and regional agencies provide guidance on appropriate and culturally sensitive collaborative opportunities for participants and researchers. The program serves several primary purposes in the community, including the following: (1) assessing health concerns from the viewpoint of community members; (2) facilitating 2-way communication with the community on how to promote health; (3) linking community members to opportunities to participate in health-related research; and (4) increasing the community's trust in research through collaboration and partnership. Most community members affiliated with the CEnR program (approximately 1900) belong to low-income, underrepresented minority communities.

Patients

Purposive sampling was used to identify patients with COPD registered in a community patient database operated and managed by the CEnR program. All patients were invited to participate by a study navigator working on behalf of the CEnR program. Patients were asked predetermined questions over the telephone to determine whether they met the following inclusion criteria: (1) diagnosis of COPD by a physician or specialist; (2) valid email address on file in the community patient database; (3) minimum 40 years of age; and (4) speak English as a first language. The minimum age of 40 was established because individuals at this age generally begin experiencing COPD symptoms such as excess mucus buildup, wheezing, and productive cough [43]. If patients met inclusion criteria, the study navigator asked whether or not the patient was interested in learning more about the study.

Informal Caregivers

Informal caregivers of patients with COPD were recruited using snowball sampling methods that capitalized on patient referrals. Snowball sampling is particularly useful when identifying and recruiting racial/ethnic minorities and individuals with low SES to participate in research [44]. Snowball sampling allows participants from these hard-to-reach populations to act as gatekeepers for recruiting others they know into a study. To identify informal caregivers of medically underserved patients with COPD in this study, patients were asked to refer a maximum of 3 informal caregivers into the study. An "informal caregiver" was defined as someone who met the following criteria: (1) family member or friend of the COPD patient; (2) at least 21 years old; and (3) responsible for helping to provide nonclinical care (eg, medication reminders, self-management support) to at least one COPD patient. The informal caregiver(s) was then provided with the contact information of a research navigator affiliated with the CEnR program, who was available to provide additional information about study enrollment.
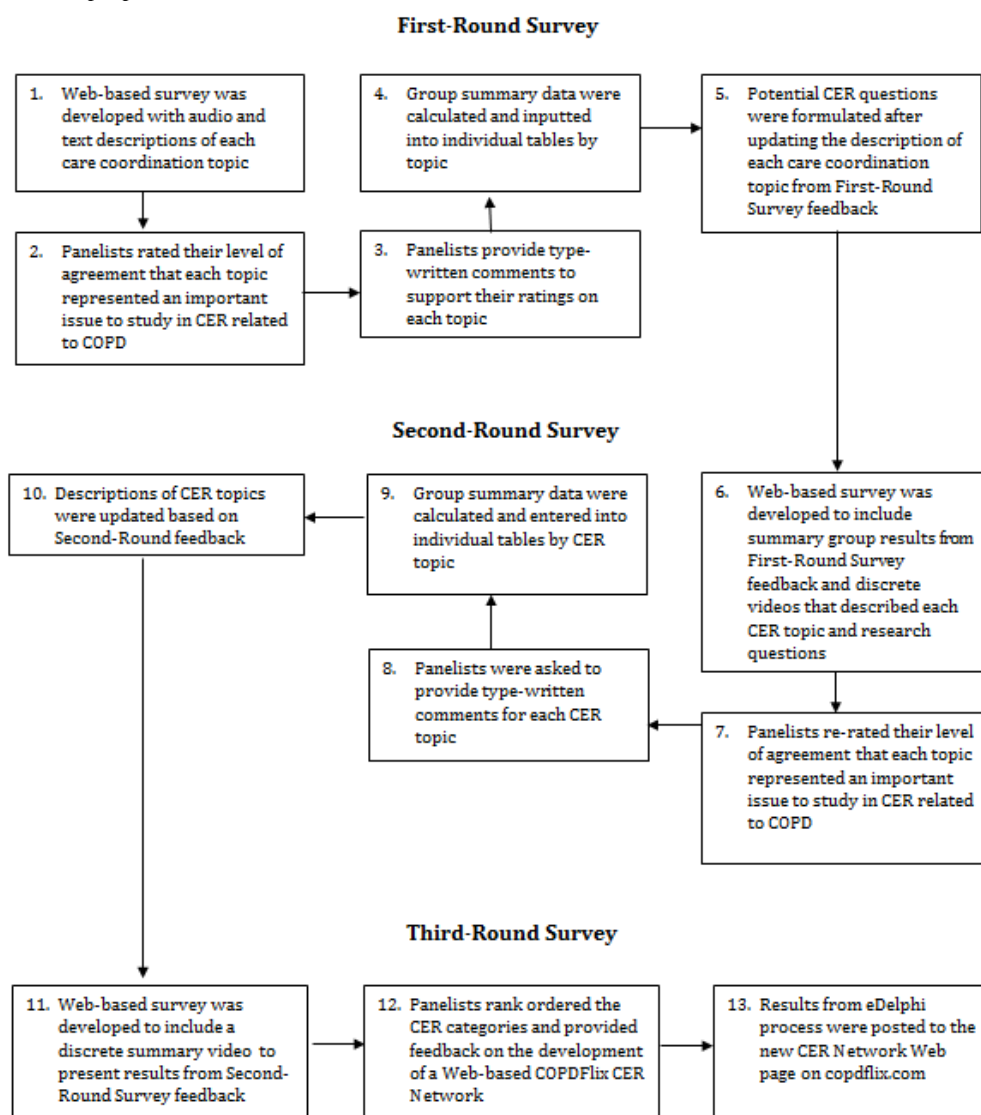
Clinicians and Research Scientists

Practicing clinicians and research scientists with professional experience studying COPD care coordination were identified through searching VIVO, an intrainstitutional semantic-Web-networking platform used to foster cross-disciplinary team science in the university where the research took place [45]. The VIVO platform uses an interactive database including a variety of scholarly variables (eg, home department/college/laboratory, number and type of grant awards, courses taught, curricula vitae) describing employed clinicians and research scientists. In this study, VIVO was queried by 2 members (MS and JA) of the research team using the following keywords: "chronic obstructive pulmonary disease," "pulmonary health (adults)," "pulmonary rehab," "respiratory therapy," "respiratory health," "care coordination," "comparative effectiveness research," "lung disease," and "oxygen therapy." All Web profiles and curricula vitae of identified research scientists and clinicians were evaluated to determine their level of involvement in COPD care coordination research. Clinicians (eg, doctors, physiotherapists, respiratory therapists, nurses) were required to be employed by a university-based clinic or health care facility for a minimum of 5 years, and research scientists were required to be current university faculty investigating at least one aspect of COPD care coordination (eg, disease management, pulmonary rehabilitation, case management, risk management) [20]. Evidence of experience investigating one or more care coordination topics was identified through reviewing grant award activity, publications, and professional presentations.

Procedures

Figure 1 depicts the sequence of 3 iterative rounds of Web-based surveys carried out over the 6-week study period. Interested panelists from each group were sent formal email invitations with an embedded Qualtrics survey hyperlink. After clicking on the hyperlink, panelists were presented with an electronic informed consent document, which provided a description of the study's purpose and procedures. Panelists were provided with the following information: (1) title of the study; (2) purpose of the study; (3) description of what would be asked of them (ie, completing 3 Web-based surveys over a period of approximately 2-3 months); and (4) description of an US$ 45 gift certificate incentive offered for their participation. Panelists were also made aware that their participation was voluntary. Information on the confidentiality of responses was also provided, including information on Qualtrics password protection, server security, and firewall protections. Panelists were made aware that a security breach of their online data was unlikely and would not likely result in adverse consequences. After providing consent, panelists were directed to the first-round survey.

Figure 1. Three-round eDelphi process.

First-Round Survey

1. Web-based survey was developed with audio and text descriptions of each care coordination topic

2. Panelists rated their level of agreement that each topic represented an important issue to study in CER related to COPD

3. Panelists provide type-written comments to support their ratings on each topic

4. Group summary data were calculated and inputted into individual tables by topic

5. Potential CER questions were formulated after updating the description of each care coordination topic from First-Round Survey feedback

Second-Round Survey

10. Descriptions of CER topics were updated based on Second-Round feedback

9. Group summary data were calculated and entered into individual tables by CER topic

8. Panelists were asked to provide type-written comments for each CER topic

6. Web-based survey was developed to include summary group results from First-Round Survey feedback and discrete videos that described each CER topic and research questions

7. Panelists re-rated their level of agreement that each topic represented an important issue to study in CER related to COPD

Third-Round Survey

11. Web-based survey was developed to include a discrete summary video to present results from Second-Round Survey feedback

12. Panelists rank ordered the CER categories and provided feedback on the development of a Web-based COPDFlix CER Network

13. Results from eDelphi process were posted to the new CER Network Web page on copdflix.com

First-Round Survey

In the first-round survey, panelists were provided with a brief (3-4 sentences) bulleted description of 10 COPD care coordination topics selected from the literature [20]: (1) management of COPD when other chronic problems are present; (2) pulmonary rehabilitation as model for care in COPD; (3) depression and mental health management in patients with COPD; (4) measurement of quality of care in patients with COPD; (5) quality of care coordination; (6) comprehensive COPD patient education; (7) cost effectiveness of care; (8) case management in COPD; (9) measuring hospitalization risk in patients with COPD; and (10) patient-centered medical home. Table 1 provides definitions of all 10 COPD care coordination topics evaluated by stakeholder panelists. All panelists were provided background information on each topic using literacy-sensitive text and audio narration. All text-based survey content followed recommended principles for developing Web-based consumer health education materials for older adults [46-48]: (1) enlarged text (14-point font) written at or below a 6th grade reading level; (2) short excerpts of text (ie, 1 primary point/sentence); (3) plain language (ie, communication an audience can understand the first time they read or hear it) with an active voice; and (4) sans-serif font (eg, Arial, Calibri) with left justification and no italics.

Panelists' level of agreement with the importance of each of the 10 COPD care coordination topics was evaluated using a 7-point Likert scale (1=strongly disagree, 7=strongly agree). Panelists were also asked to provide demographic information using items adapted from the 2014 Behavioral Risk Factor Surveillance System's Questionnaire [49]. Demographic items included the following: age (years), sex (male, female, and other), race (white, black/African American, American Indian/Alaska Native, Asian, Pacific Islander, and other), ethnicity (Hispanic/Latino/Spanish origin and non-Hispanic), highest grade or year completed in school (never attended school, grades 1-8, grades 9-11, grade 12 or general educational development diploma, college 1-3 years, and college 4 years or more), marital status (married, widowed, divorced, separated, and never married), and household income (less than US$ 10,000, less than US$ 15,000, less than US$ 20,000, less than US$ 25,000, less than US$ 35,000, less than US$ 50,000, less than US$ 75,000, and US$ 75,000 or more). Panelists were

given up to 2 weeks (August 22, 2014, to September 8, 2014)   to complete the first-round survey.

Table 1. Definitions of chronic obstructive pulmonary disease care coordination topics evaluated by stakeholder panelists.

Care coordination topic	Definition	Sample comparative effectiveness research question[a]
Management of chronic obstructive pulmonary disease (COPD) when other chronic health problems are present	Participation among multiple health care professionals in the treatment of COPD and other comorbidities experienced by the patient	Would a standard process for identifying chronic health conditions commonly found in patients with COPD help improve a doctor's ability to treat patients?
Pulmonary rehabilitation as a model for care in COPD	Formal program aimed at improving the quality of life for patients with chronic lung disease that includes a broad range of activities such as nutritional counseling, breathing retraining, exercise training, and practicing energy conservation	Which setting for pulmonary rehabilitation is most effective for different patients with COPD?
Depression and mental health management in patients with COPD	Active screening for depression and the management of mental health provided by trained depression care managers and primary care providers, including antidepressant treatment and/or psychotherapy provided by a supervising psychiatrist	Would patients undergoing regular screening for depression show improvements in mental and physical health outcomes?
Quality of care coordination	Measuring how effectively patient's needs and preferences are understood and communicated at the right time to the right people, and whether or not this information is used to provide safe, appropriate, and effective care to the patient	What factors are associated with high-quality care coordination in patients with COPD?
Measurement of quality of care in patients with COPD	The degree to which various strategies used for managing treatment across health care providers and services produces the desired health outcomes and improves the patient's quality of life	What should be measured while a patient with COPD is following a prescribed treatment plan?
Comprehensive COPD patient education	Knowledge- and skill-building programs for patients with COPD aimed at improving the patient's ability to independently self-monitor and manage COPD	What is the comparative effectiveness of different types of educational programs designed to teach patients how to use their respiratory inhaler?
Cost effectiveness of care	The direct comparison of the costs and health benefits of a treatment or intervention option	What is the cost effectiveness of different models of care coordination such as pulmonary rehabilitation versus comprehensive patient education?
Case management in COPD	Strategies that involve working with health care providers to coordinate and monitor treatments to meet individual patient needs	What is the effectiveness of case management programs for patients with other chronic conditions such as heart failure and diabetes, compared with regular care in patients with COPD?
Measuring hospitalization risk in patients with COPD	Evaluating and identifying which patients are at the greatest risk of hospitalization and rehospitalization to inform and modify risk-specific care plans	Is it possible to use a screening tool to identify which patients are at greatest risk of visiting the doctor's office or emergency room on a more regular basis?
Patient-centered medical home	Care strategy that uses a team of health care providers to monitor and improve patient care in the most accessible, convenient way for a patient	Does an individual patient with COPD experience better outcomes if he/she participates in a patient-centered medical home as compared to following other COPD treatment plans?

[a]Adapted from sample questions suggested by Krishnan and colleagues [20].

Second-Round Survey

After the first-round survey closed, 2 members of the research team (MS and JA) compiled all panelist ratings and type-written comments from the first-round survey. These data were used in conjunction with other stakeholder education materials [20] to develop a 1-2-minute video transcript describing each of the 10 COPD care coordination topics. Transcripts were used to record a series of "mini research prospectus" YouTube video presentations delivered by the lead investigator (MS). Figure 2 illustrates how topics were described and how surveys were delivered to panelists during the second-round survey. Each video was uploaded onto the Qualtrics survey interface, and all presentations followed a structured sequence of PowerPoint slides that described (1) contextual information supporting the need to investigate the topic; (2) 3-4 potential CER questions that could be examined within each topic; and (3) a brief "take-home" justification for why each care coordination topic may be important to explore in future CER. PDF versions of video transcripts were made available for users to download and review.

All consenting panelists who successfully completed the first-round survey were sent an email invitation with an embedded hyperlink to access this second-round survey. In the second-round survey, panelists were asked to review summary results from the first-round survey and watch all 10 care coordination YouTube videos developed by the research team

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using summary data from round one. Following each video, panelists were invited to enter their own comments into a textbox and rate their level of agreement with the importance of CER questions explained on each video (1=strongly disagree,

7=strongly agree). Like in round one, panelists were given 2 weeks to submit their survey responses (September 10, 2014, to September 25, 2014).

Figure 2. Item sequence during second-round survey administered on Qualtrics.
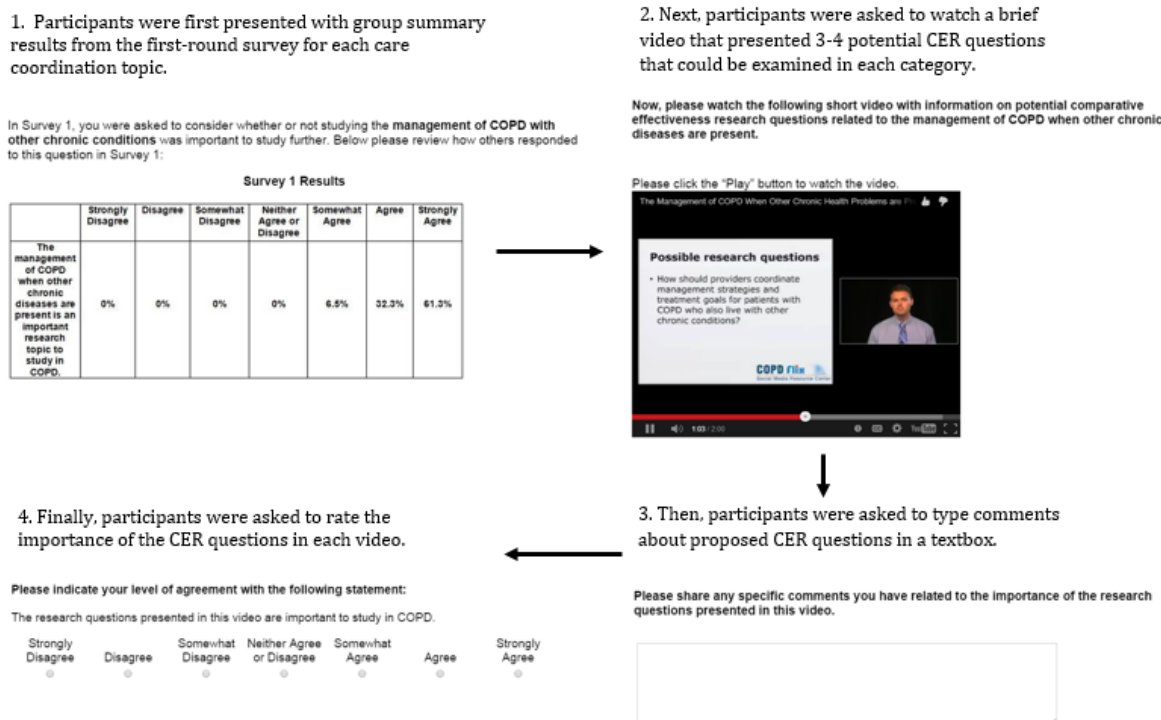
Third-Round Survey

Following the closure of the second-round survey, 2 researchers compiled all panelists' ratings and type-written comments from the second-round survey to create a final 6-minute video presentation delivered by the lead investigator. This final video summarized all eDelphi results from the first and second rounds. Specifically, it described the level of panelist convergence around the highest priority care coordination topics from the first to second rounds. The video was embedded onto the Qualtrics survey platform using the YouTube media player. After viewing the final summary video, panelists were asked to rank-order 8 remaining topics that received consensus support in the prior 2 rounds (1=most important, 8=least important). In addition, panelists were asked to comment on why they believed the topic they ranked as "1" was most important to study further.

Panelists were also asked to answer questions related to the potential impact of a Web-based stakeholder engagement network dedicated to fostering and improving CER in COPD. Panelists reported how likely they would be to visit the stakeholder engagement network website on a 6-point Likert scale (1=very unlikely, 6=very likely), and they were asked to indicate how often they would visit the website using a 5-point Likert scale (1=rarely or never, 5=every day or almost every day). Panelists were also asked to rank 5 potential purposes of the website from 1 to 5 (1=most important, 5=least important). Potential purposes of the Web-based stakeholder engagement network included learning from others, accessing research reports online, study recruitment, and building trust. Panelists could also enter in their own desired purpose using a field

marked "Other." Finally, panelists responded to the following open-ended questions: (1) "If you were to join a CER Network website, what roles or responsibilities would you see for yourself?"; (2) "What would you expect to gain from visiting a CER Network website?"; and (3) "What types of resources would you like available on a CER Network website?" Panelists could select from a list of all responses that they felt answered each question. Panelists were given 2 weeks to complete the third-round survey (October 15, 2014, to October 29, 2014), and following completion, each participant was redirected to a secure external website to provide contact information that would enable them to receive a US$ 45 gift card incentive for their participation.

Data Analysis

Once duplicate surveys were deleted from the final database and a code number was assigned to each survey, the Internet protocol addresses were deleted to eliminate any linkages between participant names and email addresses. Qualitative and quantitative data were analyzed separately and independently. Two researchers scanned all submitted comments from round one and round two surveys to determine whether any panelists reported confusion related to any of the topic categories. Round-by-round panelist response and attrition rates were computed using frequency statistics. Frequency statistics were also computed to report the sociodemographic characteristics of panelists. Panelists' ratings on each COPD care coordination topic were summarized in each round using mean (SD) statistics to quantify the collective judgment of respondents [28]. Convergence of panelists' opinions (ie, consensus) was judged

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to be reached when 80% or more of panelists' ratings were rated as "6=agree" or "7=strongly agree" on the 7-point Likert scales [50].

To determine which COPD care coordination research topics were elaborated on the most by panelists, Braun and Clarke's [51] 6-step approach to thematic analysis was completed by 2 members of the research team to evaluate third-round qualitative data describing panelists' reasons for selecting the most important care coordination topic. These steps included the following: (1) becoming familiar with the data; (2) generating initial codes; (3) searching for themes; (4) reviewing themes; (5) defining and naming themes; and (6) producing a final summary report. Each research team member reviewed transcripts independently, and all panelist comments were analyzed using open coding [52]. A codebook was developed based on open codes that included each code definition [53]. Cohen kappa statistic was calculated for each code to determine intercoder reliability; acceptable kappa statistics were .75 or more [54,55]. When disagreement occurred between coders, a third member of the research team was asked to help resolve the discrepancy. Thirty unique codes showed evidence of adequate intercoder reliability (Table 2). After codes were established, 2 researchers analyzed the qualitative data by applying the codes and grouping them into common themes. Representative comments were identified for each emergent theme.

After analyzing the third-round qualitative data with thematic analysis, both qualitative and quantitative sets of results were merged by directly comparing the quantitative rankings from the third-round survey with the qualitative feedback describing panelists' reasons for selecting the highest priority COPD care coordination topic to study in future CER. Additional qualitative feedback was used to determine which COPD care coordination topics were elaborated on to the greatest extent. Finally, frequency and descriptive statistics were computed to analyze data on stakeholders' beliefs regarding the potential impact of a Web-based stakeholder engagement network for advancing CER in COPD.

Table 2. Round three survey codes, definitions, and kappa values.

Code	Definition	Kappa
Behaviors/lifestyle	Includes patient health behaviors or lifestyle choices (eg, smoking, healthy eating)	>.99
Comorbidity	Mention of having multiple health problems at once (COPD[a] and asthma)	>.99
Coordination	Individuals working together or planning together for a common purpose; includes working as a team	.90
Coping	Patient strategies or discussion of ways to deal with health issues caused by or related to COPD	.91
Cost	Refers to money needed or spent on the care, management, or treatment of COPD	>.99
Diagnosis	Diagnosis of COPD or the health issues (eg, diagnosis of depression) stemming from COPD symptoms	.91
Doctor visits	Visits to health care providers that are involved in the treatment of COPD, NOT including emergency room visits	>.99
Patient education	References to the need to learn more or increase understanding about COPD, the treatments of COPD, or anything else related to COPD	.93
Effectiveness	References to the effectiveness of COPD treatments to manage or prevent health issues; include cost effectiveness; comparison benefits versus negative effects	.95
Emergency room visits	Mention of the occurrence or prevention of emergency room visits due to COPD symptoms or complications	>.99
Expectation	References to the patient's expectation of COPD and its treatment	.80
Follow-up	Mention of the patient or provider following up on a treatment or issue related to COPD	.80
Health effects	Mentions of any health outcome related to COPD or symptoms of COPD (eg, breathing issues)	.94
Home	Reference to the in-home care or treatment of COPD	>.99
Hospital stay	Mention of having to stay at a hospital for a day or more for a treatment related to COPD; hospital visit outside of a regular doctor visit; not including emergency room visits	>.99
Informed	Mention of all individuals involved or affected by COPD having the knowledge to make appropriate or proper decisions about treatment or care	.95
Limitations	Reference to the downfalls or possible cons of a treatment or care strategy for COPD	>.99
Management	General references to managing COPD	.96
Medicine	Mention of any type of medicine taken to treat COPD or health issues related to COPD	>.99
Mental health	Mention of mental health concerns, such as depression, stemming from COPD diagnosis, symptoms, or treatment	>.99
Monitor	Monitoring the progress or effects of COPD symptoms and treatment	>.99
Necessary/helpful	Reference to someone or something being necessary, sufficient, or helpful in the COPD treatment or management	.99
Death	Discussion or reference to passing away	>.99
Patient-provider communication	Reference to the communication or lack thereof between a patient and the health care providers involved in their treatment	>.99
Personal experience	A patient or provider references a specific event that occurred related to diagnosis or treatment of COPD	>.99
Personalization	Reference to the unique factors of patients and the need for individualized treatment, care, or consideration	.96
Prevention	Reference to the strategies and need for preventing COPD or the complications of COPD	>.99
Health-related quality of life	Reference to quality of life, such as the importance or the negative/positive effects that COPD has on quality of life	.86
Standardize	Reference to the standardization of treatment options and management of COPD for patients	.75
Statistics	References to numerical data related to COPD, such as number of deaths caused by COPD or the number of people living with COPD	.80

[a]Chronic obstructive pulmonary disease

Results

Panelist Composition

Table 3 describes the demographic characteristics of 37 stakeholder panelists who consented to participate in the study, including patients (n=23), informal caregivers (n=3), clinicians (n=2), researchers (n=6), and unidentified participants (n=3).

Table 3. eDelphi panelists' sociodemographic characteristics (n=37).[a]

Demographic variable		Patients n (%)	Informal care-givers n (%)	Clinicians n (%)	Researchers n (%)	Unidentified[b] n (%)
Sex						
	Female	11 (47.8)	3 (100.0)	0 (0.0)	3 (50.0)	2 (33.3)
	Male	11 (47.8)	0 (0.0)	2 (100.0)	3 (50.0)	1 (16.6)
	Other	1 (4.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Race/ Ethnicity						
	White	15 (65.2)	3 (100.0)	1 (50.0)	5 (83.3)	2 (33.3)
	Black/African American	6 (26.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (16.6)
	Hispanic or Latino	3 (13.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (16.6)
	Other	3 (13.0)	0 (0.0)	1 (50.0)	1 (16.6)	1 (16.6)
Highest grade completed						
	Less than a high-school degree	2 (8.7)	0 (0.0)	0 (0.0)	1 (16.6)	2 (8.7)
	High-school/general educational development	5 (21.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	Some college[c]	16 (69.5)	3 (100.0)	2 (100.0)	6 (100.0)	1 (16.6)
Household income						
	<US$ 25,000	18 (78.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	US$ 25,000-US$ 49,999	4 (17.3)	1 (33.3)	0 (0.0)	0 (0.0)	3 (50.0)
	>US$ 50,000	0 (0.0)	1 (33.3)	2 (100.0)	6 (100.0)	0 (0.0)
Marital status						
	Married or widowed	7 (30.4)	1 (33.3)	2 (100.0)	5 (83.3)	2 (33.3)
	Divorced	8 (34.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	Separated	4 (17.3)	0 (0.0)	0 (0.0)	1 (16.6)	0 (0.0)
	Never married	4 (17.3)	2 (66.6)	0 (0.0)	0 (0.0)	1 (16.6)

[a]Panelists identified with more than 1 stakeholder group (n=3).

[b]Three (n=3) individuals who did not identify their stakeholder role did not provide any demographic information.

[c]Some college is defined as completing at least 1 year of coursework in the college/university setting.

Patients

One-hundred and thirty-seven patients living with COPD in the community met eligibility criteria to serve on the virtual advisory board. Fifty-four patients (39%) agreed to participate; however, less than half of those who agreed to participate (n=23) completed the first-round survey. An equal number of female (n=11) and male (n=11) patients joined the panel (mean age 57.65 years, SD 6.80 years). Most patient panelists identified as being white (n=15, 65%), with fewer identifying as black/African American (n=6, 26%). The majority of patient panelists (n=16, 70%) reported completing at least one year of

college; yet over 75% of patients (n=18) reported annual household incomes less than US$ 25,000/year. Almost three quarters of patients were either divorced (n=8), separated (n=4), or never married (n=4).

Informal Caregivers

Only 3 informal caregivers agreed to join the virtual panel. All informal caregiver panelists were women, white, and reported completing at least one year of college. The mean age of informal caregivers was 41 years (SD 9.54 years). Annual household income for each informal caregiver varied, with a panelist reporting an income less than US$ 25,000, another

reporting US$ 25,000-US$ 49,999, and another reporting US$ 50,000 or more. Two informal caregivers indicated they had never been married, and 1 was currently married or widowed.

Clinicians

Thirty-seven clinicians working at the university where the research took place were eligible to serve as panelists, but 2 clinicians could not be reached via email. Of the 35 clinicians who were successfully contacted, only 2 (retention rate, RR, 6%) agreed to participate. All clinician panelists were men (mean age 36.50 years, SD 12.02 years). One clinician identified as being white, and the second clinician noted his race as "other."

Research Scientists

Seventeen research scientists from the university where the research took place were eligible to serve as panelists, but 1 researcher could not be reached via email. Of the 16 researchers who were successfully contacted, 6 (RR 38%) agreed to participate. There were an equal number of female (n=3) and male (n=3) research scientists (mean age 38 years, SD 6.48 years). Research scientists identified as being white (n=5, 83%) and non-Hispanic (n=6, 100%).

Unidentified

Three panelists (8%) either did not want to disclose their stakeholder role or did not select one of the available stakeholder group options. Panelists who did not associate with one particular group reported a mean age of 50.33 years (SD 1.53 years), and identified their race/ethnicity as white (n=2, 33%), black or African American (n=1, 17%), Hispanic/Latino (n=1, 17%), other (n=1, 17%), or missing (n=1, 17%). All panelists in this group reported an annual household income less than US$ 25,000.

Study Drop Out

Eight panelists who completed the first-round survey did not complete the third-round survey. Study drop out was observed among all stakeholder groups: patients (n=2), informal caregivers (n=1), clinicians (n=1), and research scientists (n=2). A greater number of women (n=4) dropped out as compared with men (n=2). The highest dropout rate was observed among those who identified as white (n=5). Panelists reporting 1 year of college education or more (n=5) dropped out more often than panelists with other education levels. Most panelists who dropped out reported annual household incomes less than US$ 25,000 (n=6).

Panelist Responses

First- and Second-Round Surveys

Of the 189 stakeholders representing all groups who were successfully contacted about participating on the virtual panel, 37 completed the first-round survey (RR 20%). Table 4 lists the mean (SD) ratings for each care coordination topic evaluated in the first and second rounds (1=strongly disagree, 7=strongly agree), with the corresponding percentage of panelists "agreeing" or "strongly agreeing" that the COPD care coordination topic was important to study using CER methods.

In the first-round survey, all care coordination topics received mean importance ratings of 6 or higher. "Measuring hospitalization risk," received the highest mean rating (mean 6.55, SD 0.67), with over 90% of panelists (n=35) agreeing that this topic was important to investigate in future CER. Over 90% of the panelists also agreed that 4 other topics were especially important areas for future CER: "management of COPD with other chronic conditions" (n=35, mean 6.54, SD 0.61), "pulmonary rehabilitation as a model for care in COPD" (n=34, mean 6.47, SD 0.60), "quality of care coordination" (n=34, mean 6.54, SD 0.65), and "measurement of quality of care" (n=34, mean 6.43, SD 0.96). The care coordination topic that received the lowest mean rating was "patient-centered medical home" (mean 6.29, SD 1.00). As much as 72% of panelists (n=27) agreed that this topic was important to investigate.

Thirty-five of the 37 original panelists completed the second-round survey (RR 95%). As was the case in the first-round survey, all 10 care coordination topics received mean importance ratings above 6. In the second-round survey, "comprehensive COPD patient education" received the highest mean rating (mean 6.65, SD 0.81), with 91% of panelists (n=32/35) agreeing that this topic was important to investigate in future CER. Two other topics were also highly rated by a majority of panelists (≥88%; n=31/35): "pulmonary rehabilitation as a model for care in COPD" (mean 6.45, SD 1.12) and "quality of care coordination" (mean 6.39, SD 1.36). Interestingly, the topic, "management of COPD with other chronic conditions," which was highly rated in the first round, scored lowest on perceived importance in the second round (mean 6.14, SD 1.44); however, over 85% of the panelists (n=30/35) agreed that this topic was important to study in future CER. Conversely, less than 80% of panelists agreed that "measuring hospitalization risk" (n=24/35) and "patient-centered medical home" (n=26/35) were important topics. Because consensus agreement was not reached on the importance of these 2 topics, panelists were not asked to evaluate either of these topics in the round-three survey.

Table 4. First- and second-round survey ratings for chronic obstructive pulmonary disease care coordination topics.

COPD care coordination topic[a]	Round one (N=37)		Round two (N=35)	
	Mean (SD)	Consensus agreement n (%)[b]	Mean (SD)	Consensus agreement n (%)[b]
Management of COPD with other conditions	6.54 (0.61)	35 (94)	6.14 (1.44)	30 (85)
Pulmonary rehabilitation	6.47 (0.60)	34 (91)	6.45 (1.12)	31 (88)
Depression and mental health management	6.38 (0.76)	33 (89)	6.44 (0.70)	30 (85)
Quality of care coordination	6.54 (0.65)	34 (91)	6.39 (1.36)	30 (85)
Measurement of quality of care	6.43 (0.96)	34 (91)	6.46 (0.78)	31 (88)
Comprehensive COPD patient education	6.50 (0.77)	32 (86)	6.65 (0.81)	32 (91)
Cost effectiveness of care	6.54 (0.78)	31 (83)	6.53 (0.71)	30 (85)
Case management	6.34 (0.84)	31 (83)	6.36 (1.14)	29 (82)
Measuring hospitalization risk	6.55 (0.67)	30 (81)	6.33 (0.89)	24 (68)
Patient-centered medical home	6.29 (1.00)	27 (72)	6.18 (1.07)	26 (74)

[a]Chronic obstructive pulmonary disease

[b]Consensus agreement was calculated by reporting the percentage of stakeholders who selected either 6 (agree) or 7 (strongly agree) on the 7-point Likert scale when evaluating each COPD care coordination topic.

Third-Round Survey

Twenty-nine participants completed the final third-round survey (RR 78%). Table 5 lists the mean (SD) importance rankings (1=most important, 8=least important) for the 8 remaining topics that received the greatest panelist support in the first 2 survey rounds. "Measurement of quality of care" (mean 2.73, SD 1.95) was ranked as the most important care coordination research topic to investigate in future CER. Other highly rated topics included the following (in order of importance with lower mean scores indicating greater importance): "management of COPD with other conditions" (mean 2.92, SD 1.67), "pulmonary rehabilitation as a model for care in COPD" (mean 3.73, SD 1.93), "quality of care coordination" (mean 4.12, SD 2.41), and "comprehensive COPD patient education" (mean 4.27, SD 2.38). Care coordination topics with the least amount of panelist support were "cost effectiveness of care" (mean 5.61, SD 2.33) and "case management" (mean 6.00, SD 2.38).

Table 5. Mean (SD) rankings of 8 remaining COPD care coordination topics (n=29).[a]

COPD[b] care coordination topic	Mean (SD)
1. Measurement of quality of care	2.73 (1.95)
2. Management of COPD with other conditions	2.92 (1.67)
3. Pulmonary rehabilitation	3.73 (1.93)
4. Quality of care coordination	4.12 (2.41)
5. Comprehensive COPD patient education	4.27 (2.38)
6. Depression and mental health management	4.62 (2.04)
7. Cost effectiveness of care	5.61 (2.33)
8. Case management	6.00 (2.28)

[a]Topics were ranked from 1 (most important) to 8 (least important).

[b]Chronic obstructive pulmonary disease

Panelists provided 22 type-written comments that described reasons for their final rankings. Almost all of the comments (n=18/29, 62%) discussed the overall importance of strategies for COPD management. One panelist commented,

> Given that comorbid conditions are commonly encountered together, along with a number of other chronic medical conditions and medications, clear

> *management strategies in these types of populations are important.* [Clinician, Male, Age 28]

Patients described difficulty when attempting to manage medications intended to treat multiple health conditions. One patient stated,

> *I believe that if you manage this condition it will help overall with the other situations that one is faced with. I have thyroid disease along with vertigo and COPD.*

Having multiple conditions is very hard to manage; taking more than one medication and the different effects that they can have. [Patient, Female, Age 51]

Panelists from almost all groups also commented on the need to determine the most effective ways to facilitate effective patient-provider communication. Miscommunication between stakeholder groups was cited frequently by panelists (n=20/29, 69%). One panelist who identified as both an informal caregiver and a clinician noted,

It has been my experience as an RN and family caregiver of my parents who both had COPD that there is a lack of communication between medical disciplines and grasp by the medical team of the overall health of COPD patients. [Informal Caregiver/Clinician, Female, Age 42]

One research scientist also observed that

There are so many miscommunications between patients [with COPD] and providers. [Research Scientist, Male, Age 36]

In addition, panelists noted the difficulty experienced by patients and providers in terms of identifying which patient education topics need to be covered with individual patients dealing with various stages of COPD. One panelist noted,

Although all the topics are very important for the care and results of the treatment of COPD, if a patient doesn't understand the basic importance of them, I don't believe they will be as effective. Especially the procedures. [Patient, Female, Age 61]

When panelists were asked about the potential impact of a Web-based stakeholder network devoted to CER in COPD, they noted the importance of accessing results from recent CER studies (mean 2.34, SD 1.19). Patients, informal caregivers, and research scientists all indicated a strong desire to learn from others affected by COPD to build reciprocal trust and communication (mean 2.34, SD 1.19). Most panelists (n=22/29, 76%) also reported that they were likely to visit such a network website at least a few times/month. Panelists perceived their roles/responsibilities for network involvement to be primarily meeting with others interested in COPD (n=19/29, 66%), and suggesting, commenting on, and voting for new CER ideas in COPD (n=18/29, 62%). Finally, more than half of the panel noted the importance of accessing and learning from the following resources: COPD educational videos (n=24/29, 83%), news updates on CER taking place in COPD (n=18/29, 62%), and downloadable CER summaries (n=18/29, 62%). Patients and research scientists primarily requested access to educational videos on COPD care coordination, whereas clinicians preferred having Web access to recent research articles on CER in COPD.

Discussion

Principal Findings

The coordinating capacity of health care settings is often determined by the approaches and coordination activities used to deliver care. Achieving a good fit between coordination needs and coordinating capacity is key for effective and efficient care;

however, the adequacy of fit is perceived differently by different stakeholders who are involved in processes of care at different levels. Traditionally, patients, informal caregivers, and health care providers have different perspectives on health care processes [56]. Yet, patients and informal caregivers are rarely included in the design of studies that test interventions or treatments. Paternalist approaches to research design and analysis often overlook important underrepresented groups who have increasingly requested that their voice be heard when conceptualizing CER relevant to health care problems they perceive to be important [57]. Because stakeholders from these groups are rarely afforded the opportunity to offer insight during both the decision- and priority-making processes for patient-centered health care [26], actively eliciting feedback from these stakeholder groups is becoming essential.

Because of this shift to patient-centered research designs, the primary purpose of this eDelphi study was to use a Web-based structured communication process to connect community-based stakeholders to discuss, generate, and evaluate potential COPD care coordination research topics that can be studied using CER methods. In this study, a team of faculty and clinical staff, in collaboration with research navigators working on behalf of a CEnR program, helped to organize a virtual advisory board consisting of stakeholders that represented 4 different stakeholder groups (patients, informal caregivers, clinicians, and research scientists). Results suggested that measuring quality of care delivered was the most important care coordination topic perceived by members of the virtual advisory board. Quality of care during the care transition process is especially critical for patients with COPD who are often treated for breathing exacerbations in the hospital or emergency room (ER). Often, these patients must proactively maintain pharmacotherapy and rehabilitation regimens based on changes in respiratory and physical condition [10]. In addition, quality of care measurement likely extends outside of primary care and into patients' lives in the community and into linkages between medical practices and specialty clinics, ERs, and inpatient care settings [10]. Identifying measurement of quality of care as a high-priority COPD care coordination topic represents the first step in beginning a continuum of patient-centered outcomes research that will test the comparative effectiveness of alternative approaches to measuring care quality in this patient population. Further development of measurement models will require continued communication and input from stakeholders who will ultimately be affected by the findings from such CER.

The virtual advisory board further commented on the importance of disease management, communication, and education as key components to consider when assessing quality of care. For example, comprehensive patient education was noted to be tied to most all other care coordination topics evaluated. Collaborative patient education and stakeholder communication based on shared objectives were identified as critical to high-quality COPD care coordination both inside and outside of the clinical setting. Specifically, panelists commented on the need to evaluate different self-management education tools that patients could benefit from by successfully coping with the day-to-day challenges they encounter. Direct stakeholder feedback on these important needs can now be used as the basis

for the development and evaluation of care-quality metrics assessing alternative COPD care coordination approaches used in this patient community.

Finally, to facilitate continued communication regarding research priority setting, a follow-up informal needs assessment was conducted following the main study to evaluate stakeholder interest in belonging, and contributing, to a collaborative Web-based community network for advancing CER in COPD. Findings suggested that the existence of a Web-based community would promote stakeholder understanding, engagement, and shared decision making, while building a new social media channel for generating, evaluating, and disseminating CER in COPD. Most panelists reported that they would be willing to regularly participate on a Web-based stakeholder engagement network to provide feedback on how to improve CER methods in COPD and review research summaries on the latest CER findings in COPD. This feedback will now be used to shape the purpose, scope, and function of the proposed Web-based stakeholder engagement infrastructure.

Comparison With Prior Work

Previous research suggests that organizations often fail to capitalize on stakeholder engagement opportunities by only fostering one-way communication [58,59]. The current eDelphi study highlighted that user-friendly, survey technology can enable patients to become active contributors and partners throughout the CER process, especially during the development of study materials, data collection, and dissemination of research findings. Furthermore, the use of a Web-based stakeholder engagement platform helped to ensure that CER topics were communicated clearly and accurately in a manner conducive to understanding [60]. Results from this small-scale stakeholder engagement study shared some similarities with results of previous research conducted nationally in the United States. Krishnan and colleagues [20] reported the following COPD care coordination topics as being highly ranked by representatives of multiple stakeholder groups: (1) management of COPD with other chronic conditions; (2) pulmonary rehabilitation as a model for care in COPD; (3) depression and mental health management; (4) measurement of quality of care; and (5) quality of care coordination. In this eDelphi study, these topics were also rated highest in priority; however, measurement of quality of care was identified as the highest priority topic in this patient population. One exception was "depression and mental health management," which was ranked just outside of the top 5 highest priority topics in this study. However, several panelists in this study commented on the worry and anxiety that patients experience due to their shortness of breath, which can often be mitigated by greater psychiatric care coordination and social support.

Similar to prior research [20], our prioritization study also identified "comprehensive COPD patient education" among the highest ranked topics. Many panelists submitted comments on the importance of patient education in care coordination for COPD. The need for comprehensive patient education resources that help patients and their informal caregivers manage the symptoms and treatments associated with obstructive lung disease has been emphasized in the literature. One qualitative study by Holland and colleagues [61] explored the content of education in pulmonary rehabilitation through semistructured interviews with patients diagnosed with interstitial lung disease. In their qualitative study, many patients emphasized the value of patient education, yet stated the education they generally received was often not applicable to their specific condition. Patients described the need for tailored symptom- and condition-specific education that was often missing in their treatment and action plans. Many panelists in our study confirmed that lack of communication is common among patients and providers, particularly with regard to access and use of inhalers and breathing medications.

COPDFlix CER Network

A recent systematic literature review by Moorhead and colleagues [62] suggests there are several overarching benefits to using social media to reach patients, health professionals, and the general public for health care purposes. These benefits include (1) increased interaction; (2) more information that is available, shared, and tailored; (3) greater health information accessibility; (4) enhanced instrumental support at the peer, social, and emotional levels; and (5) the potential to influence health policy. Through the utilization of CEnR methods, Stellefson and colleagues [63] consulted with experts in health ICT to create the COPDFlix Social Media Resource Center, which was codesigned with medically underserved patients living with COPD, who experience low computer literacy [64]. The purpose of this Web-based stakeholder engagement network is to disseminate knowledge on COPD self-management, and strengthen COPD research collaborations at multiple ecological levels [65]. Using the feedback received from stakeholders during this eDelphi study, our research team built on the existing COPDFlix social media website to create the technical infrastructure for the COPDFlix CER Network. It is expected that this additional Web-based community engagement center will include CER collaborations in COPD with diverse stakeholders including patients and informal caregivers. At present, the site displays a stakeholder-orientation video describing the intended purpose of the network (Figure 3) along with selected COPD care coordination/CER videos evaluated by the virtual advisory board members in this study (Figure 4).

On the network home page, users can click on videos uploaded using the YouTube media player that describe the 5 most important care coordination topics as rated by panelists in our study. Users are also able to post and respond to comments regarding the video content using textboxes attached to each video. Figure 4 shows a screenshot of one of the care coordination topic videos that users can rate (like/dislike), share, and comment on by signing into the network home page. Based on suggestions provided by the virtual advisory board, the COPDFlix CER Network is being used to post relevant educational videos, research articles, and news reports on CER in COPD. By uploading discrete videos on various care coordination topics, we foresee opportunities for continued stakeholder engagement around selected CER questions of interest. Further development of the COPDFlix CER Network will enable researchers to post available research opportunities, involve representatives from multiple stakeholder groups, and disseminate results from CER studies in COPD to the public

at-large. Translating results from this study into the development   next step to advance patient-centered CER in COPD.
of specific study designs and research proposals is an important

Figure 3. Screenshot of prototype version of the COPDFlix CER Network home page.

Figure 4. Screenshot of care coordination topic video and user comment box on COPDFlix CER Network page.
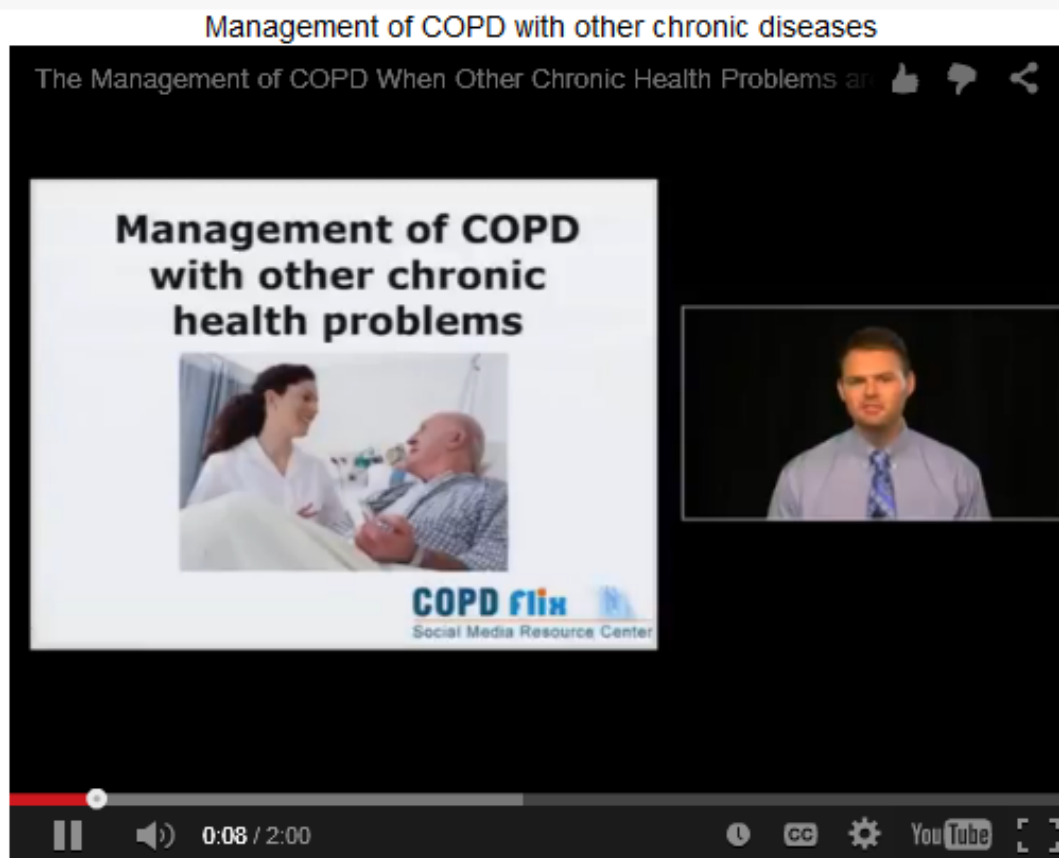
Limitations

Low initial response rate was one limitation of this study, with only 37 of 189 contacted (20%) stakeholders participating on the virtual panel. Reasons for the low response rate included

the following: (1) lack of patient access to a computer; (2) low knowledge on how to use a computer; and (3) time constraints. While the use of only 1 CEnR program for recruitment may have limited the total number of respondents, the focus of this study was on gathering opinions from community-based

stakeholders who could potentially be involved with the development and evaluation of CER proposals in COPD. Adding a paper-based alternative for the round-by-round questionnaires may have increased the response rate from patients and informal caregivers. In addition, the use of Web-based surveys may have limited the generalizability of findings to only those medically underserved patients with computer access and experience. However, it is important to note that several patients were able to travel to the CEnR program headquarters and complete the Web-based survey in their computer laboratory with assistance from program staff. The low initial response rate for this research priority-setting study highlights the need for future Web-based stakeholder engagement research within low SES populations. This type of research would benefit from incorporating computer and Internet literacy trainings prior to and during all research-related activities.

Few informal caregivers (n=3) were enrolled into the study at any point in time, which we attributed, in part, to the snowball sampling referral method used to recruit stakeholders from this group. Informal caregivers could not be contacted directly by research navigators affiliated with the CEnR program, because of patient privacy risks and the potential for informal caregivers feeling coaxed into participation. In addition, several individuals living with COPD felt that they did not need assistance from a family member or friend to manage their COPD, and therefore, they reported having no informal caregivers. Future studies seeking input from informal caregivers may benefit from using alternative sampling methods and seeking out members from informal caregiver registries operated by local/regional health care agencies and organizations.

Similarly, few eligible research scientists (n=6) agreed to participate on the virtual panel. Initial panel recruitment occurred primarily in the summer months, which may have conflicted with the regular academic calendar (fall/spring) for some researchers. Clinicians were the least represented stakeholder group on the panel, with only 2 of the 35 clinicians agreeing to serve as a panelist. Potential reasons for the very low response rate among clinicians may have included lack of time, interest, and limited incentive for participation (US$ 45 gift card). Because of the nonrandom and very small samples in several stakeholder groups, findings from this study may not be representative and generalizable to the populations they represent. Nevertheless, the purpose of this Web-based stakeholder engagement study was to establish the validity and reliability of using the eDelphi technique to generate CER priorities in a community where previous research has not been conducted, and therefore, our methodological emphasis was appropriately on maximizing internal validity versus establishing external generalizability. Future stakeholder consensus-building effort may benefit from investing more time developing collaborative relationships with key clinician/research scientist gatekeepers (eg, leadership of local medical societies, senior clinicians, chairs of respiratory health departments) prior to study recruitment. Further development of our COPDFlix CER Network is expected to improve stakeholder recruitment effort in future CER studies.

Finally, the expertise of eDelphi panelists (patients, informal caregivers, clinicians, and research scientists) was not uniform.

Stakeholders from different groups likely possessed different levels of knowledge regarding CER and COPD care coordination. Some panelists chose not to identify their stakeholder group affiliation, because they may have felt uncomfortable providing this information in this university-based study. There was also potential for intellectual, financial, and clinical conflicts of interest, which may have biased rankings, especially among research scientists and clinicians. To our knowledge, and as acknowledged by other researchers [20], no standards exist for managing and disclosing potential conflicts of interest when setting CER priorities. The eDelphi technique may be subject to both researcher and subject biases because panelists may change their own opinions to fit their own personal, research, and clinical agendas. Notwithstanding this potential, the collaborative aspect of the eDelphi technique supports acknowledging and considering the perspectives of others to achieve meaningful consensus, which is considered a key strength of this structured communication process [30].

Conclusions

Although engaging representatives of diverse stakeholder groups is feasible and can be used to identify support for CER topics in COPD [20], engaging individuals who actually belong to important stakeholder groups is sometimes overlooked. Patients from medically underserved communities are rarely afforded the opportunity to provide feedback on compliance with intervention protocols and experimental treatments. This study effectively used the eDelphi method to engage medically underserved patients to identify community-specific priorities in COPD care coordination. The inclusion of low-income, traditionally underrepresented patients with COPD provided a myriad of perspectives, which helped to identify care coordination topics that may have been overlooked with a typical homogeneous panel. Identification of measurement of quality of care coordination should be viewed as a preliminary finding to structure both Web-based and offline discussions regarding future CER proposals/protocols. Moreover, future CER in COPD care coordination should incorporate measurement mechanisms for care coordination activities and approaches, which can positively impact patients, their families, health care professionals, and the overall health care system.

Effectively engaging patients with COPD from various racial, ethnic, aged, and low-resourced backgrounds is important during all stages of the CER process (eg, planning, data collection, choice of intervention, analysis of results, and implementation of findings into clinical practice). Findings from this study support the need to conduct more CER that explores whether the use of eHealth and social media represents an acceptable and effective way to engage low-income and racial/ethnic minority populations for CER in COPD. Web-based stakeholder networks have the potential to engage more stakeholders and improve the study of COPD care coordination using CER methods. Future studies would benefit from collecting more robust data from larger, more representative samples of community-dwelling stakeholders interested in improving COPD care.

Conflicts of Interest

None declared.

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Abbreviations

CEnR: community engagement and research
CER: comparative effectiveness research
COPD: chronic obstructive pulmonary disease
ER: emergency room
ICTs: information and communication technologies
RR: retention rate
SES: socioeconomic status

Original Paper

Designing an Internationally Accessible Web-Based Questionnaire to Discover Risk Factors for Amyotrophic Lateral Sclerosis: A Case-Control Study

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Abstract

Background: Amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disease with a typical survival of three to five years. Epidemiological studies using paper-based questionnaires in individual countries or continents have failed to find widely accepted risk factors for the disease. The advantages of online versus paper-based questionnaires have been extensively reviewed, but few online epidemiological studies into human neurodegenerative diseases have so far been undertaken.

Objective: To design a Web-based questionnaire to identify environmental risk factors for ALS and enable international comparisons of these risk factors.

Methods: A Web-based epidemiological questionnaire for ALS has been developed based on experience gained from administering a previous continent-wide paper-based questionnaire for this disease. New and modified questions have been added from our previous paper-based questionnaire, from literature searches, and from validated ALS questionnaires supplied by other investigators. New criteria to allow the separation of familial and sporadic ALS cases have been included. The questionnaire addresses many risk factors that have already been proposed for ALS, as well as a number that have not yet been rigorously examined. To encourage participation, responses are collected anonymously and no personally identifiable information is requested. The survey is being translated into a number of languages which will allow many people around the world to read and answer it in their own language.

Results: After the questionnaire had been online for 4 months, it had 379 respondents compared to only 46 respondents for the same initial period using a paper-based questionnaire. The average age of the first 379 web questionnaire respondents was 54 years compared to the average age of 60 years for the first 379 paper questionnaire respondents. The questionnaire is soon to be promoted in a number of countries through ALS associations and disease registries.

Conclusions: Web-based questionnaires are a time- and resource-efficient method for performing large epidemiological studies of neurodegenerative diseases such as ALS. The ability to compare risk factors between different countries using the same analysis tool will be of particular value for finding robust risk factors that underlie ALS.

Introduction

Amyotrophic lateral sclerosis (ALS, also known as motor neuron disease or MND) is a progressive neurodegenerative disease of adults with a usual survival of three to five years after diagnosis [1]. Epidemiological studies using traditional methods of collecting data via mailed paper questionnaires or via telephonic or in-person interviews have so far not revealed any widely accepted environmental or lifestyle risk factors for ALS.

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Previous epidemiological studies of ALS have had a number of limitations. ALS has an incidence of about 2-3 per 100,000 in most populations, so it is not a common disorder and obtaining large numbers of respondents has been difficult [2]. No intercountry comparisons of risk factors for ALS using the same survey tool have been undertaken. Restricting the geographical region of recruitment to one country or continent prevents identification of risk factors that vary across countries [3] or ethnic groups. As new criteria to classify ALS into its sporadic and familial forms are proposed, changing diagnostic criteria will make characterisation of cases in previous studies difficult [4]. In addition, new potential environmental risk factors for ALS are continually being proposed, but it is inconvenient to add questions to non-Web surveys.

We became aware of these and other limitations of paper-based questionnaires during the course of an Australian study looking for risk factors for sporadic ALS. Despite this being a continent-wide survey undertaken over 11 years (2000-2011) with active recruitment of participants by state-based ALS associations, responses were obtained from only 812 ALS patients and 793 nonrelated controls in a population of 23 million people. Although this remains one of the largest epidemiological case-control databases in ALS with several publications arising from the study [2,3,5-10], numbers were too small to analyse subgroups in many categories, such as those for less common occupations. The majority of respondents were English-speaking and of western European descent although people from many language groups live in Australia (some of this bias can be explained by the questionnaire being available only in English). The criteria we used for separating familial and sporadic ALS are under revision, and many of the patients we classified as having familial ALS would now be considered to be in the sporadic group [4]. The financial cost to obtain and process information was high and when funding for staff and consumables came to an end, the survey had to close. We did not ask questions about topics such as psychiatric conditions since the respondents had to identify themselves, and this understandably would have made many reluctant to give out such information.

Many of the limitations experienced during our paper-based study have been overcome by migrating to an online questionnaire, where respondents are not asked for personally identifiable information. Our Web-based questionnaire can be easily translated into other languages for both reading and answering questions, which will aid recruitment and allow for international comparisons of risk factors. We describe our approach to designing this online questionnaire to look for risk factors in ALS and present the initial responses to this survey. We also summarise the advantages and disadvantages of Web-based versus paper-based questionnaires as they pertain to looking for risk factors for neurodegenerative diseases.

Methods

Questionnaire Software

Questionnaire platforms from a number of providers were evaluated as potential sources of Web-based survey software. Most offered user-friendly survey design, secure storage of respondent data, an online log-in portal that allows users to access the survey from any Internet browser, and the ability to download survey data in several formats. Qualtrics [11] was identified as a good platform for our project because it is flexible and provides a large diversity of question types.

Questionnaire Design

Overview

Relevant questions from our original paper-based ALS questionnaire were entered into the Qualtrics platform using the appropriate question formats (see Multimedia Appendix 1 to view the original paper-based questionnaire). The design of our online questionnaire was based on recent recommendations of best practice in this field [12-14].

Pay Careful Attention to the Wording of Questions to Ensure Clarity

Our experience with our previous paper-based questionnaire was helpful in identifying types of questions that tended to result in ambiguous answers.

Use Predetermined Choices to Ensure Standard Answers

For example, questions requiring a written answer in a paper-based questionnaire (eg, "In which country are you currently living?") can be formatted as a single-choice drop-down menu in a Web-based format. The number of answers requiring text entry, which can cause transcription difficulties and delay access to the data, was reduced to a minimum in the online questionnaire.

Place Questions Into Topic Groups

The online questionnaire is organised according to topics of interest (eg, occupation, exercise). This improves coherence of the questionnaire, and it also allows easier topics to be placed towards the beginning of the survey to increase respondents' confidence about entering data into the questionnaire.

Use Automated Question Logic

Question logic shows or skips certain questions based on previous answers. This relieves respondents of the responsibility of following the logic of a paper-based questionnaire, and ensures they only need view questions that apply to them. Question logic largely eliminates commission errors (ie, answering questions that are not applicable) and omission errors (ie, not answering questions that are applicable) [14]. Question logic applies to about 25% of our online questions.

Avoid Use of a Progress Bar

A progress bar, which shows respondents how far into the survey they are, was not used. First, a progress bar would have been misleading because it does not take into account the show/skip logic within the questionnaire. Second, a progress bar is not recommended on longer surveys because it discourages completion [14].

Access for Patients With Physical Disabilities

Access to the questionnaire was a concern given that respondents with ALS could have limited mobility. We therefore ensured the questionnaire is compatible with speech-to-text programs

and spoken commands. To aid visibility, we set the default font size at 12 point, made the text of all questions in bold font, and implemented a software feature that highlights the question being worked on.

Access in Different Languages

We plan to translate the questionnaire into many languages, including all languages spoken in countries within the International Alliance of ALS/MND Associations. Respondents will select their preferred language from a list of available translations before entering the questionnaire. For text entry, respondents will be able enter answers in their own language. Since only a few questions are answered by entering text, translations to English will not be onerous.

Google Translate is used to perform the first rough translation of non-English languages, but fluent speakers of both English and the language to be translated need to spend many hours amending this to obtain the correct meaning and grammar in the text, based on the English version. For example, in our question about skin color, the word *fair* in most languages is translated as *reasonable* rather than the intended meaning of *light in color*. Qualtrics has a function in which the English and Google-translated non-English version of the questionnaire can be presented side-by-side, so the translator can readily edit the non-English version with reference to the meaning in the English version.

We have chosen first to check and adjust the translation of simplified Chinese, one of the languages where Google Translate appears to give the greatest number of ambiguities. Fluent speakers of other languages are in the process of checking other Google translations. The Google-translated languages that have been checked for accuracy (only simplified Chinese at the time of manuscript submission) will be indicated in the language list as available translations.

New Content in the Web-Based Questionnaire

General

The content of our paper-based questionnaire was compared to the Stanford University ALS Consortium of Epidemiologic Studies (ACES) questionnaire [15], and questions were added or modified on topics such as alcohol and tobacco use, medical history, hobbies and pastimes, and pesticide and chemical exposures. The differences in our paper- and Web-based questions can be viewed by comparing the paper-based questionnaire in Multimedia Appendix 1 and the online questionnaire [16].

Defining Familial Versus Sporadic ALS

Controversy persists as to the definition of familial versus sporadic (or isolated) ALS, with some clinicians classifying a patient as having familial ALS only if close family members also have the disease [4]. Based on studies of the heritability of familial ALS, the questionnaire now asks for the number of first-, second-, and third-degree relatives as well as more distant relatives who have ALS [4,17,18]. It further asks for the total number of first-, second-, and third-degree relatives in the respondent's family overall, since the familial nature of a disease is harder to detect in a small family. Having this detailed family history will allow researchers who have access to our survey data to use their own criteria to define familial and sporadic ALS.

Dementia

Questions are now asked about the number of family members diagnosed with frontotemporal dementia (FTD), a recently recognised component of an ALS/FTD disease continuum [19]. This will allow our study to identify families where one member has ALS while another has FTD.

Genetic Variants

We now ask whether any ALS patient or relative has been identified as having a genetic variant associated with ALS. We do not ask respondents to identify the particular genetic variant since rare variants could constitute personally identifiable information.

ALS Functional Status

People with ALS are asked to complete the ALS Functional Rating Scale (ALS-FRS) [20] to assess their physical state at the time of taking the questionnaire. This will allow an assessment of the rate of progression of the disease, which can be calculated from the time of disease onset. A Web-based format for the ALS-FRS has previously been validated by comparing Web and in-person evaluations [21].

Physical Activity

To evaluate physical activity, which has been suggested to be a risk factor for ALS [22], questions were obtained from surveys used by the European Amyotrophic Lateral Sclerosis Consortium (EURALS) [23] and the European Multidisciplinary ALS Network Identification to Cure Motor Neuron Degeneration (Euro-MOTOR) [22].

Ratio of Finger Lengths

The ratio between the length of the ring finger and index finger, associated with prenatal exposure to testosterone, has been implicated as a risk factor for ALS [24]. A diagram has been included to show respondents how to perform and report these measurements (Figure 1). The reliability of these self-reported finger measurements is currently being investigated by photographing 100 volunteers' hands and comparing their own finger measurements with measurements by researchers using the photographs.

Figure 1. This diagram in the questionnaire shows respondents how to measure the length of their index and ring fingers. Below the question, boxes are provided (not shown) for respondents to select the measurements from a drop-down menu.

Please measure the lengths of your index (second) and ring (fourth) fingers on each hand. The diagram below shows you how to make the measurements.

If you can only straighten out the fingers on one hand, only record the measurements for that hand.

If possible, please take off any rings prior to measuring your fingers.

First lay the back of your hand out flat on a level surface, with your fingers together. Then, with a rigid millimetre ruler (not a tape measure), measure from (1) the tip of the finger to (2) the middle of the crease at the bottom of the finger. The ring finger often has two of these creases, so here measure from the crease that is closest to the wrist.
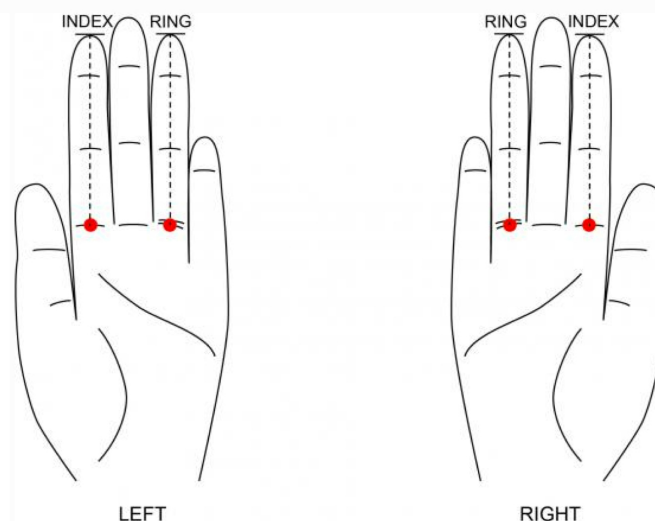
Male Pattern Baldness

It has been suggested that men with early-onset alopecia have a higher risk of ALS [25]. We therefore included a question used by the Physicians' Health Study in which men estimate the pattern of any hair loss they may have had when they were 45 years old by selecting one of 5 images ranging from no to marked hair loss [26,27].

Head Trauma

Head trauma has been implicated as a risk factor for ALS [28]. To gauge a history of head trauma, we added questions from the Retrospective Screening of Traumatic Brain Injury (RESTBI) Questionnaire [29].

Sun Exposure

Vitamin D deficiency has been implicated as a factor in ALS [30]. In most countries, sun exposure is the main source of vitamin D [31], but assessing sunlight exposure over long periods of time with a questionnaire is difficult [32]. We therefore asked about two aspects of sun-induced vitamin D generation, skin color and the reaction of the skin to sunlight, as used in the NSW Prostate Cancer Care and Outcomes Study [33].

L-BMAA

Because of the interest in a possible connection between the environmental toxin β-N-methylamino-L-alanine (L-BMAA) and ALS, we included questions related to L-BMAA exposure based on the French BMAALS program questionnaire [34].

Stress

Stress has been suggested as a potential risk factor for ALS [35]. Our questionnaire asks systematic questions about stress as a risk factor for the disease. To assess lifetime stress we used the Social Readjustment Rating Scale which scores the stress associated with a variety of events [36]. To evaluate the likely impact these stressors would have had on respondents, we used the Big Five personality traits assessment [37-39], the Connor-Davidson Resilience Scale [40], and the Geriatric Anxiety Inventory [41,42]. A Web-based administration of a scale similar to the Geriatric Anxiety Inventory has been validated by comparing Web and telephone interview surveys [43].

Diagnosis of ALS

On our previous paper-based questionnaire, we asked neurologists of ALS patients to send us copies of their clinical notes so that the type of ALS the respondent had could be assessed (there are four major types of the disease). This required a consent form specific to Australia, and individual neurologists around the country had to be contacted. No response was received from neurologists for about 15% of respondents, whose questionnaire data could not then be used. Since we designed the current questionnaire to be used for international comparisons of ALS risk factors, a direct approach to neurologists in different countries was not ethically feasible. On the online questionnaire, we therefore ask ALS patients to choose which type of ALS they have been diagnosed with from a predetermined list, and ask them to contact their neurologist or family doctor if they are unsure about the type.

Avoidance of Culturally Specific Questions

All questions were checked for content that could cause misunderstandings in different countries and cultures. We avoided questions that relate specifically to cultural or environmental aspects of any country.

Information for Participants

Text providing information for participants (administrative details about the questionnaire), comprehensive instructions (how to complete the questionnaire), and guidelines (tips for using the questionnaire) appear after respondents access the questionnaire. Respondents then need to answer a few questions before being able to fully access the questionnaire. Respondents are asked to select age, gender, and whether they have ALS. They are asked to describe their connection to ALS if they do not have the disease. If they have a friend or partner with ALS, respondents are asked to list the length of the relationship. Last, respondents are asked how they heard about the questionnaire. After these are answered, an online consent form is displayed; once this is completed, respondents enter the main body of the questionnaire. All other questions are voluntary, but if a question is not able to be answered there is usually an option to explain why (eg, not applicable).

Pairing of Cases and Matched Controls

ALS patients are asked to nominate (if available) a spouse/partner and friends to complete the questionnaire. ALS patients create a unique code and provide it to their spouse/partner and friends. The code is then used to link the ALS patient to these matched controls. This enables paired statistics to be performed on people who are likely to have similar environmental exposures; these statistics will be used for comparisons with nonmatched controls. The code does not allow participants to view other responses.

Questionnaire Distribution

Qualtrics provides two means by which a questionnaire may be distributed: via an anonymous link or via an email invitation with a link specific to each respondent. We chose the anonymous option to maintain participant confidentiality. The questionnaire does not ask for any personally identifiable information such as name, email address, employer name, or exact locations lived. This preserves the anonymity of respondents, which is important considering the sensitivity of some of the data (eg, psychiatric history) being collected. In addition, the anonymous option allows distribution of the questionnaire to a wide international group of potential respondents.

Recruitment of Participants

People both with and without ALS are being sought to complete the questionnaire. The only exclusion criterion is being under the age of 18 years, so there is little possibility for confusion about eligibility criteria. ALS patients in Australia are recruited via newsletters, Facebook pages, and meetings of ALS associations in each state. Nonmatched controls are recruited in particular among community groups such as Rotary International. In the United States, participants are recruited through the government-funded National ALS Registry at the Agency for Toxic Substances and Disease Registry (Centers for Disease Control and Prevention), which has been used by other researchers to recruit participants for ALS online epidemiological surveys [44]. Participants in other countries will be recruited through their respective national ALS associations with the assistance of the International Alliance of ALS/MND Associations.

Data Collection and Storage

Responses to the questionnaire are initially placed on password-protected Qualtrics servers in the countries that host these servers. The Qualtrics servers in the United States are used in countries that do not have their own Qualtrics servers. Completed questionnaire responses are downloaded and transferred from the Qualtrics server into Excel (Microsoft Corporation) and SPSS (IBM Corporation) program files on a regular basis. The original responses are deleted from the Qualtrics servers every six months. Questionnaire responses are kept in a password-protected file on a password-protected computer at the University of Sydney. This computer is connected to Wi-Fi only via password-protected networks.

Results

Cases and Controls

Major groups in the study comprise those who have been diagnosed by a neurologist as having ALS (cases), spouse/partners and friends of people with ALS (matched nonrelated controls), blood relatives of people with ALS who do not have the disease (matched related controls), and persons completing the survey who do not fall into the other categories (nonmatched controls).

The Online Questionnaire

The questionnaire can be viewed online [16]. Examples of multiple choice questions are shown for Single Choice (Figure 2), Select All That Apply (Figure 3), and Drop-Down Menu (Figure 4) questions. An example of a Side-by-Side question is shown in Figure 5.

Figure 2. Example of a single-choice question. Only one choice of place of birth is allowed.

Which of the following best describes the place you were born?

○ Urban (population greater than 50,000) - Inner City

○ Urban (population greater than 50,000) - Suburb

● Regional centre (population less than 50,000)

○ Rural (non-farm)

○ Rural (farm)

Figure 3. In an all-that-apply question respondents can tick as many answers as they want. In this particular question about occupational exposures there is a possible mix of tick-boxes and script entries.

As part of your occupation, have you ever worked with any of the following? Please check any that apply. If none, select "None of the above" in the last row.

☑ Lead

☐ Mercury

☐ Cadmium

☐ Copper

☑ Other metal/mineral (please specify):

  `nickel`

☐ Other metal/mineral (please specify):

☐ Other metal/mineral (please specify):

☐ None of the above

Figure 4. In these three questions about caffeine consumption respondents pick predetermined answers from drop-down lists.

Caffeine consumption

How often do you have a drink containing caffeine? `2-3 times a week ⌄`

How many drinks containing caffeine do you have on a typical day? `1 or 2 ⌄`

How often do you have five or more caffeinated drinks on one occasion? `Less than monthly ⌄`

Figure 5. A large amount of information about the type, duration, intensity, and category of an activity can be obtained using side-by-side drop-down menus and script entry.

Please list the physical and/or athletic activities you have participated in.

Please categorise the activity as either leisure activity (that is, activity in your own time), recreational organised sport (that is, a competitive unpaid sport), or professional sport (that is, paid sport).

If you have participated in more than 15 activities, please list the ones you participated in for the longest.

	Type of Activity	Description of Activity	Number of Years Participated	Hours per week (estimate)	Intensity of Activity	Indoors/Outdoors
Activity 1	Organised Sport	soccer	15	5	Strenuous	Both Outdoors and Indoors
Activity 2	Leisure Activity	tennis	25	2	Mild	Mostly Outdoors
Activity 3	Professional Sport	swimming	8	20	Strenuous	Mostly Indoors
Activity 4	Leisure Activity	running	30	7	Moderate	Mostly Outdoors
Activity 5						
Activity 6						
Activity 7						
Activity 8						
Activity 9						
Activity 10						
Activity 11						
Activity 12						
Activity 13						
Activity 14						
Activity 15						

Pilot Assessment

Ten people were asked to complete the questionnaire and provide feedback to test the clarity of the questions and the functionality of the questionnaire on multiple Internet browsers and devices. Based on this feedback, we adjusted some of the instructions for completing the questionnaire and edited the wording and format of some questions and choices of answers. In addition, after the survey first went online we received email feedback from some of the first 112 respondents. On the basis of this feedback a few minor changes were made and some questions were added. These changes did not affect the validity of the initial 112 responses.

Acceptance and Initial Uptake of the Questionnaire

After approval from an institutional ethics committee, the questionnaire was placed online on 30 January 2015. Four months later, 379 responses (204 from ALS patients and 175 from controls) had been collected. In comparison, after 4 months we had received only 46 respondents from the same population using our paper-based questionnaire.

Spontaneous feedback via email; verbal feedback at meetings of ALS patients (including those with physical disabilities) and their partners; and comments from scientific and medical colleagues concerning the questionnaire format, its content, and ease of use have been positive. However, because we did not formally ask for this information from all respondents this feedback is not quantifiable.

Respondents report taking about two hours to complete the survey, and some appeared to complete it over multiple sessions.

The majority of respondents so far have been from Australia since recruitment from countries outside Australia is in the initial stages. We will be promoting the non-English language versions of the questionnaire as their Google-translated versions are checked.

Ages of Respondents in the Paper- and Web-Based Questionnaires

The average age of the first 379 respondents to the online questionnaire was 54 years (SD 15, range 18-86) compared to an average age of the first 379 respondents to the paper-based questionnaire of 60 years (SD 11, range 28-90).

Discussion

Advantages of Web-Based Questionnaires in Neurodegenerative Diseases

Large numbers of responses can be acquired at low cost with minimal staff requirements and within a short period of time. This is especially relevant to some of the less common neurodegenerative disorders with short survival periods where traditional survey methods have had difficulty recruiting adequate numbers of respondents. Questions can be added easily when newly proposed risk factors are suggested. New risk factors for neurodegenerative diseases are continually being proposed, and with the advent of next generation DNA sequencing, the search for gene-environment interactions underlying these diseases is likely to accelerate. Automatic transfer of response data into database, spreadsheet, and statistics programs virtually eliminates the possibility of transcription errors and speeds up the data analysis. It also reduces the cost

of running these surveys so they can be operated for longer periods, an important consideration when recruiting respondents with rare diseases. Other advantages of Web-based questionnaires have been well documented [45-49].

Studies Comparing Online Versus Other Survey Modes

A review of 29 studies with a combined total of more than 15,000 respondents comparing different survey modes (postal mail, fax, email, and Web-based surveys) reported that Web-based surveys provided a better quality of response, greater level of detail, and greater compliance in answering open-ended questions than mail surveys [50]. The authors calculated similar response rates for the Web-based (52%) and mailed (51%) modes but found that average response times for Web surveys (7 days) were shorter than for mail (17 days). A population survey of 3148 Danish parents concerning their children's health and welfare found similar response rates comparing paper, paper with Web option, Web-only, and Web with incentive formats [51].

The Black Women's Health Study of 59,000 African-American women reported that Web-based surveys were filled out more completely than paper surveys and cost only 25% of paper surveys. Web-based response rates were greatest for younger age groups [52]. In the French NutriNet-Santé study of lifestyle and health, 94% of 147 volunteers stated a preference for the Web-based over the paper version [53]. Furthermore, this study found that the Web-based version prevented the omission of approximately 2% of answers (more than 550 values), which increased the value of each response. It also noted the cost benefits of the Web-based approach.

These studies demonstrate that Web-based surveys are as effective or better than other modes in garnering survey responses and obtaining sound data. These findings largely address the fundamental concerns of maintaining data validity and obtaining sufficient numbers of responses raised when making the decision to migrate to a Web-based platform.

Online Surveys in Epidemiological Research

Despite results showing that Web-based questionnaires are as good or better than other survey modes, the field of epidemiological research has been slow to adopt Web-based methodology. A meta-analysis of epidemiology-related publications in seven high-impact general medical and epidemiological journals in 2008-2009 found that only 1% had used any form of Web-based data collection, while interviews were used in 28% and paper-based questionnaires in 29% (some used multiple formats) [45]. There is therefore potential for growth in the use of Web-based data collection tools for epidemiological purposes. The migration to Web-based questionnaires is likely to increase as a growing proportion of the population gains Web access. For example, World Bank data show that 83% of Australian and 46% of Chinese populations now use the Internet [54].

Online Surveys in ALS Research

There appears to be only one other Web-based epidemiological study of ALS [44]. In that study, ALS patients who had enrolled electronically with the US National ALS Registry were recruited via email. Inclusion criteria were a diagnosis of ALS confirmed by a physician, knowledge of English, residence in the United States for at least 10 years, and age 21 years or older. Exclusion criteria were having also been diagnosed with Parkinson disease, parkinsonism, Alzheimer disease, dementia, poliomyelitis, or post-polio syndrome or having a family member with ALS. From the 2232 emails sent, completed surveys were received from 256 respondents who fulfilled the eligibility criteria, an enrollment rate of 11.5%. Among the topics covered in the survey were lifetime occupational history, occupational exposures, residential history, hobbies, physical activity, and military history.

We have also been given permission to recruit ALS patients from the US National ALS Registry. It will be of interest to compare our enrollment rate with that of Malek et al [44] since we have fewer exclusion criteria. Also, because our questionnaire is anonymous we predict more people will feel comfortable supplying personal information about themselves.

Limitations of a Web-Based Questionnaire

Nonresponse Errors

A major concern in any survey is that the responses received are not representative of the population sampled (ie, nonresponse errors). It has been noted that the demographics of Internet users differ from the general population in that they tend to be younger and more educated [46,47]. However, one study that examined computer literacy and educational status among Web survey participants found that a substantial portion of their respondents considered themselves inexperienced in computer and Internet skills, and that those with less education were more accepting of the burden of completing an Internet survey [34].

A review of 11 Web-based surveys of people aged 65 years or older found that limitations for this age group were similar to those among all age groups [55]. One of the studies included in this review found that the mean age of Web-based participants (70 years) was lower than the age of face-to-face respondents (81 years) [56]. In our study, the average age of Web-based respondents (54 years) was slightly younger than that of paper-based respondents (60 years). This may imply some preference for the Web-based questionnaire among younger people, but direct comparisons between respondents in these two questionnaires are difficult to make. In our paper-based questionnaire, for example, all respondents also had to give a blood sample, which may have discouraged some younger people from participating.

Of note in our study, respondents are likely to be in the 40 to 70 year age group since this is the typical range for ALS. Therefore, age and educational status are unlikely to substantially limit participation in our Web-based questionnaire. We think that nonresponse error for our questionnaire will be minimal since most respondents are likely to have a strong interest in the subject.

Concerns About Safety of Personal Information

As with all uses of the Internet, there are concerns about safety and confidentiality of the data provided [45]. Our questionnaire largely circumvents this issue because all data are being

collected as anonymous responses, and our data are secured on password-protected servers and computers.

Inability to Get Further Information or DNA Samples From Respondents

Since we have no identifying details on our respondents, we cannot contact them individually to ask them further questions or to ask for DNA samples to look for gene-environment interactions. However, there are now a number of databases containing large numbers of DNA samples from ALS patients, and should our study find risk factors for ALS, the same factors could be sought from patients who have donated DNA to these registries.

Inability to Obtain Physician Confirmation of Diagnosis

Since the responses are anonymous, we cannot obtain physician confirmation of the diagnosis of ALS or classify the cases using El Escorial criteria [57]. This is unlikely to be a major limitation since most ALS patients are well aware of their diagnosis. For example, of 88 people who self-reported a diagnosis of ALS to the US National ALS Registry, a check of their physician reports identified only 5 (6%) who did not have ALS [44]. We think the accuracy of the self-reporting of ALS diagnosis by our respondents will be improved by requesting them to select which subtype of ALS they have and asking them to contact their physician if they do not know this.

Conclusions

The majority of epidemiological studies have been conducted using paper-based questionnaires, face-to-face interviews, or telephone surveys. The literature now shows that Web-based questionnaires offer many advantages over traditional methods with few drawbacks. Our experience creating an online questionnaire illustrates these advantages. Furthermore, our questionnaire is being translated into non-English languages and opened up to participation worldwide. We hope the data obtained from this project will accelerate our understanding of ALS and lead to the development of effective treatment options and preventative strategies.

Conflicts of Interest

None declared.

Multimedia Appendix 1

The previous paper-based ALS risk factor questionnaire used by the Australian MND DNA Bank. A number of these questions were modified to fit the present online format.

[PDF File (Adobe PDF File), 75KB - resprot_v4i3e96_app1.pdf]

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Abbreviations

ALS: amyotrophic lateral sclerosis
ALS-FRS: ALS Functional Rating Scale
FTD: frontotemporal dementia
MND: motor neuron disease

<u>Original Paper</u>

Collecting and Analyzing Patient Experiences of Health Care From Social Media

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Abstract

Background: Social Media, such as Yelp, provides rich information of consumer experience. Previous studies suggest that Yelp can serve as a new source to study patient experience. However, the lack of a corpus of patient reviews causes a major bottleneck for applying computational techniques.

Objective: The objective of this study is to create a corpus of patient experience (COPE) and report descriptive statistics to characterize COPE.

Methods: Yelp reviews about health care-related businesses were extracted from the Yelp Academic Dataset. Natural language processing (NLP) tools were used to split reviews into sentences, extract noun phrases and adjectives from each sentence, and generate parse trees and dependency trees for each sentence. Sentiment analysis techniques and Hadoop were used to calculate a sentiment score of each sentence and for parallel processing, respectively.

Results: COPE contains 79,173 sentences from 6914 patient reviews of 985 health care facilities near 30 universities in the United States. We found that patients wrote longer reviews when they rated the facility poorly (1 or 2 stars). We demonstrated that the computed sentiment scores correlated well with consumer-generated ratings. A consumer vocabulary to describe their health care experience was constructed by a statistical analysis of word counts and co-occurrences in COPE.

Conclusions: A corpus called COPE was built as an initial step to utilize social media to understand patient experiences at health care facilities. The corpus is available to download and COPE can be used in future studies to extract knowledge of patients' experiences from their perspectives. Such information can subsequently inform and provide opportunity to improve the quality of health care.

KEYWORDS

patient satisfaction; social media; health care; natural language processing; consumer health information

Introduction

In the current era of information technology, patients often post their experiences with health care providers to social media websites, similar to reviews of restaurants or hotels. A 2012 survey by the University of Michigan found 65% of the US population was aware of online physician ratings [1]. Another survey by PwC Health Research Institute in 2013 [2] suggested that

nearly half of all consumers had read health care reviews online and, of those, 68% utilized the information within the review to assist with the selection of their health care provider. The same survey cited 24% of consumers have written a health care review, up from the 7% estimate in a 2011 survey [3].

Besides numerical ratings, the textual content in patient reviews can be a valuable resource for health care providers to improve their services. Data on patient experience is becoming a critical

component in the value-based purchasing program proposed by the Center for Medicare and Medicaid Services (CMS) [4]. In contrast to Press Ganey or Hospital Consumer Assessment of Healthcare Providers and Systems (HCAHPS) [5,6], the peer-to-peer nature of patient reviews on social media websites provides a unique perspective for health care providers to understand patient satisfaction. This study is one of a few which focuses on utilizing online peer-to-peer communications to learn about patient experiences and concerns about health care providers [7,8].

Several researchers have studied online patients reviews [7-20], but most of them analyzed doctors rating website [13-20]. Greaves et al [7] conducted a sentiment analysis study on 6412 online comments about hospitals on the English National Health Service (NHS) website in 2010. They applied machine learning approach to classify reviews into positive and negative classes. In addition, Alemi et al [9] studied 995 online comments at the RateMDs website [21] and showed that real-time satisfaction surveys were possible.

Yelp is a popular social media website that allows customers to share their business experiences with other customers. Previous studies suggest that Yelp can be a reliable source to study patient experiences with health care providers [22]. Yelp has made available an Academic Dataset of the 13,490 closest businesses to 30 universities for researchers to explore [23]. Many methodological papers have been published on analyzing restaurants [24-26] using this data set. However, this data set has yet to be studied in the context of health care.

A PubMed search of "Yelp" resulted in only 3 papers. Kadry et al [17] conducted a study to analyze 4999 physicians' ratings in the 10 most visited websites including Yelp. They found that most patients gave physicians favorable ratings: the average rating was 77 out of 100. Bardach et al [21] found the Yelp ratings correlate well (*P*<.001) with traditional measures of hospital quality (HCAHPS) and suggested that Yelp can be a reliable source to study patient experience. Recently, Butcher [27] reported that health care providers are starting to pay attention to the Yelp ratings. All 3 papers analyzed Yelp ratings but did not utilize the wealth of information contained in the corpus of Yelp reviews.

We addressed this gap by using a corpus of Yelp reviews to characterize patient experience. A "corpus" is a collection of texts presented in electronic form. In this study, we used the Yelp Academic Dataset to construct a corpus of patient experiences. Several natural language processing (NLP) methods and tools were utilized to clean the data and tag the parts-of-speech such as noun phrases and adjectives, and to create parse and dependency trees. A sentiment score for each sentence was also projected and insights from summary statistics of the corpus are presented here.

Methods

We used 26 health care-related categories (examples include hospitals, urgent care facilities, and medical centers) to extract health care related businesses (a list of categories is provided in Multimedia Appendix 1) from the Yelp Academic Dataset. After identifying 6914 reviews, Stanford Core NLP [28] was used to split reviews into sentences. Porter Stemmer [29] was applied to stem each sentence. Stanford Core NLP was further used to produce parse trees and dependency trees for the sentences and part-of-speech tags for each word. Hadoop was used to run the NLP in parallel to create the corpus. Dragoon Tool was used to extract nouns and adjectival phrases [30]. Sentiment score for each sentence were derived using SentiWordNet [31]. In addition, each sentence was tagged to classify whether or not it was negated. The Hidden Markov Model was used in our negation detection tool [32]. By filtering out terms, which appeared <5 times, 7612 words were selected to form a COPE vocabulary list. The COPE vocabulary list was compared with the consumer health vocabulary (CHV) [33] which is the gold standard in this domain. The CHV covers all health topics. The latest CHV of 2011 contains 158,519 words. To identify co-occurring pairs of terms in each review, we tokenized words and then removed stop words. A Chi-square test was conducted and the odds ratio for each pair for each term which appeared at ≥25 times (empirical cutoff) in the corpus was calculated. Finally, a network of the pairs with high Chi-square (>100), significant *P* values (*P*<.05) and odds ratios >1 was built.

Results

Overview

The first observational study of how patients communicate with their peers regarding their health care experiences using the social media website Yelp is presented here. To analyze these communications, a corpus was established and characterized with descriptive statistics.

Corpus of Patient Experience (COPE)

The COPE contains 79,173 sentences from 6914 patient reviews of 985 health care facilities near 30 universities in the United States. The top 10 cities with the most reviews incorporated into COPE are summarized in Table 1. For each sentence in COPE, a part-of-speech analysis was conducted (Figure 1) and made available for future research.

The list of the most commonly encountered nouns, adjectives, and verbs in the corpus and rates of frequency are shown in Table 2.

Table 1. The number of health care facilities and reviews from the top 10 cities covered by the COPE.

City	Health care facilities, n	Reviews, n
Palo Alto, CA	123	988
La Jolla, CA	122	872
Pasadena, CA	76	831
Cambridge, MA	50	611
Los Angeles, CA	75	541
Austin, TX	31	239
San Diego, CA	31	252
Houston, TX	58	261
San Luis Obispo, CA	56	235
Seattle, WA	28	255

Table 2. The top 20 noun phrases, adjectives, and verbs in COPE (after lemmatization).

Noun phrase	Frequency (per1000 sentences)	Adjectives	Frequency (per 1000 sentences)	Verbs	Frequency (per 1000 sentences)
Time	52.24	Good	52.90	Be	381.42
Doctor	38.20	Great	35.51	Have	197.99
Massage	32.43	Nice	19.89	Go	83.18
Place	31.08	First	17.78	Get	80.35
Staff	30.11	New	16.09	Do	68.72
Office	28.97	Friendly	16.01	Make	40.97
Care	28.68	Few	13.08	See	39.87
Appointment	25.96	Bad	13.02	Take	35.85
Experience	25.45	Sure	11.27	Feel	32.85
Dentist	21.39	Dental	11.24	Give	31.69
Eye	18.79	Little	11.08	Come	31.17
Patient	17.68	Clean	10.90	Say	31.08
Service	16.88	Many	10.82	Tell	30.59
Room	16.50	Professional	10.52	Know	28.49
Insurance	16.47	Last	10.18	Find	23.13
Hour	15.75	Live	9.97	Want	21.78
People	15.66	Medical	9.85	Think	20.36
Surgery	15.19	Next	9.66	Ask	20.25
Pain	14.77	Much	9.25	Recommend	18.99
Review	14.09	Same	8.94	Visit	15.88

Figure 1. Part-of-speech analysis conducted on each sentence in COPE.


```
<Sentence id="0" negated="false" sentimentScore="1.1240823864964697" text="The nurses are very
nice and very supportive.">
        <Parse>(ROOT (S (NP (DT The) (NNS nurses)) (VP (VBP are) (ADJP (ADJP (RB very) (JJ
nice)) (CC and) (ADJP (RB very) (JJ supportive)))) (. .)))</Parse>
        <Dependecy>det(nurses-2, The-1)|||nsubj(nice-5, nurses-2)|||cop(nice-5, are-3)|||advmod(nice-5,
very-4)|||root(ROOT-0, nice-5)|||cc(nice-5, and-6)|||advmod(supportive.-8, very-7)|||conj(nice-5,
supportive.-8)</Dependecy>
        <Nouns>nurses</Nouns>
        <NounPha>The nurses</NounPha>
        <Adjs>very nice|||very supportive</Adjs>
        <Verbs>are</Verbs>
</Sentence>
```

Descriptive Statistics of Reviews in COPE

Over the years, there has been a rapid growth of the number of COPE reviews posted on Yelp (Figure 2). The earliest COPE review was published in 2005, and the most recent was published in 2012. The earlier years, between 2005-2007, were associated with a very high year-over-year growth rate, with a doubling time every 6 months. From 2007-2012, growth stabilized at a rate of 1.5 times annually. Note that 2012 was only a partial year of data collection.

Although most facilities (93.0%, 916/985) received <20 reviews, 2 facilities (%0.2, 2/985) received >100 reviews (Figure 3). The median length of each review was 635 characters (Figure 4) and the median number of sentences in each review was 9 (Figure 5).

Figure 2. Number of reviews per years.
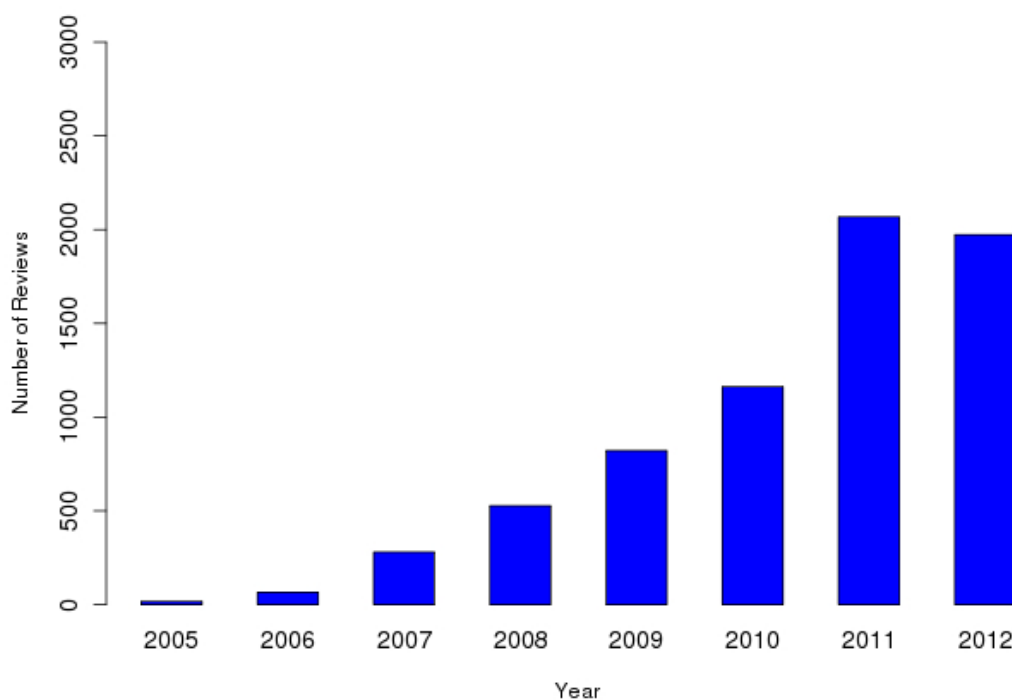
Figure 3. Distribution of reviews.
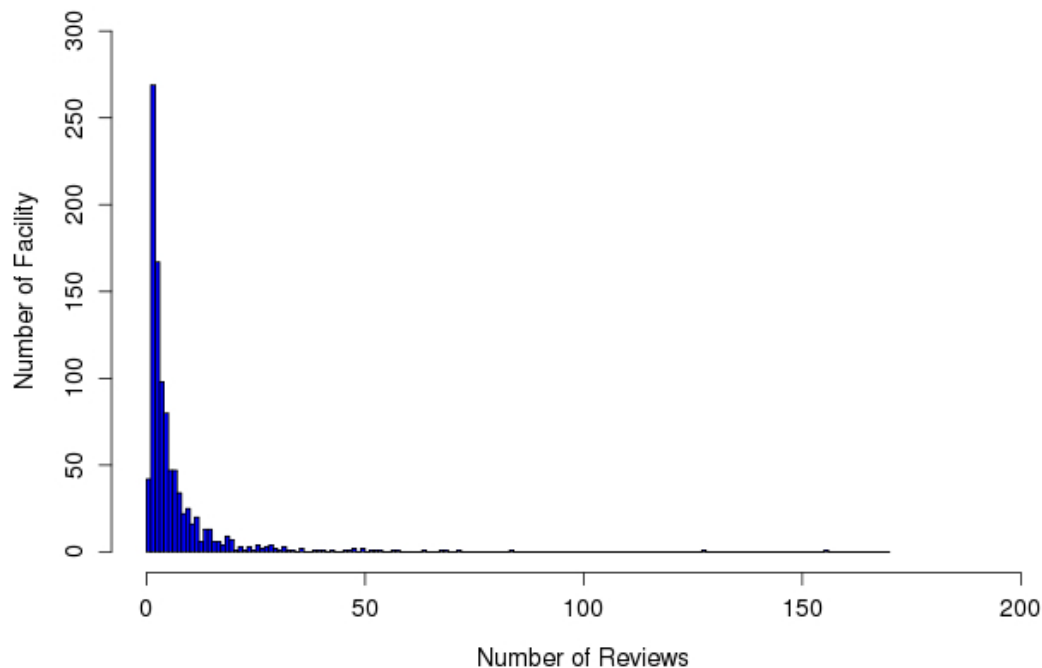
Figure 4. Distribution of review length.
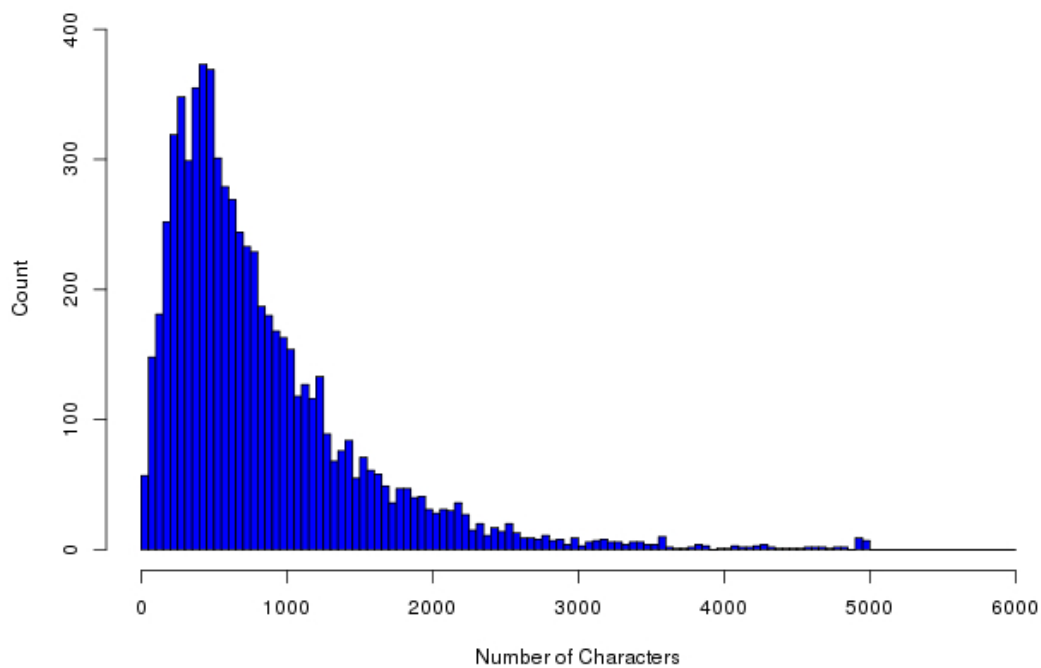
Figure 5. Number of sentences per review.
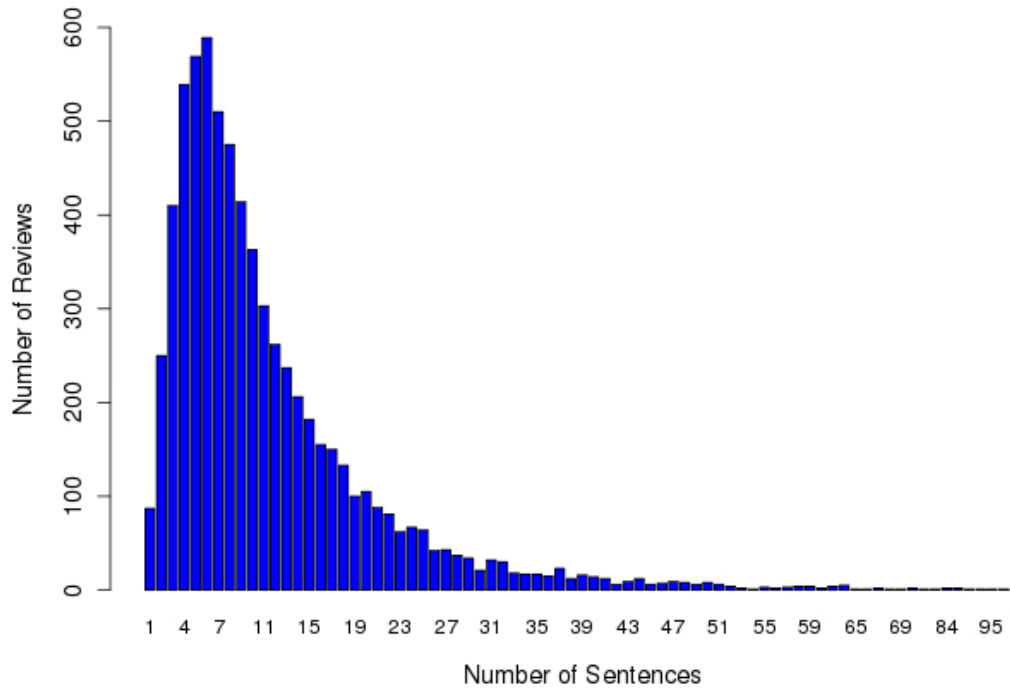
Consumer Rating and Sentiment Analysis of COPE

On a scale of 1-5 (with 5 being the best), 69.68% (4817/6914) patients rated the facility favorably (≥4 out of 5) (Figure 6). A trend was identified between length of patient reviews and perception of a negative experience (correlation=-.5829, *P*<.001) (Figure 7). Figure 8 illustrates the distribution of sentiment score per sentence. The computed sentiment score was compared with the consumer-generated rating (*P*<.001, Pearson correlation test) (Figure 9). The sentiment score reflects the degree of accumulation of sentimental words in a sentence, which can be signified by *positive* words such as "pleasing" and "perfect," and *negative* words such as "unhappy" and "disappointing." Longer sentences tended to carry stronger sentiment score (Figure 10).

Figure 6. Distribution of the rating scores per review.
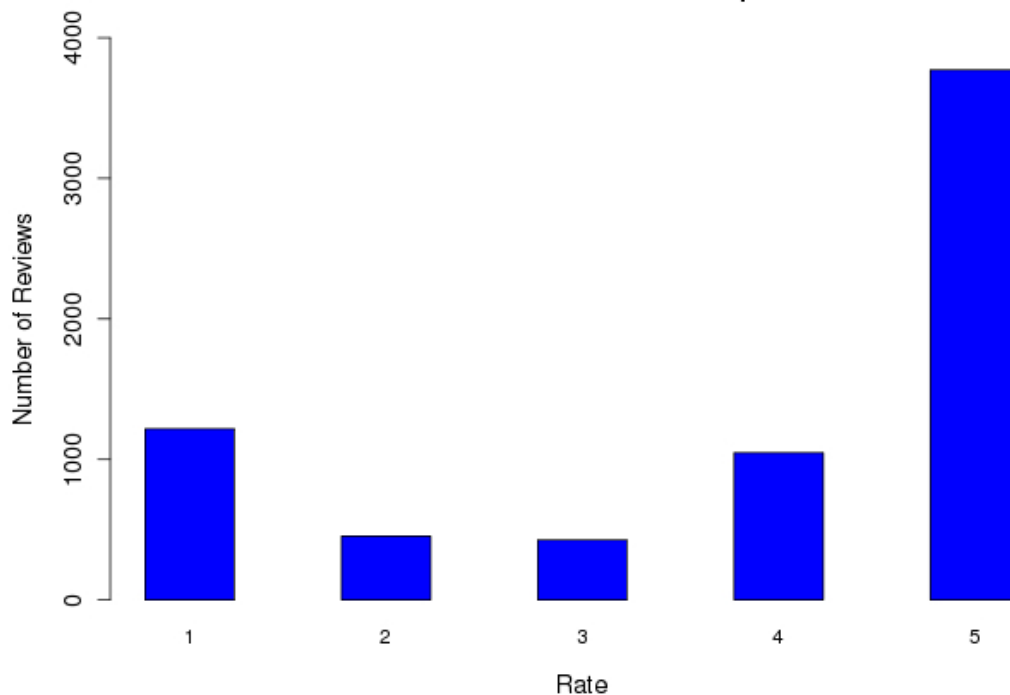
Figure 7. Length of review versus rating score.
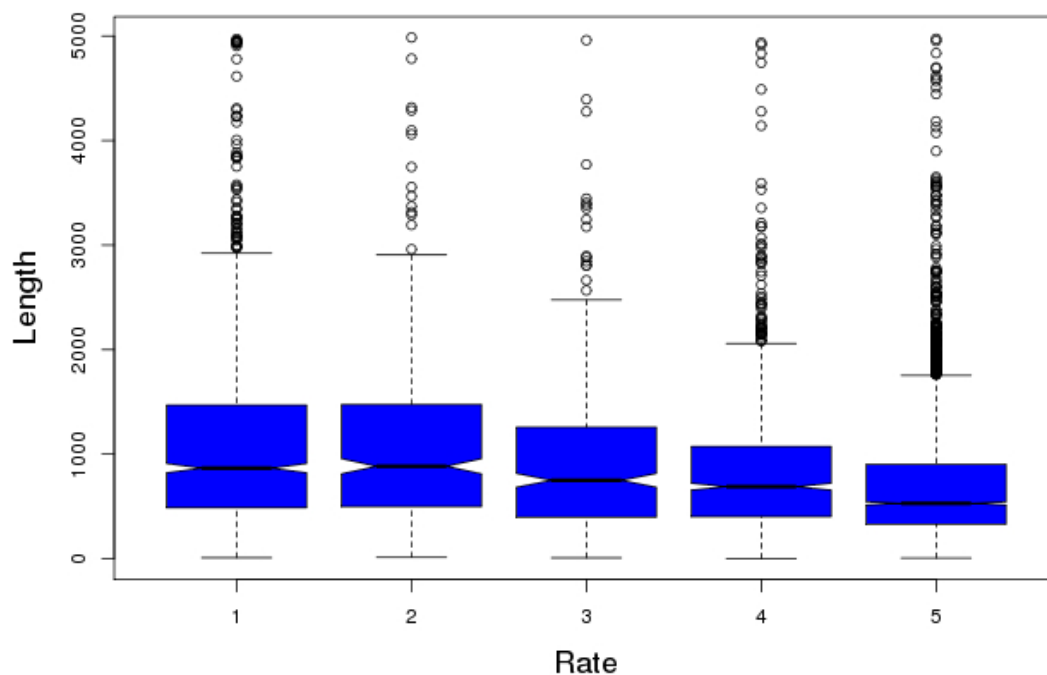
Figure 8. Distribution of the sentiment score per sentence.
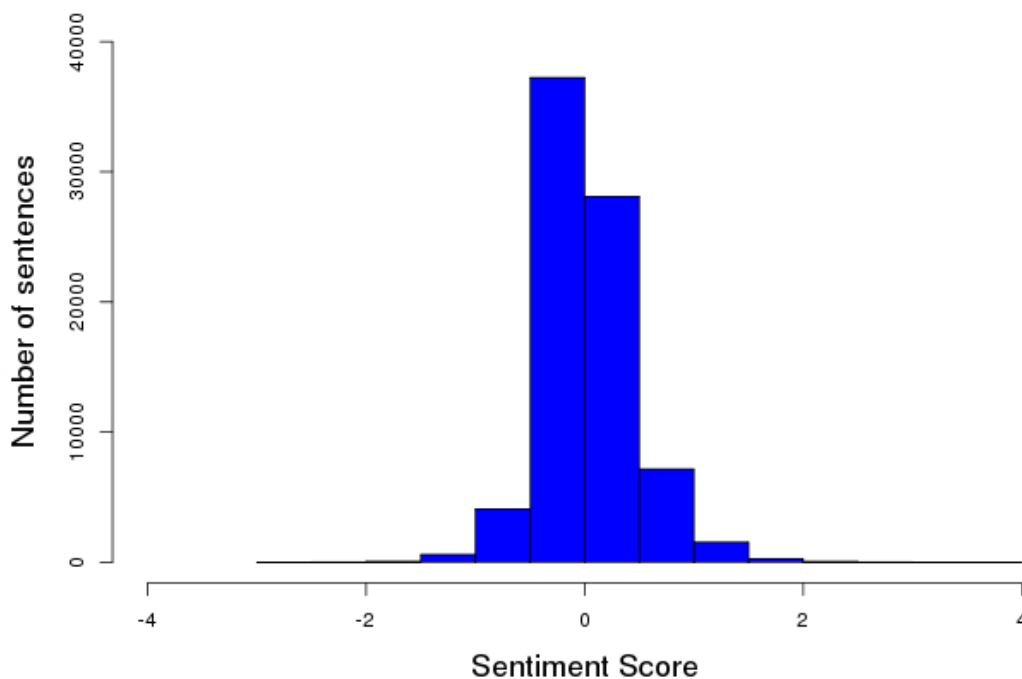
Figure 9. Mean sentiment score of sentences in each review per patient-generated overall rating.
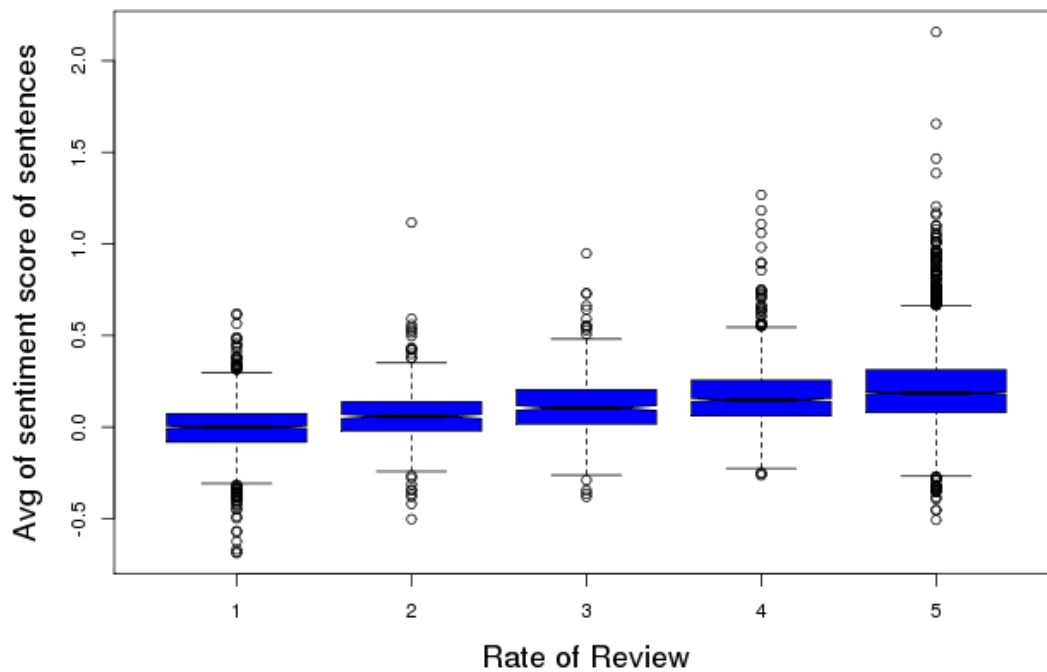
Figure 10. Sentiment score per length of sentence.
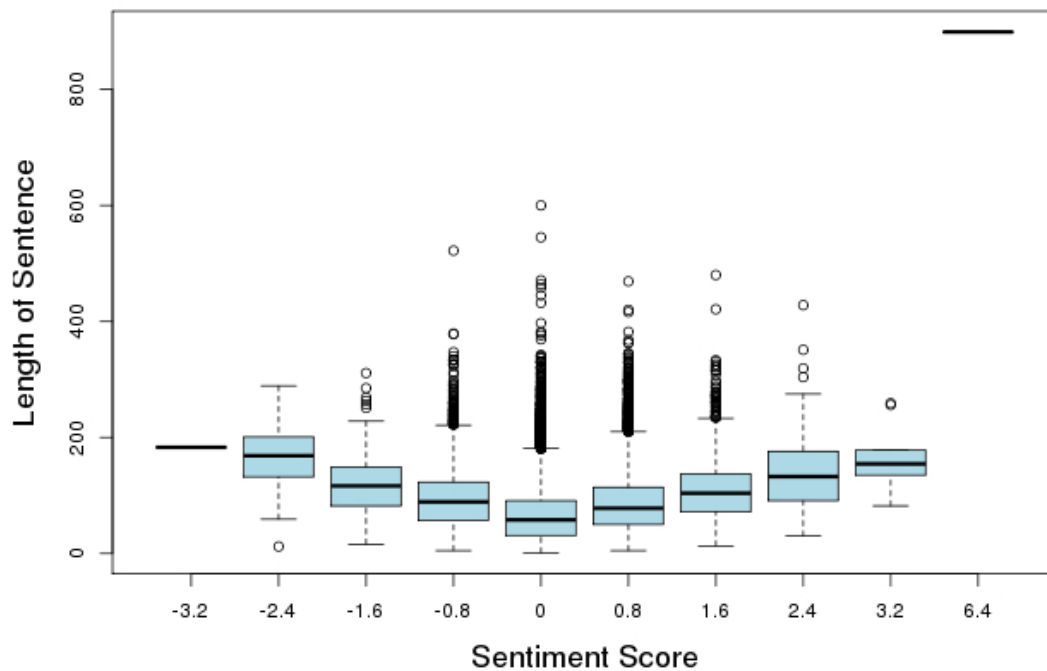
A Consumer Vocabulary Derived From COPE to Describe Their Health Care Experience

A total of 25,692 words were derived from COPE. Consistent with vocabulary used in other domains, the top 25% of the vocabulary covered 92% of the usage (Figure 11).

COPE vocabulary was also compared to the CHV [32]. Of all the words in the COPE vocabulary, 8136 (31.67%, 8136/25692) were found in the CHV. The top 20 overlapping and non-overlapping words within the CHV are shown in Table 3.

Table 3. The top 20 overlapping and non-overlapping words within the CHV.

Overlapping		Non-overlapping	
Word	Frequency (per 1000 sentences)	Word	Frequency (per 1000 sentences)
Good	53.54	Take	36.43
Time	52.21	Give	31.69
Like	40.91	Tell	30.59
See	39.87	Care	28.68
Doctor	38.20	Know	28.49
Back	35.85	Call	24.70
Great	35.84	Wait	23.98
Feel	35.06	Find	23.13
Massage	32.43	Ask	20.25
Come	31.17	Nice	19.99
Place	31.08	Room	16.50
Work	30.50	Friendly	16.16
Staff	30.11	Visit	15.88
Office	28.97	Help	15.72
Appointment	25.96	Use	14.22
Experience	25.45	Seem	11.74
Look	23.96	Clean	11.55
Dentist	21.39	Check	10.29
Think	20.96	Exam	10.21
Well	19.37	Explain	9.06

A co-occurrence analysis [34] revealed that these words formed a network. For example, the following words formed a tight cluster when patients described their experience with platelet donation ("blood", "donor", "platelets"), the snacks offered ("cookie" and "juice"), and the thank-you items given ("movie" and "ticket") (Figure 11).

Figure 11. Cumulative usage of terms versus rank of terms.
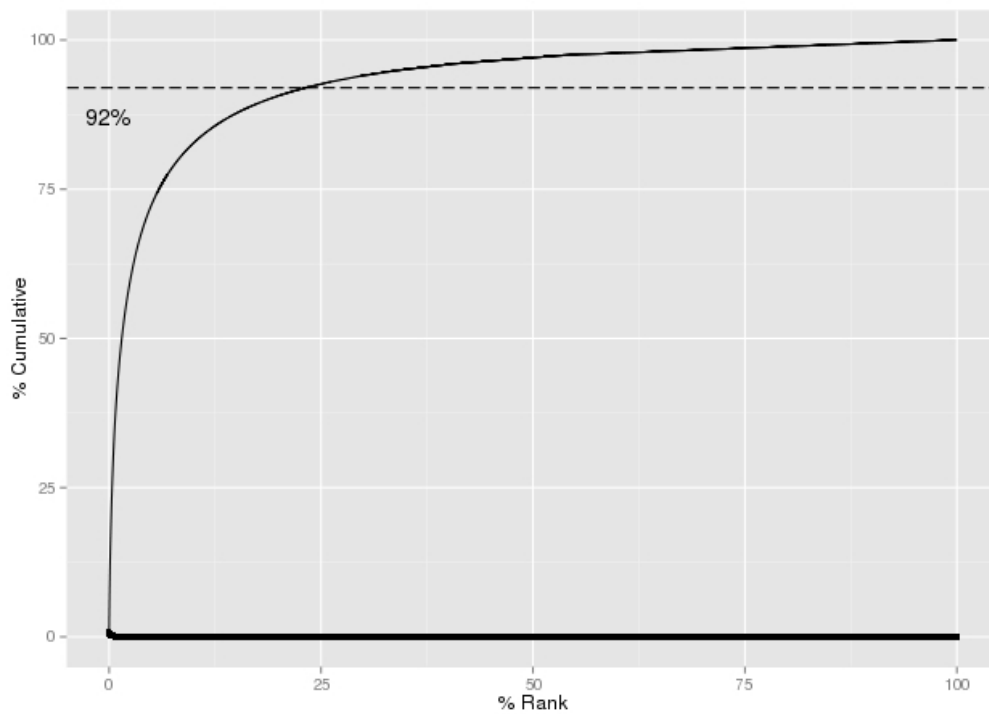
Figure 12. A network of words used by customers to describe their experiences. The size of the node indicates the frequency of the word and the width of the lines indicates the number of co-occurrences of the word-pair in the same review. An example of usage of the word "platelet" is shown in the call-out box.
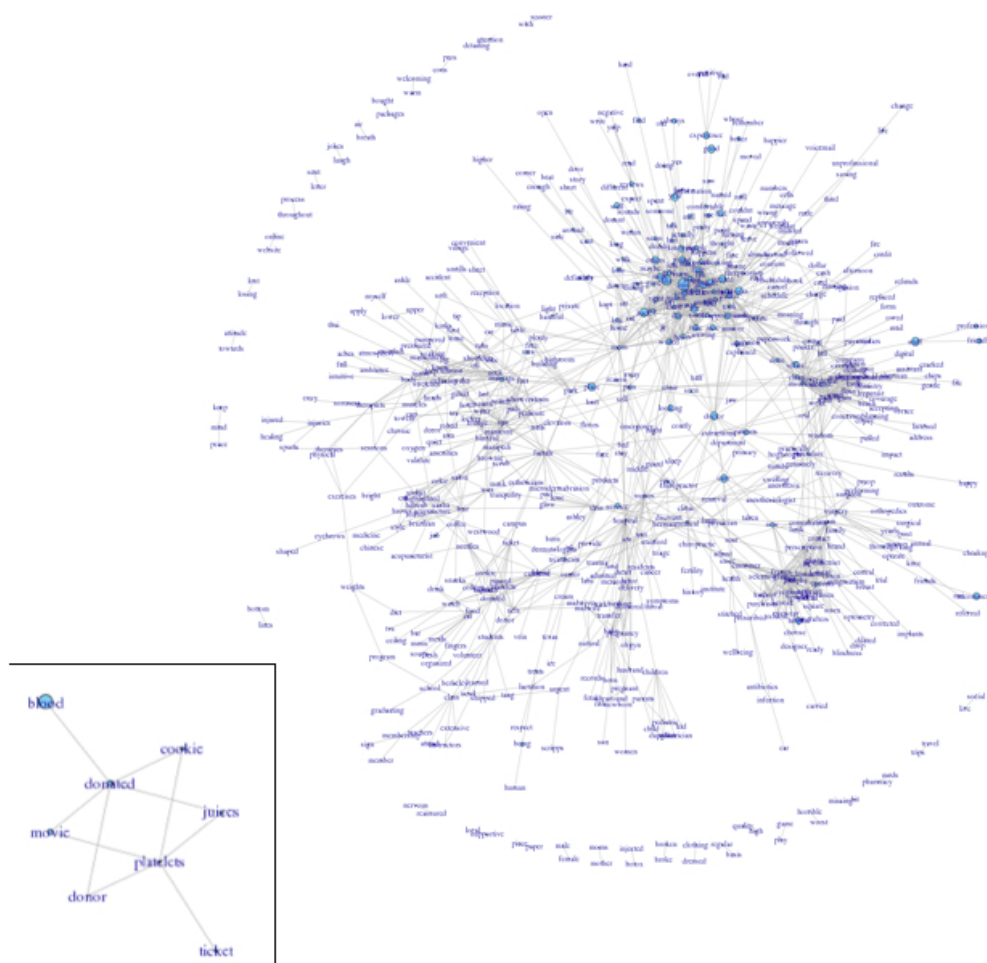
Discussion

Principal Findings

This study yields insightful results following a statistical analysis of 79,173 sentences from 6914 patient reviews of 985 health care facilities. The trend that we observed between length of patient reviews and perception of a negative experience is consistent with a previous study of consumer reviews [35]. Figures 4 and 5 suggest that the texts in COPE are much longer than Twitter (140 characters), which allow more sophisticated content analysis such as identifying the debates among different reviewers in future research studies.

Findings in this study indicate that online reviews could be used to understand important aspects of business from the customers' point of view. Consistent with a previous report on CHV [33], we also observed that a small vocabulary set (25%) covered a majority (92%) of the content (Figure 10). In examining Table 2 and considering the most frequent noun phrases (ie, time, doctor, massage, place, staff, office, care, appointment) we can see important aspects of health care business as the most frequent terms used by patients. Table 3 further suggests that the COPE vocabulary list covers more about the patient experience with health care providers, including sentiment words such as "nice" and "friendly" and experiential words such as "wait" and "visit". Moreover, the co-occurrence analysis revealed a statistical "wordnet", which can recover some interesting associations in the context of health care (Figure 11).

Our comparison of the computed sentiment score with consumer-generated rating (Figure 9) showed good correlation between the mean sentiment score of sentences and patient-generated. This result further validated our computational approach for sentiment analysis and the consistency of rating by the patients.

Limitations

The data source of the Yelp Academic Dataset used herein was associated with the following study limitations. First, it was geographically biased with businesses surrounding 30 universities in the United States. Table 1 suggests that the data set is highly concentrated in the east and west coasts, and Texas. Second, the date range of the reviews was limited from 2005-2012. There were no updates available from the Yelp Academic Dataset. However, this dataset is the accessible Yelp data for academic research, since the Terms of Service by Yelp Inc prevents any automatic data retrieval of Yelp contents. In addition, there is an implicit selection bias toward "patients" (we cannot verify they are truly patients) who choose to write a review at Yelp. Moreover, the credibility and content of some reviews has been challenged by physicians and provider organizations on whether the review content truly reflects an unbiased patient experience or is representative of the actual quality of care [27].

Conclusions

The created and characterized COPE corpus includes patient reviews, ratings, parse trees, dependency trees, and a vocabulary list. The COPE corpus further enables future policy studies, such as using machine learning techniques such as unsupervised learning of topic analysis or supervised analysis of classifications [7] to analyze the patient reviews in the context of six domains of quality established by the Institute of Medicine [36]. COPE is available for academic use [37].

Conflicts of Interest

None declared.

Multimedia Appendix 1

List of the 26 Yelp health care categories in the study.

[PDF File (Adobe PDF File), 99KB - resprot_v4i3e78_app1.pdf]

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Abbreviations

CHV: Consumer health vocabulary
COPE: Corpus of Patient Experience
HCAHPS: Hospital Consumer Assessment of Healthcare Providers and Systems
NLP: Natural language processing

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Original Paper

Social Media Use in Research: Engaging Communities in Cohort Studies to Support Recruitment and Retention

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Abstract

Background: This paper presents the first formal evaluation of social media (SM) use in the National Children's Study (NCS). The NCS is a prospective, longitudinal study of the effects of environment and genetics on children's health, growth and development. The Study employed a multifaceted community outreach campaign in combination with a SM campaign to educate participants and their communities about the Study. SM essentially erases geographic differences between people due to its omnipresence, which was an important consideration in this multi-site national study. Using SM in the research setting requires an understanding of potential threats to confidentiality and privacy and the role that posted content plays as an extension of the informed consent process.

Objective: This pilot demonstrates the feasibility of creating linkages and databases to measure and compare SM with new content and engagement metrics.

Methods: Metrics presented include basic use metrics for Facebook as well as newly created metrics to assist with Facebook content and engagement analyses.

Results: Increasing Likes per month demonstrates that online communities can be quickly generated. Content and Engagement analyses describe what content of posts NCS Study Centers were using, what content they were posting about, and what the online NCS communities found most engaging.

Conclusions: These metrics highlight opportunities to optimize time and effort while determining the content of future posts. Further research about content analysis, optimal metrics to describe engagement in research, the role of localized content and stakeholders, and social media use in participant recruitment is warranted.

Introduction

In 2000, Congress authorized the National Institutes of Health to conduct the National Children's Study (NCS); a prospective, longitudinal study of US children and their parents, designed to examine the effects of environment and genetics on children's health, growth and development. The NCS Vanguard (pilot) Study began in 2009, evaluating methods for the larger Main Study, including community engagement techniques to increase recruitment and retention of participants [1-3]. Historically, recruitment of participants for population-based, longitudinal studies has presented many challenges [4-7]. Young adults, including women of childbearing age (the target demographic for the NCS), represent a particularly challenging cohort for recruitment and retention due to their increased mobility [8-11]. Social media (Facebook, Twitter, blogs, YouTube) is increasingly a first information source for this demographic group, and has been shown to be an effective tool for participant retention in longitudinal research [12-15]. Social media

circumvents geographic differences between people and provides a cost effective, convenient method of study recruitment and retention [11,13,15]. Social media also provides an interactive platform and encourages the free sharing of information.

However, using social media in biomedical research raises important considerations. Utilizing social media in the highly regulated clinical research environment requires a nuanced understanding of potential threats to confidentiality and privacy and the role that posted content plays as an extension of the informed consent process (eg one must avoid overpromising benefits or underestimation of risks) [16,17]. Additionally, institutional review boards require that researchers make every effort to minimize human subject risks when engaging participants via social media [16].The regulatory review process can slow posting frequency to a pace that threatens timeliness, relevance and response which are strengths of social media use.

This paper presents the first formal evaluation of social media use in the NCS. While few metrics exist to guide best practices for the use and evaluation of social media in the NCS and for biomedical research generally, we present here a pilot project testing the feasibility of collecting and analyzing social media metrics from multiple sites with the primary goal of determining best practices for social media use in research engagement.

Methods

Participants

Study Centers (SCs) utilizing Facebook as part of their community outreach and engagement efforts were invited to participate. Four SCs (Queens County, New York; Waukesha County, Wisconsin; San Diego County, California; and Cumberland County, Maine) elected to participate thus providing geographic diversity.

Participating SCs collected 4 months of data between December 2011 and March 2012 from various social media accounts and websites (see Table 1). Only Facebook data is presented in this paper because it was the only modality consistently used by all of the participating locations. SCs met via 4 monthly conference calls to report and discuss social media use. All SCs downloaded their Facebook data and provided it to the MSC for analysis.

Metrics

We used several metrics in our Facebook analysis. We started with basic Facebook use metrics including lifetime number of likes, average likes per month (number of lifetime likes divided by the number of months on Facebook) and number of posts. At the time of this analysis, EdgeRank score (see Textbox 1) was collected as an effectiveness measure because it is an algorithm developed by Facebook to govern what is displayed on the News Feed [18]. The EdgeRank formula includes the variables of affinity, time, and weight [19]. An EdgeRank score of 20 or higher is generally considered by social media experts as positive for potential exposure in the News Feed [20].

A multitude of metrics exist in Facebook to describe engagement but at the time of this analysis there was no standard metric for engagement with content. We conducted a literature search of existing Facebook metrics for assessing user engagement using Facebook Insights data [21-24]. Although no single common metric exists, a combined Insights data set is commonly used, albeit with distinctly different approaches. Facebook collects deidentified data for pages, as well as for individual posts (see Textbox 1). Page level data describes how users engage with the Facebook page, offering cumulative metrics for fans, reach, and engagement. Post level data is collected for each individual post, yielding a more focused assessment of what prompts fans (users who have liked the Facebook page) to interact with individual posts.

In page level analyses, the rate of Page Consumption (number of page clicks or video views) over Total Daily Page Reach (number of people who saw your page content) is commonly used as an engagement metric, however Page Consumption does not include post likes, shares, or comments. In Post level analyses, current engagement metrics measure the rate of comments and likes on a post over the number of impressions (number of times a post is displayed, regardless of whether it is seen or not in the News Feed).

The Facebook pages used in this study had a relatively low number of page likes. SC Facebook pages count likes in the mid to low hundreds compared to commercial products that count fans in the millions (Nike has over 22 million fans). The engagement metrics for Page and Post level Insights described above did not accurately describe the activity we saw on the pages. To better understand how our fans engaged with our posts, we determined that it was essential to include all activities of engagement when analyzing our data. This included any interaction between a fan and a post—any click on a post, like, comment, or share. We chose to use Post Total Reach in our engagement analysis as well. Post Total Reach is the total number of unique people who see the post in their News Feed, as defined and measured by Facebook.

Table 1. Study center characteristics and social media use by location.

Study center location	Social media modalities used	Months on Facebook	Rural/Urban	Population (US Census 2010)
Queens County, New York	Facebook, Twitter, YouTube, Blog	12	Urban	2,230,722
Waukesha County, Wisconsin	Facebook	18	Rural	389,891
Cumberland County, Maine	Facebook, Twitter, Blog	14	Rural	281,674
San Diego County, California	Facebook, Twitter	17	Urban	3,095,313

Textbox 1. Key Facebook analytic terms.

EdgeRank - As of 2011, the Facebook algorithm that determined what is displayed on a user's News Feed [19]

Page level data - Data that provides an overview of the overall Page performance and metrics related to change in audience [13]

Post level data - Data about a particular post [13]

Reach - The number of persons who have seen content associated with your Page [13]

Consumption - The number of clicks or video views [13]

Impressions - The number of times a post is displayed, regardless of whether it is seen in a News Feed or not [13]

Analysis

Content analysis examines the topics that SCs posted about during the study period. Since Facebook does not collect metrics about the content of posts, we developed a unique analysis, conducted by collecting SC posts and assigning each post to one of nine content categories, classifying the overall intent of each post (see Textbox 2). Inter-rater reliability testing of post-content classification was performed with four raters assigning posts to categories and produced a kappa ranging from 0.67-0.75 indicating adequate inter-rater agreement.

By assigning each post to one category, the prevalence, or frequency of a SC posting about that topic was calculated. Prevalence of each post category was represented as a percentage of the total posts (see Figure 1). Using the lifetime total reach and lifetime engaged user metrics from each post, an overall total reach and engagement was summed for each content category. The engagement score was then calculated by dividing the total engagement for a category by its total reach. This method of analysis was applied to each study center.

This project was declared exempt from review by the Maine Medical Center Institutional Review Board. All social media activity strictly followed NCS social media policies [17,25].

Textbox 2. Categories used to analyze the topics of posts.

National Children's Study (including updates, newsletters, publications)

Holidays

Activity (focusing specifically on local or regional events)

Kids (content directly related to or for children)

Health and fitness (focusing on physical fitness and active living)

Health education

Nutrition

Education (including parenting)

Awareness (health observances and monthly causes)

Figure 1. Facebook cumulative Likes over a 4 month period and average number of likes per month for the 4 participating SCs.
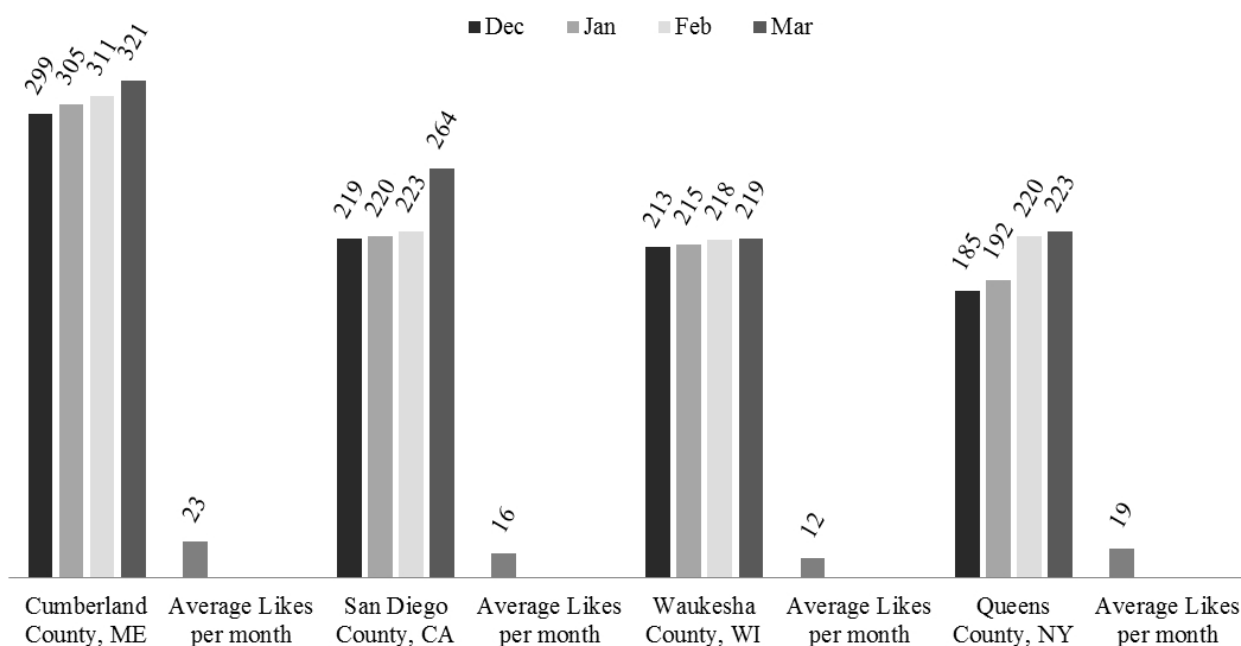
Results

We present here both basic use metrics for Facebook, as well as the Facebook content and engagement analysis described above.

Basic Use Metrics for Facebook

The 4 sites experienced an average of 229 (range 185-299) Facebook Likes in December 2011; by the completion of the pilot in March 2012, this average jumped to 257 (range 219-321), an average increase of 28 likes (range 6-45) over the pilot period. Likes is a cumulative metric over the period of Facebook use, therefore we calculated "Likes per Month". The SC Facebook pages averaged 16 (range 12-18) months of

publishing and the Likes per Month ranged from 12 to 23 (see Figure 2). SCs averaged 17 posts per month (range 7-35) and generally increased to 37 posts per month (range 13-53) over the study period.

EdgeRank scores for the strength of post placement in the News Feed were variable over the sites, as shown in Figure 3, and the monthly average by site ranged between 34 and 42 (see Figure 3). We expect a positive correlation between EdgeRank scores and number of posts [19,20]. Waukesha County, WI and Queens County, NY demonstrates this relationship, however, Cumberland County, ME does not. As the number of posts increases in Cumberland County, ME, the EdgeRank score decreases.

Figure 2. Number of posts and EdgeRank scores for the study period by month and SC.
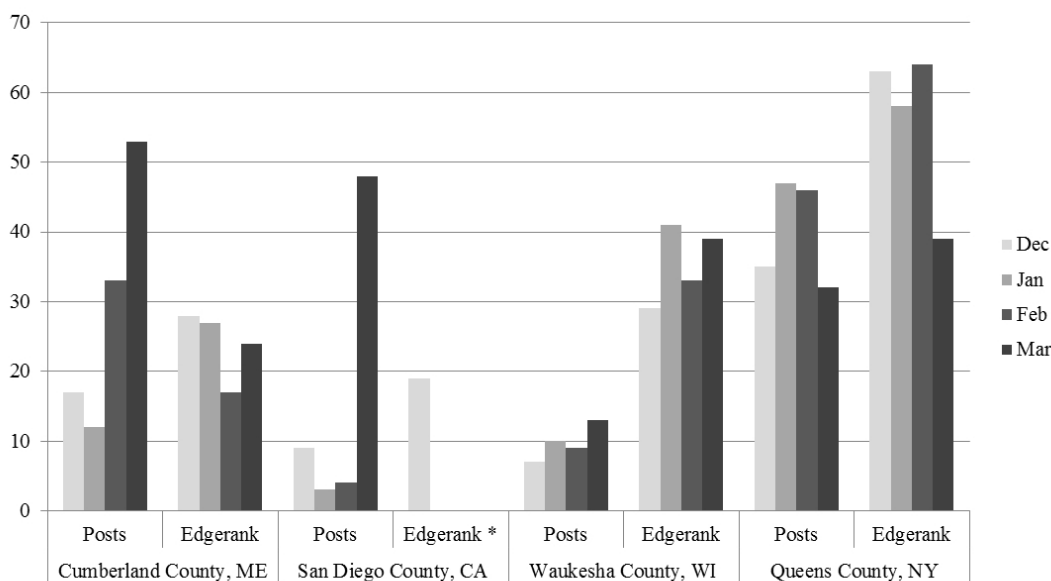
* Edgerank scores were unavailable for San Diego County, CA for the entire pilot period.

Figure 3. Content posted by each Study Center over the pilot period.

Cumberland County, ME: Content of Posts
- Holiday 5%
- Education 6%
- NCS 8%
- Activity 21%
- Awareness 8%
- Kids 8%
- Health and fitness 3%
- Health education 25%
- Nutrition 16%

Queens County, NY: Content of Posts
- Holiday 3%
- Education 3%
- NCS 8%
- Activity 17%
- Awareness 11%
- Kids 5%
- Health and fitness 20%
- Health education 21%
- Nutrition 12%

San Diego County, CA: Content of Posts
- Holiday 5%
- NCS 5%
- Education 8%
- Nutrition 13%
- Activity 11%
- Awareness 27%
- Health education 25%
- Kids 5%
- Health and fitness 1%

Waukesha County, WI: Content of Posts
- Activity 8%
- Awareness 3%
- Holiday 11%
- NCS 10%
- Education 0%
- Nutrition 13%
- Kids 21%
- Health education 24%
- Health and fitness 10%

Facebook Content Analysis and Engagement Analysis

For each SC we analyzed the post content throughout the pilot period (Figure 1). Analysis of post content showed that SCs posted most commonly about health education (24.3%, (range 21%-27%)), activity (14.3%, (range 8%-21%)), and nutrition (13.8%, (range 13%-16%)). Content of showed some variability between SCs. For example, San Diego County, CA posted mostly about health awareness issues (27%), while Waukesha County, WI posted most frequently about children's topics (21%).

Table 2 shows the engagement analysis for each Study Center by content category. We calculated the overall engagement per view as well as the overall views per post for each Study Center. There was some variation in the views per post (ranging from 66.095-84.875) and engagement per view (range 0.053-0.039). Posts about the NCS have high engagement per view across all Study Centers. Posts about holidays had the highest views in Waukesha County, WI, while posts about nutrition had the most views per post in Cumberland County, ME. Additionally, some Study Centers had high engagement on activity and nutrition-related content. Content analysis demonstrated overall

low engagement scores with health education topics, but regional variation was seen with other topics. Waukesha experienced high engagement on posts related to activity or awareness, but the other sites had significantly lower engagement in these categories. Interestingly, three sites (Cumberland County, ME; Queens County, NY; and San Diego County, CA) experienced higher engagement with child related content, but Waukesha County, WI experienced little engagement relative to the number of posts about this content.

Interestingly, in Cumberland County, ME, we notice an inverse relationship between views per post and engagement per post. When looking at the overall engagement in Cumberland County, ME, (Table 2) many people saw each post as reported by the high views per post, yet few people engaged with post as indicated by the lowest rate of engagement per view. This pattern supports an acknowledged relationship in Facebook where as a Page reaches more people, a lower proportion of that audience will engage with content. By comparing the engagement of each content category to the overall engagement, we can derive which topics are of most interest to each Study Center and tailor social media content to local community interests.

Table 2. Content engagement variance as a function of Study Center.

		Overall content engagement variance	By Content Category								
			Activity	Awareness	Kids	Health and fitness	Health education	Nutrition	Education	NCS	Holiday
Cumberland County, ME	Engagement per view	0.039	0.052	0.019	0.045	0.034	0.031	0.040	0.029	0.052	0.034
	Views per post	84.875	80.591	86.125	81.375	88.667	88.308	90.176	80.833	77.444	87.400
Queens County, NY	Engagement per view	0.040	0.044	0.030	0.032	0.031	0.035	0.034	0.042	0.093	0.046
	Views per post	82.079	87.654	79.471	82.125	82.071	78.563	83.842	76.750	83.917	77.600
Waukesha County, WI	Engagement per view	0.040	0.032	0.039	0.038	0.030	0.035	0.045	0.000	0.062	0.034
	Views per post	75.778	73.000	76.000	78.000	66.500	76.900	76.200	0.000	68.500	87.000
San Diego County, CA	Engagement per view	0.053	0.048	0.055	0.080	0.019	0.040	0.064	0.044	0.103	0.030
	Views per post	66.095	54.000	71.176	67.000	54.000	62.563	74.750	68.600	71.000	55.333

Discussion

Principal Findings

Social media use is new in research recruitment and retention and holds significant potential, however there are currently no well defined best practices and metrics for evaluation.

We describe here a pilot project testing the feasibility of data collection through Facebook, as well as the creation and analysis of social media metrics from multiple SCs with the primary goal of determining best practices for future use. Primarily, this pilot demonstrated the feasibility of creating linkages and databases to collect and measure social media metrics from multiple SCs for comparison of content and engagement. Shared posting schedules and best practices combined with coordinated engagement (eg liking each other's posts to increase reach) contributed to a measurable increase in engagement during the study period.

Facebook was the only social media modality evaluated in this pilot study. Assessment of engagement across SCs and modalities was complicated by a lack of commonly used and/or accepted metrics. We describe here basic Facebook metrics, along with the nascent creation of content and engagement analysis metrics tailored for NCS evaluation. Likes are commonly used as a measure of engagement; however, likes are garnered and not often lost. Therefore likes are a cumulative, static metric and not a moving metric like engagement. Number of likes does not indicate engagement, but does represent a "fan base" and potential for engagement. The difference in likes per month demonstrates that these online communities can be

quickly generated (see Figure 2). For example, Cumberland County, Maine was able to yield a similar number of likes as the two NCS locations that were the most established on Facebook in a shorter amount of time, although other factors (eg authorization for mass communications campaigns and the use of social media) must be considered in interpretation. Because of the limitations of using likes in measuring engagement, we describe here the evaluation of new engagement metrics.

EdgeRank is commonly used to measure overall success and impact on Facebook, however it does not allow analysis of the content of posts, nor does it inform on how to serve interesting and engaging content to individual communities. The algorithm that EdgeRank uses includes variables of affinity, time, and weight [18-20]. Cumberland County, Maine's EdgeRank scores continued to be low despite posting significantly more frequently in the last study month, which, as a variable in EdgeRank's algorithm, should have yield an increased score (see Figure 3). This example highlights the challenges of using this algorithm to see and respond to our community's variable interests in content.

Content and engagement analysis yielded new and improved metrics for the use of social media in the NCS. These analyses allowed us to describe what content of posts SCs were using, what content they were posting about, and what the online NCS communities found most engaging (see Figure 1). Engagement metrics shed light on where to focus time and effort in determining the content of posts (see Table 2). The purpose of this study was to demonstrate the ability to measure differences in engagement, yet an important realization is that not all centers

should necessarily post the same content—rather the content posted should reflect their community and study activity. Questions remain; What messages were different between centers when it came to the topics of children? What role does localized content play in engagement on Facebook? Future research could further explore the role of content on engagement, as well as the optimal metrics to describe engagement in the research setting.

Limitations and Challenges

This pilot project had several limitations and challenges. This pilot study was not a representative sample of all SCs. The study proposed new metrics that lack baseline data to which to compare our engagement scores, making it difficult to interpret the data relative to other Facebook sites. We minimized subjectivity through inter-rater analysis, however, subjectivity in content categories and the sorting of posts must be acknowledged. The use of social media in the research setting is necessarily restricted by regulations for human subject protections. As such, we were limited in the content we could post and were unable to directly solicit engagement from our

target market— NCS participants— and instead targeted the general community corresponding to each Facebook site. While ethical review of using social media to support the conduct of research is evaluated by federal restrictions through institutional review, many social media users neither read nor understand complex social media terms of service agreements and may not see themselves as potential research subjects. This latter point will continue to be a source of challenge for this field of study.

Conclusions

This pilot developed the infrastructure to analyze social media use in 4 SCs in the NCS, as well as demonstrating some preliminary best practices. Our analysis supports the use of social media, specifically Facebook, to increase awareness of the Study. Facebook's strengths include the ability to engage in a two way dialogue and the open sharing of information, but understanding how best to utilize this forum's user base and strengths for the changing goals and regulations of the use of social media in research. Further research examining content analysis, the role of localized of content and stakeholders, and social media use in participant recruitment is warranted.

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Abbreviations

NCS: National Children's Study
MSC: Maine Study Center
SC: study center
SM: social media

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<u>Original Paper</u>

Ecological Momentary Assessments and Automated Time Series Analysis to Promote Tailored Health Care: A Proof-of-Principle Study

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Abstract

Background: Health promotion can be tailored by combining ecological momentary assessments (EMA) with time series analysis. This combined method allows for studying the temporal order of dynamic relationships among variables, which may provide concrete indications for intervention. However, application of this method in health care practice is hampered because analyses are conducted manually and advanced statistical expertise is required.

Objective: This study aims to show how this limitation can be overcome by introducing automated vector autoregressive modeling (VAR) of EMA data and to evaluate its feasibility through comparisons with results of previously published manual analyses.

Methods: We developed a Web-based open source application, called AutoVAR, which automates time series analyses of EMA data and provides output that is intended to be interpretable by nonexperts. The statistical technique we used was VAR. AutoVAR tests and evaluates all possible VAR models within a given combinatorial search space and summarizes their results, thereby replacing the researcher's tasks of conducting the analysis, making an informed selection of models, and choosing the best model. We compared the output of AutoVAR to the output of a previously published manual analysis (n=4).

Results: An illustrative example consisting of 4 analyses was provided. Compared to the manual output, the AutoVAR output presents similar model characteristics and statistical results in terms of the Akaike information criterion, the Bayesian information criterion, and the test statistic of the Granger causality test.

Conclusions: Results suggest that automated analysis and interpretation of times series is feasible. Compared to a manual procedure, the automated procedure is more robust and can save days of time. These findings may pave the way for using time series analysis for health promotion on a larger scale. AutoVAR was evaluated using the results of a previously conducted manual analysis. Analysis of additional datasets is needed in order to validate and refine the application for general use.

KEYWORDS

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Introduction

Person-Centered Research and the Idiographic Approach

Evidence-based treatment guidelines in health care are predominantly based on nomothetic, group-based research. Samples of patients are investigated to find general laws of symptomatology and functioning, which are then generalized to all individual members of the investigated population [1,2]. Several authors have criticized the dominance of this approach [3-6], which leads to knowledge that is "true on average" [2]. Although nomothetic research is useful to study variability between patients in a sample, the results do not necessarily generalize to individual patients. In fact, between-persons and within-person associations can diverge in both magnitude and direction [6]. In a study investigating the occurrence of desirable and undesirable events in the daily life of individuals with chronic pain, Tennen and Affleck [6] showed that, on average, there was a moderate positive association between desirable and undesirable events (r=0.50), indicating that patients experiencing more desirable events (relative to other people), also experienced more undesirable events. However, the within-person correlations showed an inverse relationship (mean r=-0.25), indicating that on days that patients reported more desirable events, they experienced fewer undesirable events. Another study focusing on personality traits in the general population shows that the Big Five factor structure, which resulted from a between-person analysis, could not be generalized to individuals. Within-person analysis showed differences between persons in both the number of factors and in how the factors related to the personality items [5]. The above examples illustrate that outcomes of nomothetic research need not be valid for individuals, as they tend to relate to what Gordon Allport in 1937 called "a nonexistent average individual" [7]. According to Allport, researchers should put more emphasis on the unique patterns within individuals over time. This is what he named the "idiographic approach."

Allport was an early advocate of the idiographic, individual-based approach. In the 1960s and 1970s, the enthusiasm for idiographic research diminished. It was qualified as unscientific [8] and unrealistic [9], as there were no adequate methods for carrying out quantitative idiographic research [10]. At that time, idiographic research mainly referred to case study-based qualitative research. However, in the last 2 decades, new quantitative methods have been developed to perform idiographic research and researchers took up Allport's ideas again, calling for a new person-centered approach in health research [3,5,6]. One of the most promising research methods that can be used to employ idiographic research is ecological momentary assessment (EMA), also called experience sampling method or diary methods [11]. EMA is aimed at repeatedly assessing experiences, activities, and physiological parameters, once or multiple times a day, and is typically characterized by real-time data collection in a natural setting [3]. EMA data can be analyzed at the group level by, for instance, multilevel analysis [12]. However, a more recent development is time series analysis, which allows for the analysis of EMA data on an individual level (level of the idios). The combination of EMA

with time series analysis, which we refer to as "intensive time series design," has recently brought the idiographic approach back to life.

Intensive Time Series Designs in Health Research

A number of research examples can be found in which intensive time series designs are used to map the mental and physical functioning of individual people [13-18]. For instance, Bouchard et al [13] investigated the temporal relationships between dysfunctional beliefs, self-efficacy, and panic apprehension in a diary study of 12 patients suffering from anxiety. Multivariate time series analysis identified substantial heterogeneity between the patients in the dynamic associations between variables. In 3 patients, changes in panic apprehension were predicted by changes in dysfunctional beliefs, in 6 patients they were predicted by changes in self-efficacy, and in 2 patients they were predicted by both changes in dysfunctional beliefs and self-efficacy.

In another study, Rosmalen et al [18] used time series analysis to investigate the causal direction of associations between physical activity and depression in 4 patients who had experienced a myocardial infarction. They found that in 2 patients, depression predicted physical inactivity; in 1 patient, physical inactivity predicted depression; and in another patient, only a cross-sectional association between depression and physical inactivity was found. These results could be translated into concrete indications for treatment advice. For 1 patient, 1.5 hours of sports every 4 days led to a desirable degree of decrease in depressive symptoms, whereas for the other patients physical activity did not have beneficial effects on depression. These 2 studies indicate the potential of EMA combined with time series analysis for health care practice. The identification of individual patterns of symptoms, behaviors, and experiences sheds light on the most important functional and dysfunctional dynamics of a given person, providing concrete indications for tailored treatment advice [18].

Gap Between Research and Health Care Practice

Despite the promising examples described above, there still is a significant gap between the research context in which intensive time series analysis is experimented with and health care practice in which individual patients may profit from its results. An important challenge is the substantial burden that data collection and processing puts on patients and researchers. Patients have to complete at least 50 assessments, and preferably even more [19]. Researchers have to be experienced in advanced time series methodology, which they have to apply at an individual level, for each person separately. This has led some researchers to conclude that the idiographic approach is too time-consuming and too expensive for implementation on a large scale [20].

Intensive time series analysis can only be applied in daily care practice when certain requirements are met. First, data collection and data management should be standardized to some extent, as to enable professionals and patients to select relevant assessment domains from a prespecified set of measures. This is to prevent a situation in which intensive time series data collection needs to be built from scratch for every individual patient. Second, to deploy intensive time series in the course of

a treatment process, as a diagnostic means, or as a method to evaluate treatment effects, time series data need to be available real-time so that the outcomes can be used immediately. Third, it should be possible to conduct a reliable analysis of time series data, without extensive statistical training. Fourth, professionals and patients should be able to interpret the output of intensive time series and to understand how the results relate to their particular care context.

The latter 2 conditions, which allow for a situation in which the researcher becomes superfluous, may be the hardest and most fundamental conditions to meet. So far, analysis of time series data has always required advanced statistical expertise, including extensive knowledge of the statistical procedures and a high level of experience.

Statistical Modeling of Time Series

There are several forms of time series data. Time series can be event-based, in which the assessments follow a specific event, or time-based in which the assessments are performed at specific time points. Moreover, time-based assessments can be conducted either at fixed or random moments. Each method has its own purposes. If data is collected at fixed moments, with equidistant intervals in between time points, temporal dynamics between variables can be analyzed by a method such as vector autoregressive modeling (VAR) [19,21,22].

The "vector" term in vector autoregressive modeling refers to the multivariate character, which is an extension of the single variable autoregressive model. VAR models consist of a set of regression equations in which all variables are treated as endogenous variables, meaning that they function as both outcome and predictor. VAR analysis can be conducted without a prior hypothesis about the direction of the association between variables. A statistical test called the "Granger causality test" can be used to examine whether the lagged values of one variable x are useful in the prediction of values of another variable y. If so, it is said that variable x *Granger-causes* variable y [23]. VAR analysis can thus elucidate dynamic relationships between 2 or more variables, providing an impression of putative causal associations. The identification of these dynamic relationships, in turn, paves the way for unveiling detailed and patient-specific patterns of symptoms or experiences, their triggers, and their effects on functioning. An extensive description of the VAR technique can be found elsewhere [19,21,22]. At this point we should note that in the practice of EMA assessments, the distance between two consecutive time points often is not equal. In these cases, the raw time series data would not meet the VAR modeling assumption of equidistant time intervals. The EMA data can, however, be preprocessed such that they do meet this assumption. One such way of reprocessing is to use spline smoothing, followed by resampling at equal sampling intervals [24,25].

In the VAR modeling process, researchers are broadly faced with 2 main tasks, namely (1) to build statistical models and conduct a reliable, iterative analysis to evaluate the validity of these models and (2) to choose the best model with which they can work. The first task is predominantly a statistical one. Although the researcher has to make some choices, such as which variables to include in the VAR and the maximum lag length (ie, the maximum number of previous observations that contain relevant information for estimating the current observations), the biggest part of this task consists of statistical analysis conducted with predefined tests. By means of residual diagnostics, the models are checked for assumptions of stability, "white noise" (ie, no residual autocorrelation), homoscedasticity, and normality based on which valid models can be selected. The second task is less statistical. Choosing the "best" model out of all valid models mostly is an informed choice of content. It is based on a combination of statistical parameters (eg, model selection criteria like the Akaike information criterion (AIC) or the Bayesian information criterion (BIC)) theoretical assumptions about the data, and common sense. The researcher plays a crucial role here.

Aim

Quantitative idiographic assessment has shown to be promising, but application of this method in health care practice is hampered because analyses are conducted manually and advanced statistical expertise is required. This study aims to show how this limitation can be overcome by introducing innovative technology.

We provide a proof-of-principle that might bring idiographic assessments closer to health care practice by automating analytical processes. We developed a Web-based application, called AutoVAR, which automates time series analyses of EMA data and provides output that is intended to be interpretable by nonexperts. We report on our experiences with the program in re-analyzing a set of time series data.

Methods

Patients and Measures

To evaluate the outcomes of our automated analysis, we reanalyzed data that were previously analyzed in a manual analysis in a study by Rosmalen et al [18]. This data was obtained from 5 middle-aged (55-59 years old) Caucasian male patients suffering from post-myocardial infarction, recruited from screening for a psychoeducational prevention module (PEP) at the Máxima Medical Center in Eindhoven-Veldhoven, the Netherlands. The PEP module focuses on regaining emotional stability and dealing with cardiac disease as part of a cardiac rehabilitation program. Patients were considered eligible for study participation if they had a score of 10 or higher on the Beck Depression Inventory (BDI) [26], meaning that they suffered from mild to moderate depressive symptoms. The BDI is a self-report questionnaire assessing depressive symptoms in a reliable and valid manner [27]. The questionnaire addresses both cognitive and somatic depressive symptoms during the past week, such as hopelessness, guilt, fatigue, and weight changes. The BDI has 21 items, scored on a scale ranging from 0 to 3. Exclusion criteria for the study were significant cognitive impairments, life-threatening diseases, and severe problems with physical activity. Written informed consent was obtained from all patients. The study was approved of by the Medical Ethical Committee for mental health institutions in the Netherlands. Data collection took place in the first semester of 2010.

Patients were asked to complete daily measures of depressive symptoms and physical activity every evening, during a period of 3 months. Depressive symptoms were measured with the depression module of the Patient Health Questionnaire [28], which was adapted for daily use. The Patient Health Questionnaire includes 9 items assessing depressive symptoms based on the DSM-IV criteria for major depressive disorder. The items were rated on a 4-point scale ranging from 0 to 3. The sum score (0-27) was used as a measure of depression severity. Level of physical activity was measured by 7 items describing physical activities (eg, commuting activities, work activities, household activities, sports, and other leisure activities), of which patients had to report the amount of time in minutes they had spent on them [18]. The total daily amount of time being physically active was used in the analysis.

To encourage compliance to the daily assessments, patients were promised that they would be provided with a personal report of the assessments results after completion of the assessments. They were also offered a small gift certificate of €25. During the study period, one patient dropped out after 2 weeks because he was too busy at work and could not manage to complete the daily assessments. This patient was not included in the analysis.

Automated Time Series Analysis With AutoVAR

Our starting point was the study by Rosmalen et al [18]. We aimed to investigate whether the complex time series analysis using VAR modeling, which was conducted manually in the Rosmalen study, could be automated. To automate the analysis processes performed by Rosmalen et al, one of the authors (AE) developed an open source R package that includes a front-end Web application. This application reads raw data in an SPSS or STATA file and fits the data into VAR models. For the VAR modeling, the existing R package for VAR modeling is used [29]. In the new application, one can upload a data file, select variables for time series analysis, specify the maximum number of lags, and run the program (see Figure 1). For this paper, we selected the variables Activity and Depression from the Rosmalen dataset. The right column in Figure 1 shows all variables included in the dataset. Under the tab "Exogenous variables" one can add exogenous variables. Under the tab "Advanced settings" one can change settings (eg, change ordering from AIC to BIC scores).

AutoVAR is developed to take over those actions that in the manual analysis can only be conducted by a statistical expert. The solution that AutoVAR follows is to test all possible models within given restrictions and to summarize outcomes of all valid models. When the program is running, AutoVAR creates time plots for each selected variable, defines the possible VAR models, checks all models for validity, and finally presents all valid models. AutoVAR is freely accessible online and it is accompanied by documentation and a user example [30-32]. For a discussion of AutoVAR from a computing science perspective, see also Emerencia et al [33]. (We would like to note that the AutoVAR package is work in progress. We are currently working on improving the package's functionality.)

The total number of possible VAR models is determined by the combinatorial search space. AutoVAR's combinatorial search space is defined by multiple factors:

1. The lag length. The lag length refers to the maximum number of previous observations that contain relevant information for estimating the current observations. AutoVAR tests all lag lengths, up to a maximum set by the user by typing the number into the box "Max. lag." In this paper, the maximum lag length was set to 2, following the procedure by Rosmalen et al [18]. In a manual analysis, a researcher tests those lag lengths that seem to make sense, based on theoretical plausibility, common sense, and lag length selection criteria (eg, the likelihood ratio test, final prediction error, Akaike information criterion, Hannan-Quinn information criterion, and the Bayesian information criterion).

2. Potential need for inclusion of a trend variable. AutoVAR checks whether a time series is stationary around a trend with the Phillips-Perron test [19]. If this test is significant, a trend term is added to the model as an exogenous variable. In a manual analysis, the presence of a trend variable is determined either by looking at the time plots and judging whether the mean of the time series changes over time or on the basis of a stability test (eg, the Eigen value stability condition [19]).

3. Potential need for inclusion of seasonal variables. AutoVAR checks whether seasonal variables should be included using dummies for the weekdays (if AutoVAR's option "timestamps" is checked). AutoVAR evaluates, by default, every model twice. Once with and once without dummy variables for weekdays. In a manual analysis, dummy variables for weekdays are added when it seems to make sense, for instance when a lag of 7 is indicated by lag length selection criteria.

4. Potential presence of outliers. Outlier values that violate model assumptions are accounted for in AutoVAR and manual analyses by including a dummy variable as an exogenous variable (eg, 0/1). In AutoVAR, outliers are defined as values larger than 3.5, 3.0, or 2.5 standard deviations from the mean of the residuals. AutoVAR will first test a model without outliers; if this model is invalid, it will test a model with outliers that deviate 3.5 standard deviations from the mean of the residuals; if the model is still invalid, it will test a model with outliers that deviate 3.0 standard deviations. If this still yields no valid model, AutoVAR will stop, unless the option is checked to look for outliers of 2.5 standard deviations. In a manual analysis, the presence of outliers is determined by looking for extraordinary values in the time plots of the (residuals of the) variables and based on additional information provided by the patient.

5. Log transformation. AutoVAR constructs and calculates each model with and without log transformation. In a manual analysis, a researcher determines whether a log transformation is necessary based on a normality test, such as the Skewness-Kurtosis test [19]. If this test is significant, the residuals do not have a normal distribution. A log transformation is applied when this non-normality is caused by a skew to the right. This skew to the right can be

determined by checking the histogram, the time plot, or the box plot of the residuals.
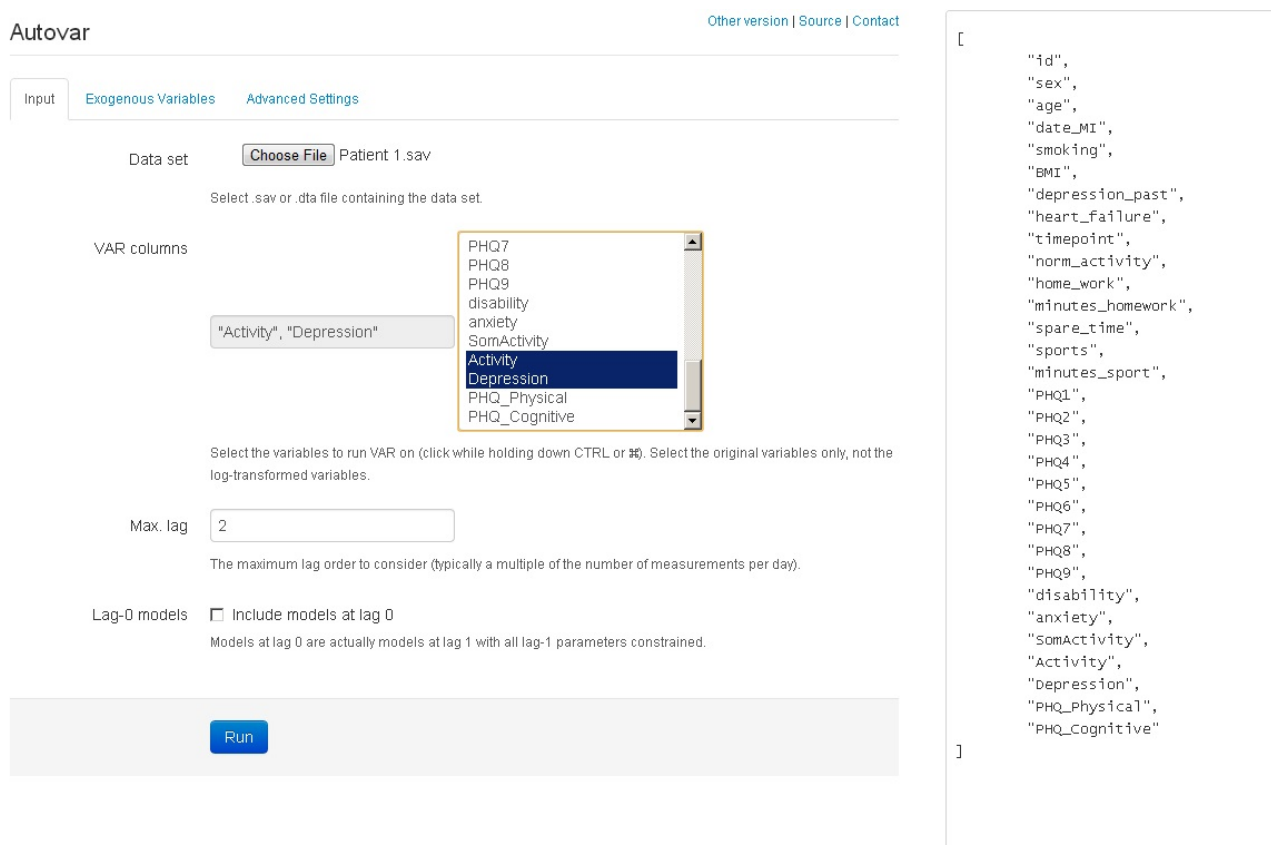
6. Potential need for constraints put to model parameters. Like the manual procedure, AutoVAR sets to "0" those parameters that do not significantly contribute to the model, starting with the parameter that has the highest *P*-value. After each constraint, the VAR model is rerun, until the chosen goodness-of-fit criterion (AIC or BIC) ceases to become smaller. In addition to the manual procedure, AutoVAR checks assumptions for stability, "white noise," homoscedasticity, and normality after every constraint has been set (see also below).

7. Potential need for exogenous variables added to the model, based on additional patient information. Sometimes time plots show strange characteristics (eg, an unexpected increase in activity) that may be explained by external factors (eg, change of jobs). In AutoVAR, these external factors can be added to the model, by having the user select them as "additional exogenous variables." In a manual analysis, the researcher adds additional exogenous variables to the model as part of the regular analysis procedure.

After each model is estimated, AutoVAR checks them for validity by means of an automated residual diagnostics procedure, in which 4 assumptions are tested. The stability assumption is checked by the eigenvalue stability condition, the "white noise" assumption by a Portmanteau test on the residuals, the homoscedasticity assumption by a Portmanteau test on the squares of the residuals, and the normality assumption by the Skewness-Kurtosis test (see [19]). All tests must be nonsignificant for all variables for AutoVAR to consider a model valid. If one of these tests indicates a violation of the model assumptions, the model is adjusted, reestimated, and reevaluated in an iterative model building process until all assumptions are met (or until meeting all assumptions appears impossible, meaning that no valid models can be found). This process is similar to the manual procedure.

The validity of models also plays a role in the total number of models that AutoVAR runs. Strictly speaking, AutoVAR does not run all possible models defined by the combinatorial search space, but only the nonredundant ones. Of all the models that AutoVAR considers, it filters out the redundant models prior to running the final model calculations. AutoVAR considers a model redundant when it is not needed for optimization of the data modeling. For instance, a valid model without modeled outliers makes a model with the exact same model specifications but with modeled outliers redundant. This is to say that AutoVAR always tries to fit the most simple model (eg, without outliers) to the data first and only resorts to more complex models (with outliers) when these simple models do not suffice (ie, when they invalidate one or more of the model assumptions). This procedure has consequences for the number of valid models that can be fitted to the data. If simple models do not suffice to fit the data, AutoVAR has to resort to more complex models and thus the total number of possible models increases. For instance, if a model without outliers is not valid, AutoVAR will widen the combinatorial search space to include models with outliers. As a result, the total number of valid model fits for complex models often will be higher than the total number of valid model fits for more simple models. Finally, for all valid models, AutoVAR calculates AIC and BIC scores. AutoVAR orders the valid models on ascending order of the best (ie, lowest) AIC or BIC score. If the ordering of models based on AIC scores differ from the ordering based on BIC scores, AutoVAR will present the ordering based on AIC by default. However, users have the option to change the ordering based on BIC score by checking a box on the Advanced Settings page. Results of Granger causality tests are summarized in an image.

The AutoVAR procedure deviates from the manual procedure in two important respects. First, AutoVAR tests all possible VAR models within a given combinatorial search space, whereas a researcher tests a selection of models based on statistical and theoretical considerations. Second, AutoVAR orders the valid models and presents all of them in a Granger causality image, whereas a researcher evaluates the models and chooses one "best" model.

Figure 1. AutoVAR screenshot.

VAR Model

The basic VAR model used in this study was the same model as the one used by Rosmalen et al. The model consists of a system of two endogenous variables, namely, depression and physical activity, which are shown in Figure 2 below.

In these equations α_i, β_i, Υ_i, and δ_i are the coefficients to be estimated, p is the number of lags considered in the system, and the ε_t is the stochastic error term. Each endogenous variable is made up of a constant, a regression coefficient determined by its own p lagged value, a regression coefficient determined by the p lagged value of the other variable, and a random error component. The error terms should be serially uncorrelated but can be contemporaneously correlated. Potential confounding factors can be accounted for by adding a control variable to the VAR model (not included in the formulas). This control variable is an exogenous variable, meaning that the variable can affect the model but cannot be affected by the model.

There are 4 main assumptions that need to be met for a VAR model to be valid: (1) the stability assumption requires that the VAR model is stable (ie, that it is stationary over time), (2) the "white noise" assumption requires a model to leave no autocorrelation in the residuals, (3) the homoscedasticity assumption requires homogeneity of variance over time, and (4) the normality assumption requires the residuals to be normally distributed.

In the Rosmalen et al study, the VAR analyses were performed in STATA 11 software, using the suite of VAR commands [34].

AutoVAR uses the existing R software package for VAR modeling [29].

Figure 2. The endogenous variables for depression and physical activity used in this study.

$$Activity_t = \alpha_0 + \sum_{i=1}^{p} \alpha_i\, Activity_{t-i} + \sum_{i=1}^{p} \beta_i\, Depression_{t-i} + \varepsilon_{1t}$$

$$Depression_t = \beta_0 + \sum_{i=1}^{p} \gamma_i\, Activity_{t-i} + \sum_{i=1}^{p} \delta_i\, Depression_{t-i} + \varepsilon_{2t}$$

Results

Output of AutoVAR

For patient 1 of the study by Rosmalen et al [18], AutoVAR generates the following output (see Table 1, first column). It provides a time plot of the activity and depression series, showing how activity and depression fluctuate over time. Furthermore, the textual output of AutoVAR summarizes the VAR model selection procedure. Forty-three VAR models out of 216 possible combinations were tested (19.9%). In the combinatorial search space, 216 is the maximum number of models that can be created, with a maximum lag length set on 2 (ie, 2 days). A total of 173 models were not tested due to redundancy. Of the 43 models tested, 2 of them appeared to be valid, meaning that they met the assumptions of stability, "white noise," homoscedasticity, and normality. Both models indicated that physical activity Granger-caused depression and that the sign of the association was negative. In AutoVAR, the best model was presented at the top, with an AIC of 631.22 and a BIC of 655.41.

Table 1. Comparison of AutoVAR output versus manual analysis output.

		Autovar analysis	Manual analysis
Patient 1 (T[a]= 83)	Granger causality Wald test	Increase activity → decrease depression (*P*=.03)	Increase activity → decrease depression (*P*=.03)
	Lag length	2	2
	Trend variable included	No	No
	Weekday dummies included	No	No
	Outlier variables	Outlier dummies for day 4 (Depression) and day 13 (Activity)	Outlier dummies for day 4 (Depression) and day 13 (Activity)
	Log transformation	No	No
	BIC	655.41	655.89
	AIC	631.22	631.70
Patient 2 (T=63)	Granger causality Wald test	Not significant	Not significant
	Lag length	1	1
	Trend variable included	No	No
	Weekday dummies included	No	No
	Outlier variables	Outlier dummy for day 12 (Depression)	Outlier dummy for day 12 (Depression)
	Log transformation	Yes	Yes
	BIC	390.07	386.15
	AIC	381.49	375.43
Patient 3 (T=63)	Granger causality Wald test	Increase depression → decrease activity (*P*<.001)	Increase depression → decrease activity (*P*<.001)
	Lag length	2	2
	Trend variable included	Yes	Yes
	Weekday dummies included	Yes	Yes
	Outlier variables	Outlier dummy for day 5 (Depression)	Outlier dummy for day 5 (Depression)
	Log transformation	No	No
	BIC	307.21	304.64
	AIC	275.06	283.21
Patient 4 (T=58)	Granger causality Wald test	Increase depression → decrease activity (*P*=.04)	Increase depression → decrease activity (*P*=.04)
	Lag length	1	1
	Trend variable included	No	No
	Weekday dummies included	No	No
	Outlier variables	Outlier dummy for day 27 (Depression)	Outlier dummy for day 27 (Depression)
	Log transformation	Yes	Log transformation yes
	BIC	398.59	398.59
	AIC	386.23	386.23

[a]T is the number of time points at which patients completed a measure.

The results of the Granger causality tests of all valid models are summarized visually, in a rather self-explanatory image in Figure 3. The thickness of the line connecting "Activity" with "Depression" indicates the proportion of valid models in which this Granger causal association was found (the thicker the line, the more models), which can be interpreted as the probability of the effect. The arrow shows the direction of the association. The line style (or, in AutoVAR, the color of the line) designates the sign of the association: continuous means a positive association, dashed with equal dashes equals a negative association, dashed with unequal dashes means a mixed positive and negative association within the model (ie, estimates show

a positive and a negative sign, at different lags, within the model), dashed with points shows mixed positive and negative association among models (ie, some models show a positive, some a negative sign). From the first image in Figure 3, one can infer that for patient 1 inactivity is likely to Granger-cause an increase in depressive symptoms, whereas there is no indication that it is the other way around.

For the other 3 patients in the Rosmalen et al study, the Granger causality images generated by AutoVAR are also presented in Figure 3. For the data of patient 2, AutoVAR concludes "Granger causality summary: none." The data of patient 2 did not show any Granger causal associations, meaning that no image could be created. For patients 3 and 4, the image shows that their depressive mood is likely to Granger-cause them to

become physically inactive, whereas there is no indication that inactivity Granger-causes depression. These Granger causality images provide diagnostic information that can be used rather intuitively to guide tailored treatment decisions. If the time series data of patient 1 show that inactivity is likely to increase depressive symptoms, then it makes sense to advise this patient to become more active, as this may have a positive effect on his mood. In contrast, patients 3 and 4 probably would not benefit from this advice. Their personal network indicates that a depressive mood has an effect on physical activity instead of the other way around. In their case, the main target of intervention would be the depressive symptoms. These patients might therefore profit more from therapy targeting their depressive symptoms, such as pharmacotherapy or psychotherapy.

Figure 3. Granger causality plots.
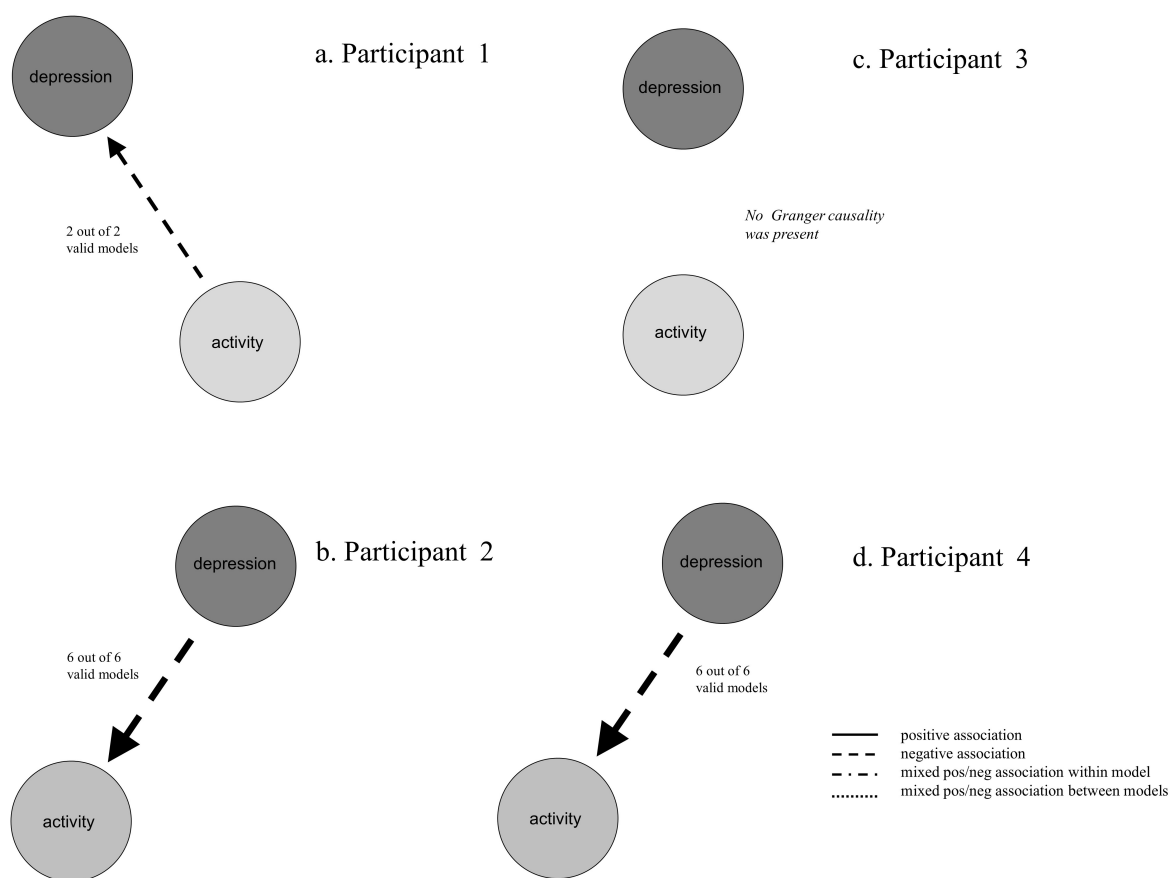
Automated Analysis Compared to Manual Analysis

Comparing the output generated by AutoVAR to the outcomes resulting from the manual analysis described by Rosmalen et al, we found rather similar results in terms of model specification, model validity, information criteria, and Granger causality estimates (see Table 1). For patient 1, both methods found an optimal lag length of 2, included no trend or seasonal variables (weekday dummies), required no log transformation, and included the same two outlier variables. Furthermore, the top model in the ordering by AutoVAR (both AIC and BIC orders) matched the best model chosen in the manual analysis

by Rosmalen et al, and both showed a significant negative Granger causal relationship between activity and depression.

Discussion

Principal Findings

In this paper, we provided a potential solution to bridge the gap between the use of intensive time series analysis in research and health care practice by automating the analysis processes. Results suggest that automated time series analysis is feasible and that the output can be presented in an intuitive way. Automated analysis can make the role of the statistical

interpretation less important and, as such, it saves a significant amount of time. Whereas AutoVAR generates results in a few seconds, manual analysis may take several days. Automated analytical procedures and accessible visual presentation of statistical outcomes might pave the way for health care professionals and patients to use methods such as EMA as an integral part of the treatment trajectory, without extensive training. As such, general treatment guidelines based on nomothetic research could be complemented by idiographic-based information. This may support health care professionals in taking a tailored treatment approach. Although the personal narrative of patients remains an important basis for tailor-made treatment, intensive time series assessments can add information that professionals are unable to see with the naked eye. EMA may be particularly valuable in those situations in which treatment trajectories have become stuck, when patients do not sufficiently benefit from treatment, and professionals do not know why. Furthermore, since completing EMA assessments can be quite an investment, an automated EMA approach may be especially suitable for settings in which patients receive long-term treatment for a chronic disease, such as depression or a heart disease in which controlling, instead of curing, is the main focus. The creation of a thorough and detailed patient profile of symptoms, behaviors, and experiences can help to shape the treatment toward individual needs.

Apart from EMA being an instrument to support professionals, we may also speculate that automated time series analysis provides opportunities for using EMA as part of self-management processes. If patients are able to analyze and interpret their own data, they may find it helpful to monitor themselves and map their symptoms or functioning in certain situations or periods. A promising perspective is sketched by Nikles et al [35] who conducted a study among patients with ADHD and osteoarthritis participating in idiographic research and found that the assessments led to increased knowledge and awareness of their condition, a better management of their bodily functions, and a sense of empowerment. We should note that if patients use EMA assessments for self-monitoring, they may change their behavior in response to their data, which implies that the resulting time series may no longer be stationary. However, these changes in behavior can be accounted for in the VAR model by adding a trend variable to the model.

Strengths and Limitations

AutoVAR is promising, but the application needs further validation and refinement prior to implementation in health care practice. In this study, we applied AutoVAR to replicate the results of the manual analysis conducted by Rosmalen et al. Analysis of additional datasets is needed in order to validate the application for general use. Whereas the output of AutoVAR was rather similar to the manual output of the Rosmalen et al study and the most important output, namely the directions of the Granger causality relationships were identical, the model selection criteria (AIC and BIC) were not exactly the same in the different procedures. This may be due to differences in optimization algorithms in STATA versus R and therefore needs a more thorough scrutiny of discrepancies between the statistical packages in future research. An important question in this context is how to determine the validity of different procedures.

In this paper, we compared automated analysis to manual analysis. Nevertheless, the manual analysis need not be the golden standard. The major advantage of a manual procedure is that a researcher can make informed decisions about the analysis process in a way that an application like AutoVAR can perhaps never do. These decisions are, however, subjective. They may depend on the researcher's experience, preference, and "staying power." As a consequence, valid time series models might be overlooked in a manual procedure. AutoVAR, in contrast, takes into account all possible models, thus following a more objective procedure. A limitation of this latter procedure is the risk of capitalization on chance. By testing many models, AutoVAR may generate more incidental findings. In the current version of AutoVAR, we tried to minimize this risk in 3 ways: (1) by not running redundant models, (2) by an extensive check of validity assumptions, and (3) by summarizing the results of the Granger causality tests in an image in which the thickness of the arrow indicates the probability of the effect.

The automated processes of the current version of AutoVAR need to be optimized. AutoVAR cannot yet handle missing data. VAR models can be processed with missing values, but this is suboptimal as this usually decreases the number of observations considerably, and thus decreases statistical power. Data collected from assessments completed at non-equidistant time intervals need to be preprocessed before AutoVAR can analyze them. There is as yet no functionality in AutoVAR to use spline smoothing and resampling of data. Moreover, AutoVAR currently functions most optimal when several settings are set manually. The lag length is one of these settings. AutoVAR also has several options that users can choose to check or leave blank, such as setting timestamps and adding additional exogenous variables based on patient information. These issues need to be solved before using automated analysis in health care practice. In addition, the user interface of AutoVAR has a rather technical look-and-feel and therefore needs a radical redesign to meet the criteria of user-friendliness for health care practice. We are currently working on an improved version of AutoVAR in which we will account for these issues.

One of the most important limitations of idiographic analyses compared to nomothetic analyses is their presumed limited generalizability. What holds for one individual is not necessarily true for another. Nevertheless, the question is whether this limitation needs to be overcome in the context of health care practice, for in this context the presumed weakness of idiographic research can also be considered one of its main strengths. If the main aim is to elucidate the specific temporal patterns of symptoms or experiences, and their triggers and effects on functioning within one specific patient, then the argument of generalizability to a larger population does not hold. The principal requirement for a meaningful use of intensive time series analysis as a supportive means in diagnostics and treatment of a specific individual is that the models selected provide a good description of the dynamic relationships in the EMA data registered by that very individual. Nevertheless, what remains is the issue of generalizability over time, within an individual. Whether the results of time series analysis need to be generalizable to the individual patient on multiple moments depends on the context. In those treatment

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contexts in which one is mainly interested in the temporal dynamics of variables in a specific time window, a single time series analysis may suffice and its results do not need to be generalizable to other points in time. Nevertheless, if one wants to generalize within one individual over time, for instance when the aim is to unveil the temporal dynamics of variables that are assumed to be rather stable, a second time series analysis is needed to confirm the explorative results of the first analysis.

Finally, instead of having nomothetic research replaced by idiographic research, the most ideal situation may be a combination of both. Gates et al [36] presented a procedure called Group Iterative Multiple Model Estimation that enables individual-level modeling while simultaneously identifying commonalities across individual models. Furthermore, time series analysis provides information about relationships between variables over time, but not about the meaning of mean levels of the variable values. To evaluate the level of variable values (eg, evaluating scores as falling into a clinical or nonclinical category), health care professionals and patients may profit from relating time series data to population-based norms.

Implementation and Future Perspectives

The benefits of automated time series analysis can only be fully exploited when it is embedded in an "EMA-friendly" health care context. Just like the analysis and interpretation processes, the collection and management of data also need to be facilitated. This may best be realized by integrating time series assessments in the existing information technology infrastructure used by professionals and patients, such as systems for routine outcome monitoring (ROM). In the Netherlands, almost all mental health organizations use electronic ROM systems, which offer professionals and patients the opportunity to select and complete questionnaires and other measurements, of which the results are automatically presented in the electronic patient files. These systems were created for the mandatory yearly routine assessments among patients in which health care effects are examined. However, several systems have been extended with functionality for frequent and repeated assessments; for instance, by means of a diary app [37].

To facilitate intensive time series measurements, the electronic monitoring systems should include a specified set of reliable instruments that are appropriate for time series analysis of particular variables. From this set of instruments, health care professionals can select the relevant variables for specific patients. Time series diaries might also be automatically composed by having variables selected based on deviating scores on completed ROM measures. Time series measurements need

not be restricted to self-report questionnaires. Current technological developments have given rise to smart and consumer-priced mobile devices measuring heart rate, activity, sleeping behavior, and so on. An increasing number of devices have a so-called open application programming interface, meaning that the data collected by these devices can be used by and be integrated into existing applications. Provided that they are validated, these devices can be excellent EMA data collectors. They often collect data automatically, so that minimal input is needed from the person who carries the device.

If patients are willing to participate in intensive time series measurement, they will have to deal with a long series of assessments. Motivation to complete the assessments is therefore crucial. A key element in motivating patients for EMA data collection is demonstrating to patients the personal and theoretical benefits EMA can have for them prior to the assessments [38]. Furthermore, during the assessment period, feedback on completed assessments may encourage patients to continue to next assessments. This feedback can consist of basic information about the percentage of successfully completed assessments or more advanced feedback about results obtained so far. Apart from the length, the repetitiveness of the assessments is an important obstacle in completing a time series [38]. A possible remedy to this problem may come from computerized adaptive testing and machine learning processes that can provide the basis for dynamic assessments, adapted to the individual [38].

Future studies should examine whether patients and care professionals are actually willing and able to use time series analysis in an individual care trajectory and how intensive time series analysis can best be integrated into the daily care practice. In addition, we need to investigate whether tailored treatment advice, based on the analysis, can improve clinical outcomes. After all, this is the ultimate test to determine the actual validity of intensive time series analysis for health care practice.

Conclusions

In this paper, we have conducted a proof-of-principle study that has demonstrated the viability of a quantified idiographic approach in health care practice by using automated time series analysis. Compared to a manual procedure, the automated procedure is more robust and saves a significant amount of time. In addition, the output of automated time series analysis can be presented in an intuitive way. These findings may pave the way for health care professionals and those in need of care to use intensive time series analysis as an integral part of the treatment trajectory, without extensive statistical training.

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Conflicts of Interest

None declared.

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Abbreviations

AIC: Akaike information criterion
BIC: Bayesian information criterion
EMA: ecological momentary assessment
ROM: routine outcome monitoring
T: time points
VAR: vector autoregressive

<u>Original Paper</u>

Using Social Media While Waiting in Pain: A Clinical 12-Week Longitudinal Pilot Study

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Abstract

Background: Chronic pain places an enormous burden on health care systems. Multidisciplinary pain management services are well documented as an effective means to improve patient outcomes. However, waiting lists to access these services are long and outcomes deteriorate. Innovative solutions such as social media are gaining attention as a way to decrease this burden and improve outcomes. It is a challenge to design research that demonstrates whether social media are acceptable to patients and clinically effective.

Objective: The aim was to conduct a longitudinal pilot study to understand what aspects of research design are key to the success of running a larger-scale study of social media use in the clinical management of chronic pain.

Methods: A 12-week study examined social media use by patients on the waiting list for the Royal Melbourne Hospital Pain Management Service. Selected social media resources were suggested for use by patients waiting for an appointment at the clinic. Patients filled out measures for pain interference and pain self-efficacy before and after the study. Follow-up was conducted at monthly intervals via telephone semistructured interviews to discuss engagement and garner individual perceptions towards social media use. A social media-use instrument was also administered as part of the after-study questionnaire.

Results: Targeted recruitment refined 235 patient referrals to 138 (58.7%) suitable potential participants. Contact was made with 84 out of 138 (60.9%) patients. After a further exclusion of 54 out of 84 (64%) patients for various reasons, this left 30 out of 84 (36%) patients fitting the inclusion criteria and interested in study participation. A final study cohort of 17 out of 30 (57%) was obtained. Demographics of the 17 patients were mixed. Low back pain was the primary condition reported as leading to chronic pain. Semistructured interviews collected data from 16 out of 17 (94%) patients who started the trial, and at final follow-up 9 out of 17 (53%) patients completed questionnaires. Low specificity of the resources to one's condition and time poorness may have been barriers to engagement.

Conclusions: Results suggest that with refinements, this study design can be implemented successfully when conducting a larger social media study. At present, comment cannot be made on what effect using social media can have on patients on hospital waiting lists, nor whether those who use social media while waiting in pain achieve better outcomes from eventual participation in a chronic pain program. Long-term follow-up should be included in future studies to answer this. Future research should focus on multicenter randomized controlled trials, involving patients in the intervention design for improved participation and outcomes and for evidence to be sound.

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Introduction

Chronic pain is one facet of chronic disease placing a significant burden on health care systems and individuals alike, through stigma, personal suffering, loss of income, and isolation. It is estimated to affect approximately 1 in 5 Australians and to cost the economy AUD $34 billion a year [1-4]. One consequence has been increased waiting list times to access clinic-based pain management services (up to 6 months). This correlates to poorer patient-reported outcomes (PROs) for quality of life (QOL), and for psychological and physical well-being [2,5].

Specialized multidisciplinary team approaches and pain management programs are well-established forms of management [1] for the primary reasons of cost, social interaction, and sensations of validation among attendees. There has been a strong national endeavor across pain services to monitor patient outcomes to ensure that treatments provided actually result in improved function and QOL for patients [6]. Regardless, the health care system struggles to provide timely access to such services. Chronic pain self-management support is, therefore, crucial.

Barlow and colleagues describe self-management as the individual's ability to manage the symptoms and treatment, as well as the physical and social consequences of lifestyle changes linked to living with a chronic condition [7]. Various self-management interventions have been described, for example the Stanford model of chronic disease self-management program, acceptance and commitment therapy, and cognitive behavioral therapy (CBT) [1]. From a broader health care system point of view, benefits of effective self-management strategies can include decreased medical consultations, hospitalizations, and imaging investigations. From a patient point of view, benefits include decreased use of analgesic and days off work, as well as improved QOL, mood, self-efficacy, and empowerment, to name a few [1,8,9].

Innovative and cost-effective strategies are recommended to alleviate the pressing need for self-management support [2,10]. Web-based resources are one area gaining attention [1,5,10]. These may be implemented as stand-alone interventions, as adjuncts to traditional care, or as tools to bridge the waiting time between obtaining a referral from a general practitioner and receiving a place in a pain clinic program [11]. Recent examples in Australia include the following: painHEALTH from Western Australia [12] and the Pain Management Network from New South Wales [13]. However, it is a challenge to demonstrate that such resources are clinically effective and accepted by patients [11].

The success of Web-based resources may lie in their ability to provide individuals with a means to tailor management to their own needs, as well as a channel for support outside of traditional clinic hours [1,11]. This is a distinct advantage over offline chronic pain management; there is the potential to reach large, diverse populations at relatively low cost and provide geographically unrestrained access to resources. Hence, their appeal for reaching people with chronic pain (PWCP) in remote areas, those with changing schedules, stigmatized and isolated individuals, and those who have mobility issues [11].

Social media—sometimes referred to as Health 2.0 tools—provide an innovative approach to Web-based resources. Unlike general Web-based interventions, social media are characterized by more highly evolved platforms that allow enhanced user engagement and autonomy, as well as greater social functionality and interaction [14,15]. This ultimately allows patients to better appraise their own individual situation. In social cognitive theory this is called self-efficacy [1] and it can be enhanced by peer modeling and support, things that social media may enable. Patients may thus become more empowered and engaged in collaborative self-management [16-18].

Studies have examined social media use in chronic pain [19-21]. However, none have examined the utility of social media for PWCP on waiting lists for specialist pain services. Nor have any studies involved patients in the study design process, with a focus on their perceptions and motivations for using different social media [22]. Results from studies conducted to date are not yet sufficient to inform design or implementation of social media interventions in clinical settings [23]. Greater emphasis is needed on conceptual research frameworks within a participatory health research paradigm for social media to become useful tools in chronic pain self-management [24].

Therefore, the aim of this pilot study was to understand what aspects of research design are key to the success of running a larger-scale study of social media use in the clinical management of chronic pain.

Methods

Overview

The methodology of this pilot study aligns with previous research into the therapeutic affordances of social media in PWCP [25-27]. This approach recognizes that each patient has individualized needs, building on the principles of participatory health care [28].

The setting chosen for the study was the Royal Melbourne Hospital—Pain Management Services (RMH-PMS). The Royal Melbourne Hospital (RMH) is a large publicly funded hospital in Melbourne, Australia. It offers one of the most comprehensive outpatient pain management services in the country. RMH-PMS has between 900 and 1100 outpatient referrals per year. At any one time, there are from 200 to 300 PWCP on the waiting list, and they have a wait time of 6 to 8 months for a first appointment. RMH-PMS provides an ideal context in which to test a social media intervention.

Ethics

The Human Research Ethics Committees of Melbourne Health and the University of Melbourne approved this study (ID No. 2014.043). During the review of the project, the ethics committee specifically considered the following areas of study design:

1. The sample: comments were made about representativeness and selection of the sample, as well as the impact using social media may have on expectations of patients for management of their condition.

2. Social media resources: feedback centered on anticipated outcomes and what impact social media would have on participants' conditions. Queries related to the appropriateness of the resources, who would be responsible for the content, and monitoring the resources.

3. Logistics and staff allocation: this covered staff and time required to recruit, to manage participant numbers during the study, to collect data, and to conduct follow-up.

Targeted Patients and Recruitment

The sample pool consisted of patients with chronic pain—pain of greater than 3-months duration [29,30]—on the RMH-PMS outpatient waiting list. Sampling was sequential and inclusion criteria were applied (see Table 1). Exclusion criteria were also applied, including the following: a change in priority status (ie, immediate intervention required) or discharge from the waiting list.

Table 1. Study inclusion criteria.

Inclusion criteria	Comments
Competent in English (reading and writing)	
Regular Internet access and competent usage abilities based on a preexisting, validated model [31]	An Internet-literate cohort was sought because Internet users were the primary point of reference for this study.
Willing to register with Gmail and Facebook (if they didn't already have accounts) and be bound to each site's terms and conditions	
Not currently undertaking any online intervention to manage their pain	
Not currently using chronic pain-related social media resources for management of this condition	We defined this as follows: being a member of a pain support group online and/or regularly reading blogs, watching videos, and contributing to forums about pain (this did not exclude general/personal social media use).
Medically appropriate (based on physical/psychological status, cognitive function, visual/hearing function)	This was determined by clinical study investigators.

A clinically relevant sample was sought. Desired cohort size for this study was estimated based on the following factors: participant numbers used in pilot studies within a similar domain [32-38], the number of referrals to the RMH-PMS program within a 3- to 4-month period, and the number of patients managed in the pain service at any particular time. Based on a combination of these factors, the aim was to enroll approximately 20 patients.

Potential patients classified as *priority 2* were sourced from the RMH-PMS Direct Access Unit referrals database. *Priority 2* includes patients receiving support via a primary care practitioner while waiting for a consult at RMH-PMS. Referrals are received from general practitioners in the local area, community health centers, other medical specialists, and internal referrals from RMH. Each referral was reviewed for preliminary suitability by two of the study's investigators who met nine times between April and September 2014. Potentially suitable participants were flagged based on matching information recorded in their referral with study inclusion/exclusion criteria (ie, English language ability, current interventions/treatments, any significant conditions requiring treatment noted in the history). Recruitment was conducted via phone calls from July to September 2014. The people reached were advised of typical waiting list times and introduced to this study as a self-management strategy available in the meantime. The phone transcript can be found in Multimedia Appendix 1.

Interested patients were emailed with a link to the study website and a unique identifier. The link led to SurveyMonkey—an online survey site—where the study information, consent form, and pretest questionnaire were hosted. After 1 week, follow-up phone calls were made to discuss the study, determine suitability, confirm Internet competence, and to ensure the prestudy questionnaire was submitted to confirm registration in the study. Once registered, contact was made to discuss final details and educational material was emailed that contained links to the suggested social media resources and instructional videos—filmed by the study's primary investigator—to act as an introduction to the resources and provide instructional information for using the resources. The educational material can be found in Multimedia Appendix 2.

Patients who were ineligible to participate in the study were provided with information about online resources (ie, painHEALTH [12]) if they desired for their future reference.

The Intervention

Each enrolled patient completed the intervention over 12 weeks and because recruitment was staggered, some commenced at different points in time. The entire intervention period ran from July 24 to December 5, 2014. Waiting list time is typically between 6 and 8 months with specialist preclinic pain education provided close to the medical admission appointment. Therefore, treatment was not delayed by completing this study. No

incentives were offered to participate. It was also explained that the study was a pilot study and that participant feedback may help to shape future consideration of social media resources for the RMH-PMS.

Patients were informed that the intervention consisted of using the suggested social media-based pain management resources in an unrestrained fashion over the allotted time period. Patients were asked to interact with these at their own pace. They were given the autonomy to be selective as to which they interacted with and how. Of interest was the impact that use might have on their condition and on their understanding about pain management, and finally, to know how they interacted with the resources—this would be examined during monthly semistructured interviews that will be described further.

The social media resources incorporated into this study included a large chronic pain support community on Facebook, a selection of chronic pain blogs, and pain management YouTube videos filmed by painHEALTH. Further detail about these resources and their selection for this study can be found in Multimedia Appendix 3. These particular platforms were suggested based on social media used by PWCP from a global online survey investigating social media use in chronic pain self-management. Also, platforms were selected based on each platform's ability to foster various therapeutic affordances that appear conducive to positively impacting health effects in chronic pain [26,27]. The resources were reviewed and agreed on by all study investigators from both the Health and Biomedical Informatics Centre at the University and RMH-PMS.

Outcome Measurement

Pre- and postintervention data were collected, as well as data collected at monthly intervals during the study. To start, participants completed a questionnaire on SurveyMonkey that amalgamated demographic information, chronic pain status, and patient-reported outcome measures (PROMs)—pain interference and pain self-efficacy—into one survey (see Multimedia Appendix 4). Patient-reported outcomes (PROs) provide insight into the patient's perception of the impact that interventions have on their health [18].

Pain interference (PI) is an example of a regularly examined standardized outcome that measures the burden on an individual across a wide range of health-related quality-of-life (HRQOL) measures [39,40]. PI was measured using 16 items from the Patient-Reported Outcomes Measurement Information System—Pain Interference (PROMIS-PI) item bank and included one item from the pain behavior item bank to measure pain severity. Unlike common legacy outcome measures used to measure chronic pain, the PROMIS-PI item bank demonstrates good reliability and validity across a variety of chronic diseases, including chronic pain, and shows strong correlations to other common outcome measures, allowing findings from this study to be compared and generalized in the future [39,40].

Pain self-efficacy (PSE), or confidence in one's ability to perform certain tasks in the face of pain, was measured using the 10-item Pain Self-Efficacy Questionnaire (PSEQ) [41]. Social cognitive theory underlying PSE was discussed briefly in the introduction [1]. Based on social media's ability to foster peer modeling and support, it was logical to include the PSEQ as a primary measure. The PSEQ has frequently been cited as a standardized outcome measure in chronic pain management. Accordingly, *efficacy* determines the effort and persistence an individual will apply when faced with hurdles and adverse experiences. Like PROMIS-PI, the PSEQ provides a means to overcome inconsistency and generalizability among previous existing legacy measures covering a range of general behaviors and activities, and directly contextualizes self-efficacy in regard to living with pain [41,42]. Similar to the argument made for the use of PROMIS-PI, the PSEQ is favored over legacy self-efficacy measures because it more effectively overcomes the variability in measurement presented by other instruments.

At the end of the study, patients were guided to a second SurveyMonkey questionnaire that amalgamated all PROMs (PROMIS-PI and PSEQ) and a social media-use instrument into one survey (see Multimedia Appendix 5). The social media-use instrument sought to examine which resources were used, the amount used, features of each used, positive/negative aspects of using the resources, and perceptions toward various therapeutic affordances. The same line of questioning was used for each resource—Facebook page, blogs, and YouTube videos. Questions about therapeutic affordances were phrased to better understand the degree to which each affordance is present and impacts PROs. Five therapeutic affordances of social media, refined through a global online survey of PWCP [26], were examined through 15 statements, each consisting of three exploratory components. These measured the following: (1) self-presentation—preferences regarding one's identity, (2) connection—using social media to connect with others, (3) exploration—guidance toward useful information, (4) narration—sharing experiences of chronic pain, and finally (5) adaptation—motivation, frequency, and type of use.

At monthly intervals during the intervention period, patients were also contacted on the phone by the primary investigator to complete a brief 10- to 15-minute, semistructured interview (see Multimedia Appendix 6). Semistructured interviews are well suited to small-scale studies with small participant numbers, and their utility lies in their ability to collect rich qualitative data that can be analyzed in a variety of ways to supplement pre- and posttest survey data [43,44]. Data collection gave people a chance to discuss participation and study progress, but more importantly offered patients the opportunity to help shape social media use in future studies and interventions by collecting information regarding social media use and perceptions toward the five therapeutic affordances free of coercion. These phone calls were not medical consultations and patients were advised of this. Any queries of a medical nature were flagged for follow-up by a member of the clinical team.

Data Analysis

Major study design procedures and the study process are the focus of the results described. Brief descriptive statistics of pre- and posttest survey data are also presented. Pertinent to the study was the examination of barriers to engagement with the resources and intervention. To explore these, thematic analysis was employed using a grounded theory *inductive*

phenomenological approach on the semistructured interview data to uncover any emergent themes.

Deductive coding of semistructured interviews was also conducted to categorize patient comments against our list of five therapeutic affordances: self-presentation, connection, exploration, narration, and adaptation. These results will be the subject of a separate manuscript.

Furthermore, the posttest PROMs were analyzed using paired *t* tests and Fisher's exact test. In order to compute the PROMIS-PI data, raw scores were first translated into a T score for each patient. The T score rescales the raw scores into a calibrated and standardized score with a mean of 50 and standard deviation of 10. The value of hypothesis testing is limited due to the small sample size and given that potential covariates such as gender, age, and educational level were not able to be stratified [45].

Results

Study Design and Processes

Recruitment

During nine rounds of referral screening at RMH-PMS Direct Access Unit, 235 referrals were examined for suitability. A total of 138 out of 235 (58.7%) were deemed appropriate for possible study inclusion. A total of 55 out of 235 (23.4%) were inappropriate for inclusion based on priority status for medical intervention and/or medical status, planned discharge, psychological status, drug-seeking behavior, and/or cognitive impairment. A further 42 out of 235 (17.9%) were from non-English-speaking backgrounds (NESBs) and, thus, inappropriate for this particular study (see Table 2).

Table 2. Referral screening process for possible inclusion into the pilot study.

Round	Date (dd/mm/yy)	Assessed, n	Suitable, n	Inappropriate, n	Non-English speaking, n
1	15/04/14	58	41	11	6
2	13/05/14	32	18	5	9
3	03/06/14	12	6	1	5
4	10/06/14	31	12	16	3
5	24/06/14	32	22	5	5
6	10/07/14	8	6	0	2
7	29/07/14	16	11	2	3
8	19/08/14	25	11	8	6
9	02/09/14	20	10	7	3
Total, n (%)	N/A[a]	235 (100)	138 (58.7)	55 (23.4)	42 (17.9)

[a]N/A: not applicable

Multimedia Appendix 7 is the recruitment spreadsheet detailing success of the recruitment effort. Unreachable patients are shaded with grey (54/138, 39.1%); these represented roughly equal numbers of males (25/54, 46%) and females (29/54, 54%), while age range of nonresponders was relatively unremarkable. Contact was made with 84 out of 138 (60.9%) potentially suitable patients. Those indicated by the color red in Multimedia

Appendix 7 were excluded (54/84, 64%). Reasons for exclusion are further broken down into *self* (19/54, 35%) or *external* (35/54, 65%). Table 3 shows reasons for exclusion. Major reasons for *self*-exclusion were as follows: no interest in participating and no connected devices. *External* reasons for exclusion included the following: patient moved to priority treatment, medically inappropriate, and non-English speaking.

Table 3. Self-exclusion and external reasons for nonparticipation.

Reason for nonparticipation	n (%)
Self-exclusion (n=19)	
Not interested in participating	8 (42)
No connected devices	4 (21)
Prolonged computer use flares pain	3 (16)
Time poor	2 (11)
Against Internet and Facebook	1 (5)
Confident with self-management	1 (5)
External (n=35)	
Moved to priority treatment	12 (34)
Medically inappropriate	8 (23)
Non-English speaking	8 (23)
Discharged from waiting list	5 (14)
Duplicate referral	2 (6)

This process left a total of 30 out of 84 (36%) patients fitting the inclusion criteria and interested in study participation. All 30 patients were emailed the study information for registration purposes; this process yielded a final study cohort of 17 out of 30—indicated in blue in Multimedia Appendix 7—who supplied pretest data, giving a participation rate of 57%. Those that did not register are highlighted in orange. The full recruitment process can be seen in Figure 1.

Figure 1. Recruitment process after screening referrals leading to final cohort.
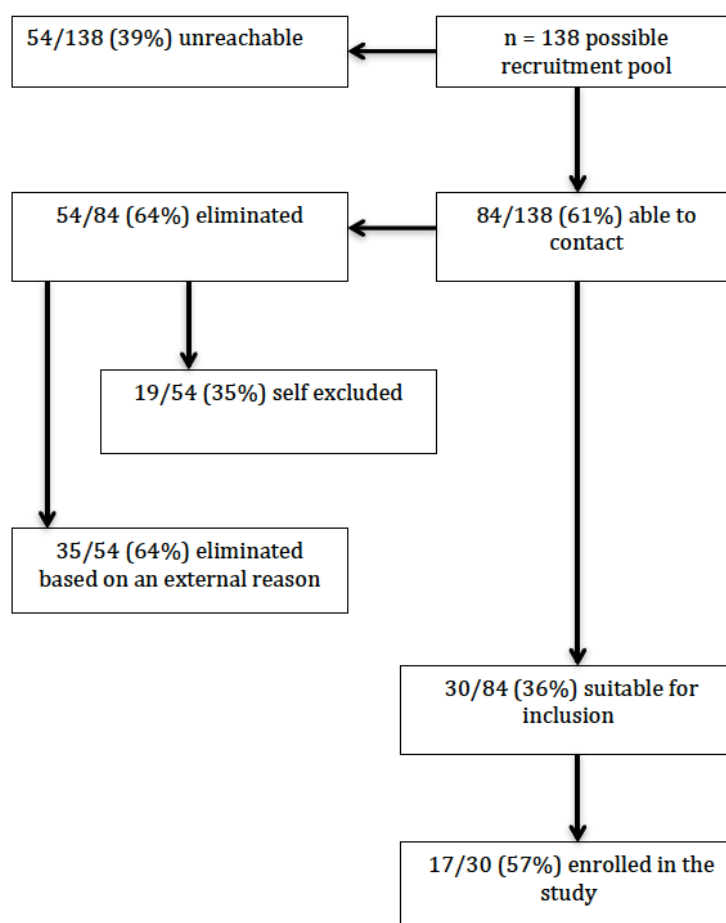
Participants

Demographics are presented in Table 4. The study included slightly more females (10/17, 59%). Age range was spread: 13 out of 17 (76%) patients were aged between 18 and 39 years, with only 1 patient aged older than 50 years. A total of 10 out of 17 (59%) patients reported never being married and 4 out of 17 (24%) were married/partnered. Education level also varied, with 9 out of 17 (53%) patients having completed high school or less and 8 out of 17 (47%) having obtained a university degree or higher. Work status indicated that more than half of the patients were not working due to ill health (9/17, 53%) and only 3 out of 17 (18%) patients were currently working full time.

Enrolled patients were asked to provide information about their chronic pain. A total of 9 out of 17 (53%) patients reported a duration of chronic pain between 1 and 5 years; 7 out of 17 (41%) reported pain duration of greater than 5 years. Low back pain was the primary ailment reported (8/17, 47%)—defined as upper/middle/lower back pain—whereas 3 out of 17 (18%)

patients reported hip/leg/foot pain as their primary pains. Various offline treatment modalities—in the last 12 months—for pain management were noted. Doctor's visits (16/17, 94%) and medication (15/17, 88%) were most reported. Physical therapies (ie, physiotherapy, massage, myotherapy) were next (13/17, 76%), followed equally by exercise classes and relaxation/meditation (8/17, 47%), and finally, psychology/counseling (5/17, 29%). Other free-text responses also highlighted acupuncture and walking.

Each patient was asked whether their pain was *flared* or *stable* at the time of the study. The majority (12/17, 71%) reporting *flared*, with 12 out of 17 (71%) patients reporting average day-to-day pain at a level of 6 to 7 out of 10 (mean 7.1, SD 1.2). Patients were also asked to indicate whether they had been formally diagnosed with a condition causing their pain and 10 out of 17 (59%) indicated this was the case. Fibromyalgia (3/17, 18%) and osteoarthritis (2/17, 12%) were most noted. Other recorded conditions included, but were not limited to, posttraumatic stress, temporomandibular joint syndrome, sciatica, and low back pain.

Table 4. Study demographics.

Patient characteristics (n=17)		n (%)
Gender		
	Male	7 (41)
	Female	10 (59)
Age range in years		
	18-29	7 (41)
	30-39	6 (35)
	40-49	3 (18)
	50-59	1 (6)
	60+	0 (0)
Marital status		
	Never married	10 (59)
	Currently married/partnered	4 (24)
	Separated/divorced/widowed	3 (18)
Level of education		
	High school or less	9 (53)
	College/university completed	6 (35)
	Postgraduate degree completed	2 (12)
Work status		
	Full time	3 (18)
	Part time	2 (12)
	Not working (ill health)	9 (53)
	Not working (other)	3 (18)

Engagement and Completion of the Study

Out of 17 patients, 16 were contactable, supplying data for this study (94% success rate).

A total of 12 patients out of 17 (71%) reported using the resources during the study. Based on the number of times each patient could be reached on the phone to collect data (n=38) and call durations of 15 minutes, on average, it is approximated

that a rich dataset of 570 minutes or 9.5 hours of qualitative interview data was collected.

Study completion rate was calculated based on the number of completed posttest questionnaires received. Despite the success of the semistructured interviews, 9 out of 17 completed posttest questionnaires were received, giving a study completion rate of 53%. Out of 17 patients, 1 (6%) dropped out between study enrolment and first feedback phone call, 1 (6%) withdrew before final follow-up as she reported no longer needing pain management services, 2 (12%) submitted the final questionnaire but reported not having used the resources (hence, were eliminated from further analysis), and finally, 4 (24%) failed to submit the posttest questionnaire despite several attempts to contact them. No contact by patients was attempted during any phase of data collection requesting assistance completing the surveys. This satisfied the research team that the data collection tools were acceptable.

Barriers to Engagement With the Social Media Resources

Coding of the semistructured interview data yielded eight separate engagement themes (see Table 5). Based on the number of times each barrier was identified, *time poor* and *low specificity of resources* to one's condition were most noted. *Effects of medication* was also highlighted; patients noted that this was due to their sedative effect and/or impact on concentration. Only 2 out of 17 patients (12%) suggested access to the Internet was an issue.

Some of these barriers were also identified in the free-text responses of the posttest survey, for example, *low specificity of resources*. According to Patient SM021, "I have a more localized pain condition and most of the resources were for generalized conditions so I had trouble relating to many of them." This was echoed by Patient SM112, who stated, "I think that because they weren't about my pain and there were none about the pain I was going through I found it not very useful."

Table 5. Barriers to engagement with the social media resources.

Theme	Participants (n=17), n (%)
Time poor	7 (41)
Low specificity of resources	6 (35)
Effects of medication	4 (24)
High pain levels	2 (12)
Pain-focused mentality	2 (12)
Internet access	2 (12)
Too much text-based information	1 (6)
Pain resolved	1 (6)

Discussion

Principal Findings

The aim of this study was to examine the pilot-testing of social media use with patients in the clinical setting, focusing on major aspects of the study design. The study also produced evidence to support social media use and PROs from earlier studies [26,27]. However, these findings are not the focus of this protocol paper.

Study Design

The use of mixed methods in eHealth research is often advocated [46-48]. This study also presents a strong case for the complementarity of such a research design. The richness of both quantitative and qualitative datasets and their value to examining the effectiveness of pilot studies has been discussed within a similar research context to this study [32,36,49].

By combining empirical PROs data from PROMIS-PI, PSEQ, and from the social media-use instrument with the qualitative semistructured interview data and free-text responses about social media use from the posttest survey, a rich dataset was obtained. This becomes particularly useful with a small sample size, such as the one in this study. It helps to cross-validate findings and strengthen converging inferences [46].

Collecting empirical data about social media use was able to corroborate semistructured interview data. Similarly, data collected regarding patient perceptions toward each of the five therapeutic affordances of social media helped validate findings from a global online survey of PWCP [26,27]. This enhances the scope to generalize study findings in future research and across different study areas and conditions within similar domains.

Recruitment

The recruitment procedure used in this study was extensive and demonstrates a targeted method aimed at recruiting the most suitable clinical cohort that might benefit from the intervention. It is the belief of the research team that the method for recruiting such a targeted cohort in this study is appropriate and would be scalable in a larger-scale randomized controlled trial (RCT) study. This is because the aim was to refine the most suitable cohort required to test the effectiveness of social media to positively impact PROs. This was not a study of readiness to adopt social media. A similar targeted approach has been seen in other pilot studies within a similar study domain [32,36,50].

However, targeted recruitment does highlight pertinent ethical considerations, such as "representativeness and selection." Internet access and English language problems were two considerations noted from the RMH-PMS population. Similarly

to this study, most social media interventions target Internet-competent, social media-using participants and/or people thinking about engaging in health behavior change [23,51,52]. While some may argue that this may limit the generalizability of findings, it has also been argued that chronic pain patients almost always self-select their own management (ie, medication, physiotherapy, exercises, surgery, etc). Hence, a self-selecting study design is still ecologically valid [11].

Demographic characteristics predicting participation in social media or other Web-based interventions for chronic disease management are also interesting and relevant. This has traditionally been skewed towards well-educated females of a relatively high socioeconomic status. Marital status and age are more varied but studies are typically slanted toward those in relationships/married and aged 30 to 60 years [53-55]. Literature has also previously reported that people living with chronic illness are typically more representative of lower socioeconomic status and educational level [51,56,57]. What was found in the present study is that the clinical setting is representative of a greater demographic spread and it was this clinical PWCP population that was of interest for examination. Patients were an equal mix of males and females, education level was generally lower (in this study, 9/17 [53%] completed high school or less), more than half were unemployed due to ill health (9/17, 53%), and age range varied from approximately 18 to 59 years. Earlier studies, such as that of Berman et al [33], reported significant improvements in PROs for older chronic pain patients (55+ years). They also reported minimal issues for participants navigating the online resources, suggesting that older adults in the chronic pain setting may also derive benefit from online interventions. In this study 19 out of 138 (13.8%) potentially suitable study recruits were aged 55 years or over.

Engagement and Completion of the Study

According to Sheaves et al [36], the study completion rate of 53% (9/17) is comparable with other Web-based health studies. Reasons for attrition according to interview data about *barriers to engagement*, may have been *low specificity of resources* to one's condition and *lack of time* to use the resources.

The semistructured interviews conducted monthly by telephone were an important tool in understanding reasons for engagement or nonengagement above. In contrast to overall completion rate, results showed that 94% (16/17) of patients were able to be engaged by phone. This enhanced collaboration between patients and the research team and placed greater emphasis on patient preferences and perceptions about using social media for their self-management. In other studies, such as that of Sheaves et al [36], email was used to collect data. The authors reported that lack of response to feedback emails was high. Hence, conducting semistructured interviews by telephone rather than via email may be a more successful data collection and patient engagement method in social media studies.

As noted from patient feedback, low specificity of resources to one's condition negatively influenced engagement. It has been reported that often those living with chronic conditions have multiple comorbid manifestations and, hence, Web-based resources can fail to cover enough of their individualized needs for them to be deemed of significant value [58]. As could be seen from the research design, general chronic pain management social media resources were suggested to patients, not those specific to any one chronic condition (eg, low back pain, rheumatoid arthritis). This was decided based on current evidence-based approaches to chronic pain management, focusing on holistic multi-faceted, versus disease-specific, management [10]. The conflict observed between a desire to deliver evidence-based practice (EBP) and patient preferences for their own management highlights the need for greater emphasis on shared decision-making models between patient and clinician to achieve success in larger-scale studies in the future [18].

Suggesting certain social media resources as a starting point was done to provide some element of quality control and uphold ethical standards of care. However, freedom was encouraged for patients to use the resources as they wished and explore different avenues using the social media resources. Unlike many earlier studies conducted in this space, the aim of the present study was to more closely replicate social media use in day-to-day life (ie, open, engaging, collaborative, participatory) rather than to create a specific online intervention that dictates exactly what patients engage with and how they engage with it.

Finally, facilitated engagement of social media interventions, or involvement of clinicians, has been reported as another positive way to improve participation and intervention adherence. In turn, this has a positive flow onto PROs [9,20,53-55]. In Hoch et al [32], the entire pilot intervention was guided by a clinical nurse. This led to a completion rate of 24 out of 28 (86%). However, unlike this study, that of Hoch et al [32] was a social media intervention that translated a traditional face-to-face intervention into one delivered in a virtual world. The nurse had an integral role in delivering each session, thus mimicking offline management. Autonomous self-management was the goal for this study, not translating an intervention into an online one. Hence, using social media resources cannot be truly facilitated in the same manner. Empowering patients to make their own decisions about using social media in this manner also has positive connotations for study logistics, suggesting that fewer clinical staff would be required to run future larger-scale studies.

Strengths and Limitations

Strengths

The foremost strength of this pilot study lay in the intervention design. The choice was to encourage participating patients to be more autonomous and decide on which social media to use and how to use them as part of self-management. This breaks away from conventional Web-based intervention design based on constrained, predefined online interventions. As discussed, this idea fits within a participatory model, suggesting, not prescribing, a Web-based intervention. It places greater weight on patients' perceptions and preferences for health self-management online.

Web-based interventions in chronic pain traditionally collect data using several disparate PROMs. As seen and described in Buhrman et al [50], the decision to incorporate several legacy

measures increases the risk of deriving findings due to chance. The authors also suggest that many chronic pain PROMs have a weak theoretical basis. Future research would benefit from utilizing standardized, validated, and generalizable measures to overcome such issues. This is another reason to advocate for the strength of using PROMs such as PROMIS within this research domain [39,40]. It is the belief of the research team that, to date, no similar studies have used PROMIS for outcome measurement in this context. PROMIS has been validated against a variety of measures and across a range of conditions. Hence, using this study as a benchmark, researchers interested in studying social media for chronic pain management will be able to compare findings across a range of contexts and conditions in the future.

Limitations

RCT designs are synonymous with robust health research. This method is strongly advocated in trials of effectiveness and has been employed in other Web-based chronic pain studies [33,50]. However, the decision was made to run this study as a single-arm trial with only an intervention group as numbers would not be sufficient to warrant an RCT at this stage. Similar designs and sample sizes have been seen in other social-media-in-chronic-disease pilot studies [32]. The recruitment process showed how difficult it is to recruit large numbers of patients into studies where no incentives are offered. As was seen, it was not until members of the clinical team began conducting recruitment phone calls that a rise in study interest was seen and, hence, enrolments. Future research warrants larger-scale studies to recruit sufficient numbers to use RCT designs to accurately test the effectiveness of social media use in the clinical management of chronic pain.

The decision to merely suggest social media resources, but allow patients to make their own decisions about which to use, meant that the resources patients actually used were not able to be verified. PROs collected may be in reference to a variety of social media resources, both reputable and not. Thus, study findings are open to interpretation bias. This is one of the reasons that emphasis is not placed on posttest PROMIS-PI and PSEQ findings in this study.

There is a trade-off between targeted recruitment of competent and enthusiastic social media-using chronic pain population members and ensuring all chronic pain patients who may benefit from social media can participate. Until social media interventions can better address the needs of chronic pain patients who suffer from a lack of Internet access, poor literacy skills, poor Internet literacy, and language barriers, they will always be biased toward self-selecting populations. Hence, any conclusions drawn from this pilot study regarding recruitment,

intervention design, and engagement are in reference to the current sample only.

Other pilot studies [32,33] have reported completion rates slightly better than those of this study (9/17, 53%). However, both of these studies utilized incentives ranging from monetary amounts through to allowing participants to keep the supplied technology. This study did not offer incentives as a way to minimize selection bias, but their value is not discounted for future study as another way to enhance recruitment and/or decrease attrition.

Recommendations and Conclusions

This pilot study has outlined key considerations for conducting social media interventional research in the clinical setting, in particular, study design, recruitment, and engagement.

Targeted recruitment of social media users indicates that enthusiastic, competent social media users may be still largely underrepresented on pain management services' waiting lists. Therefore, these interventions may not yet be appropriate for all PWCP. Further work is required to ensure that those in need of online support will also be catered to by social media's integration into clinical service models. In line with recommendations by Sheaves et al [36], future studies would be well advised to (1) include general practice sites in research, where patients may have more need for information (given that they are more likely to be earlier in the course of managing their pain) and (2) include eHealth literacy education, training, and support as part of care models for those who have low computer literacy skills, but may stand to benefit from online resources [35].

As patients become increasingly connected and active shared decision makers in their self-management, researchers would be advised to pay close attention to study designs that give patients greater flexibility and empower them to make decisions about the online resources they use. This is where the potential for social media sits above traditional Web-based interventions. Social media resources must actively engage patients as seen in this study. Finally, acknowledging patient preferences for resources that adequately address disease-specific needs is also a consideration.

Future research into the effectiveness and potential for social media use in the clinical management of chronic pain is warranted. While this study cannot ascertain what effect the use of social media resources can ultimately have on hospital waiting lists, a considered approach to conducting this type of research has been offered. Future studies need to focus on larger-scale, multicenter RCTs and involve patients in the intervention design in order to achieve desired effect sizes and for evidence to be sound.

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Conflicts of Interest

None declared.

Multimedia Appendix 1

Telephone transcript.

[PDF File (Adobe PDF File), 132KB - resprot_v4i3e101_app1.pdf]

Multimedia Appendix 2

Patient educational material.

[PDF File (Adobe PDF File), 112KB - resprot_v4i3e101_app2.pdf]

Multimedia Appendix 3

Selected study resources.

[PDF File (Adobe PDF File), 54KB - resprot_v4i3e101_app3.pdf]

Multimedia Appendix 4

Pretest questionnaire.

[PDF File (Adobe PDF File), 306KB - resprot_v4i3e101_app4.pdf]

Multimedia Appendix 5

Posttest questionnaire.

[PDF File (Adobe PDF File), 420KB - resprot_v4i3e101_app5.pdf]

Multimedia Appendix 6

Semistructured interview template.

[PDF File (Adobe PDF File), 34KB - resprot_v4i3e101_app6.pdf]

Multimedia Appendix 7

Recruitment list.

[PDF File (Adobe PDF File), 64KB - resprot_v4i3e101_app7.pdf]

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Abbreviations

CBT: cognitive behavioral therapy
EBP: evidence-based practice
HRQOL: health-related quality of life
MNSI: Melbourne Networked Society Institute
N/A: not applicable
NESB: non-English-speaking background
PI: pain interference
PRO: patient-reported outcome
PROM: patient-reported outcome measure
PROMIS: Patient-Reported Outcome Measurement Information System
PROMIS-PI: Patient-Reported Outcome Measurement Information System—Pain Interference
PSE: pain self-efficacy
PSEQ: Pain Self-Efficacy Questionnaire
PWCP: people with chronic pain
QOL: quality of life
RCT: randomized controlled trial
RMH: Royal Melbourne Hospital
RMH-PMS: Royal Melbourne Hospital—Pain Management Services

Original Paper

An Internet-Based Means of Monitoring Quality of Life in Post-Prostate Radiation Treatment: A Prospective Cohort Study

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Abstract

Background: Widespread integration of the Internet has resulted in an increase in the feasibility of using Web-based technologies as a means of communicating with patients. It may be possible to develop secure and standardized systems that facilitate Internet-based patient-reported outcomes which could be used to improve patient care.

Objective: This study investigates patient interest in participating in an online post-treatment disease outcomes and quality of life monitoring program developed specifically for patients who have received radiation treatment for prostate cancer at a regional oncology center.

Methods: Patients treated for prostate cancer between 2007 and 2011 (N=1113) at the British Columbia Cancer Agency, Centre for the Southern Interior were invited by mail to participate in a standardized questionnaire related to their post-treatment health. Overall participation rates were calculated. In addition, demographics, access to broadband Internet services, and treatment modalities were compared between participants and nonparticipants.

Results: Of the 1030 eligible invitees, 358 (358/1030, 34.7%) completed the online questionnaire. Participation rates were higher in individuals younger than age 60 when compared to those age 60 or older (42% vs 31%) and also for those living in urban areas compared with rural (37% vs 29%) and in those who received brachytherapy versus external beam radiotherapy (EBRT) (41% vs 31%). Better participation rates were seen in individuals who had access to Internet connectivity based on the different types of broadband services (DSL 35% for those with DSL connectivity vs 29% for those without DSL connectivity; cable 35% vs 32%; wireless 38% vs 26%). After adjusting for age, the model indicates that lack of access to wireless broadband connectivity, living in a rural area, and receiving EBRT were significant predictors of lower participation.

Conclusions: This study demonstrates that participation rates vary in patient populations within the interior region of British Columbia, especially with older patients, those in rural areas, and those with limited access to quality Internet services.

KEYWORDS

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Introduction

As technologies improve and Canadians become more comfortable using computers and other Internet devices, there is an increasing potential to use online platforms as a means of communicating with patients on health-related issues. This communication allows for patient-reported outcomes (PROs), patient perspectives on their health and health care experience, to be collected. PROs are increasingly used as a valuable part of understanding the impact that an intervention has on a patient's outcome. Therefore, these types of systems are progressively used to identify significant treatment-related morbidities and possess the potential for expansion in the field of clinical monitoring and quality of life (QOL) research [1-3]. Such systems also have potential to be implemented as a standard clinical process for specific health intervention programs; they could be beneficial in a number of areas, such as minimizing physician workload in routine patient follow-up consultations. Internet-based collection of PROs reduce travel time for patients requiring long-term follow-up, especially relevant for rural patients seeking specialized care [2]. Most importantly, the integration of PROs in clinical practice would allow for a more accurate reflection of patient health status, providing essential information about symptom management following treatment [1,2,4].

For this study, an Internet-based platform was designed for patient follow-up at the British Columbian Cancer Agency, Centre for the Southern Interior (BCCA-CSI), and a group of prostate cancer treatment patients treated with radiation therapy were invited to participate in an online disease-specific and QOL questionnaire. Both short- and long-term function and QOL are affected in men treated for prostate cancer, with declines in most functional domains occurring over at least 15 years of follow-up [5,6]. Therefore, future research in this area should assess both treatment efficacy and side effects so as to optimize treatment decisions and increase patient satisfaction and QOL following cancer treatment [6]. In addition, the use of PROs in this patient population could enable oncologists to identify patients or patient types that may benefit from improved postradiation therapy management.

The outcomes of interest in this study were twofold: the overall participation rate of an online PRO system implemented as a pilot and the participation rates based on readily available personal, demographic, and treatment-related factors. The overall goal of the initiative was to evaluate feasibility of a regional oncology program to eventually transition to Web-based collection of PROs following cancer treatment, so as to further inform patient-centered care and better understand the long-term impacts of cancer treatments.

Methods

Platform Design

An in-house online platform was designed to host participant data and collect the online participant response information in an automated format; it pulls information from completed surveys from an external server to a secure database and dashboard. The project was approved by the Institutional Ethics Review Board as a quality improvement project and the online platform was reviewed for institutional privacy impact and met the necessary data security standards of practice.

Patient Selection and Recruitment

The BCCA is an agency responsible for province-wide, population-based oncologic care and radiation therapy for British Columbians undergoing treatment through 6 regional cancer centers including CSI. Patients with nonmetastatic prostate cancer treated with conventional radiation therapy are discharged to their primary care practitioner within 2 years of treatment and are often not seen again unless re-referred back to the program.

In January 2014, all living individuals (N=1113) treated with radiation therapy for prostate cancer between 2007 and 2011 at the BCCA-CSI were invited by mail to complete a standardized questionnaire related to their post-treatment health. Therefore, all patients were at least 2 years out of their initial treatment during the course of this study.

These men were mailed a single letter (see Multimedia Appendix 1), which provided a description of the study, statement of their right to accept or decline participation, study code that enabled them to log into the secure online platform, and instructions on how to consent and complete the questionnaire through the online platform. Invitees were also encouraged to call the study coordinator (BP) if they had questions related to the study or questionnaire. The questionnaire consisted of questions on the urinary function, rectal toxicity, and sexual health components of the Expanded Prostate Cancer Index Composite, a validated and commonly used set of functional and QOL surveys for prostate cancer patients [7]. Individuals were given 4 months to complete the online questionnaire. They were provided with no other form of communication or invitation to participate.

Statistical Analysis

Spatial analysis was performed in ArcGIS (Esri), which is a spatial visualization and analysis software program. For the spatial analysis, each patient's address was converted into a geographic coordinate. Broadband Internet connectivity data were obtained from the 2012 Broadband Canada: Connecting Rural Canadians' National Broadband Maps derived from an initiative completed by Industry Canada [8]. Broadband Canada defined the presence of broadband services as a minimum download speed of 1.5 megabits per second. Three different types of geographical broadband data were available: cable, digital subscriber line (DSL), and wireless (ground based and satellite based). Subsequently, the broadband Internet connectivity data were joined to each geocoded coordinate based on linear proximity to the nearest broadband geographic coordinate data point. In addition, spatial statistical analysis calculated the distance of each patient from the nearest of the 5 provincial radiation treatment facilities. These distances were grouped into the following 3 categories: less than 200 km, 200-400 km, and more than 400 km. Furthermore, a rural/urban status was established for each invitee based on his postal code.

Statistical analysis was performed in SPSS version 14 (IBM Corp). A chi-square, *t* test, or the nonparametric equivalent was used to compare participation rates by patient characteristics.

The relationship between covariates of interest and participation was initially calculated through univariate binary logistic modeling. Subsequent analysis indicated that many of the covariates were associated with each other. Therefore, an age-adjusted model was developed, resulting in an age-adjusted model and odds ratio estimates for each covariate of interest. All tests of statistical significance were two sided and the threshold for statistical significance was set at $P<.05$.

Results

Patient Demographics and Participation Rates

Of the 1113 individuals invited to participate in the study, 83 were subsequently excluded due to mortality near time of letter mail out or otherwise lost to follow-up due to reasons such as a change of address. The characteristics of participants and nonparticipants are described in Table 1. Overall, 358 (358/1030, 34.7%) of the 1030 invitees completed the online questionnaire. Participation rates were higher in individuals younger than 60 years compared with those aged 60 years and older (139/334,

41.6%, vs 219/696, 31.5%). Similarly, participation rates were higher in urban areas, when compared with rural (262/700, 37.5%, vs 96/330, 29.1%), and for those who received brachytherapy versus external beam radiotherapy (EBRT; 156/380, 41.1%, vs 202/650, 31.1%). Participation was also greater from individuals who had access to Internet connectivity based on the types of broadband (DSL 337/958, 35.1%, for those with DSL connectivity vs 21/72, 29.2%, for those without DSL connectivity; cable 316/898, 35.2%, for those with cable connectivity vs 42/132, 31.8%, for those without cable connectivity; wireless 290/770, 37.7%, for those with wireless connectivity vs 68/260, 26.2%, for those without wireless connectivity).

Predictors for Participation

Both the univariate and age-adjusted model odds ratios and their statistical significance for these measures are reported in Table 2. After adjusting for age, the model indicates that rural status, lack of access to wireless broadband connectivity, and prior EBRT treatment remain as significant predictors of relatively lower participation.

Table 1. Demographic factors of participants and nonparticipants.

		Participated (N=358)	Invited, but did not participate (N=672)	P value
Age, years, at time of letter mail out, mean (SD)		73 (8)	72 (7)	.001
Rural area of residence, n (%)		96 (27)	234 (35)	.009
Residence distance from center, km, n (%)				
	<200	295 (82)	542 (81)	.495
	200-400	41 (11)	75 (11)	—
	>400	22 (6)	55 (8)	—
Types of broadband connectivity, n (%)				
	DSL	337 (94)	621 (92)	.369
	Cable	316 (88)	582 (86)	.494
	Wireless	290 (81)	480 (71)	.001
Primary radiation treatment type, n (%)				
	EBRT	202 (56)	448 (67)	.001
	BT	156 (44)	224 (33)	—

Table 2. Predictors for participation, represented in crude and age-adjusted odds ratios.

	Crude model			Age-adjusted model		
	Odds ratio	*P* value	95% CI	Adjusted odds ratio	*P* value	95% CI
Age (each year increasing)	0.973	.001	0.957-0.990	—	—	—
Urban versus rural (reference: urban)	0.686	.009	0.517-0.910	0.701	.014	0.528-0.931
Distance from center (increasing)	0.893	.324	0.714-1.118	0.915	.439	0.730-1.147
DSL connectivity (reference: yes)	0.759	.303	0.449-1.283	0.78	.357	0.461-1.322
Cable connectivity (reference: yes)	0.859	.448	0.581-1.271	0.856	.439	0.578-1.268
Wireless connectivity (reference: yes)	0.586	.001	0.429-0.801	0.601	.001	0.439-0.823
Radiation treatment type (reference: EBRT)	1.545	.001	1.187-2.010	1.39	.021	1.052-1.837

Discussion

Principal Results

The results of this study show modest participation rates; even for individuals under the age of 60, only 40% completed the survey. However, individuals were made aware of the study exclusively by a single mailed letter; reminders may have increased participation. Informing patients about this PRO aspect of care and follow-up in the time surrounding their treatment and integrating email invitations and reminders would also likely increase participation rates; however, integration of these response improvement strategies was beyond the scope of the pilot project.

Previous studies including patients with prostate and other cancers have indicated that it may be feasible to use Web-based technologies as a means of collecting PROs and follow-up [9-11]. Vickers and colleagues [10] reported a 39% participation rate for all eligible postprostatectomy patients (age range 57-65 years). Sebrow et al [9] demonstrated a 50% participation rate in prostatectomy patients (age range 38-77 years). The latter group suggested that these types of systems could be useful for collection of post-treatment QOL, especially from those patients who may not otherwise attend follow-up due lack of geographic proximity to a treatment facility. Although both of these previously reported studies had higher participation rates, they also had a younger population, different method of recruitment, and briefer interval between treatment and invitation to participate when compared to this study. As expected, participation rates were higher in individuals younger than 60 years compared to those aged 60 years and older. Internet usage is strongly dependent on user attitude, especially in areas such as perceived ease of use and perceived access barriers [12,13]. With regard to age, Porter et al [13] noted that older individuals (aged 50 years and older) typically exhibit lower perceived ease of use, in addition to perceiving more access barriers associated with Internet usage. Future action may require the development of educational tools and support to familiarize patients with the online platforms and help reduce user anxiety. In addition, it was seen that likelihood of participation rates was higher in brachytherapy patients. In contrast to patients treated with conventional radiotherapy, brachytherapy patients are never discharged but remain on regular follow-up for at least 10 years. They are accustomed to filling out the questionnaires used in this study, and their follow-up data are recorded in a provincial database operational since 1998. Furthermore, at our clinic it has been observed that brachytherapy patients are generally more involved in shared decision making and are often more self-educated than other patients. These behaviors may be associated with an increased likelihood of responding to a questionnaire invitation.

As expected, participation rates were significantly lower in rural areas and in areas without wireless broadband connectivity. The majority (96%) of the regions without wireless broadband had either DSL broadband or cable broadband. Wireless broadband connectivity requires wireless transmitters, the same technology that supplies wireless Internet to cellular phones. While online platforms have allowed for more widespread collection of PROs in certain instances, they are also prone to excluding certain populations due to access and use of Internet [14,15]. As access to wireless broadband was a significant predictor of participation in this study, it is hypothesized that those who have limited access to cellular mobile and smartphone Internet connectivity may also be less likely to use other Web-based technologies. Rural addresses were also associated with lower participation and, as the rural regions of the BC southern interior are often forested and mountainous, residents are likely to have limited and unreliable access to wireless connectivity. Furthermore, there may also be cultural differences regarding general Internet usage in rural regions compared to urban regions.

These findings are applicable and relevant to other Web-based health surveillance, health monitoring and research programs currently in development. Missing data and sample bias are two of the most serious, practical problems involved with implementing online PRO platforms. As health care institutions increasingly employ modern Web-based technologies in patient management, it will be important to monitor the uptake of these technologies by elderly patients and those living in rural areas [1,15] and develop strategies to increase uptake and minimize health disparities within these patient cohorts.

Limitations

This study has several limitations. The mailing information for the BCCA-CSI was outdated, and 55 (5%) invitation letters were returned due to an invalid address. In addition, the broadband connectivity data used within the spatial analysis was based on data published in 2012 and therefore may not be fully representative of BC's current broadband coverage.

Conclusions

These findings demonstrate that a modest proportion of prostate cancer patients treated at the BCCA-CSI are willing to use online systems to report health outcomes. Our results demonstrate that participation rates vary based on age, geographic location, and access to certain types of Internet connectivity. As specialist care increasingly uses Web-based technologies to interact with patients and monitor their health as part of standard post-treatment and long-term clinical monitoring, usage of these technologies in rural residents and older patients should be monitored to ensure that these patient cohorts continue to receive appropriate medical care.

Authors' Contributions

The author contributions were as follows: RR conceived the idea and the security architecture for the project; AM, RR, CA, and BP designed the Web platform; BP, RR, CA, and JC designed and implemented the research protocol; BP analyzed data and prepared the manuscript. All authors read and approved the final manuscript.

Conflicts of Interest

None declared.

Multimedia Appendix 1

Web follow-up letter of contact.

[PDF File (Adobe PDF File), 155KB - resprot_v4i3e115_app1.pdf]

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Abbreviations

BCCA-CSI: British Columbian Cancer Agency, Centre for the Southern Interior
DSL: digital subscriber line
EBRT: external beam radiotherapy
PRO: patient-reported outcomes
QOL: quality of life

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Original Paper

A Validation Study of the Web-Based Physical Activity Questionnaire Active-Q Against the GENEA Accelerometer

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Abstract

Background: Valid physical activity assessment in epidemiological studies is essential to study associations with various health outcomes.

Objective: To validate the Web-based physical activity questionnaire Active-Q by comparing results of time spent at different physical activity levels with results from the GENEA accelerometer and to assess the reproducibility of Active-Q by comparing two admissions of the questionnaire.

Methods: A total of 148 men (aged 33 to 86 years) responded to Active-Q twice and wore the accelerometer during seven consecutive days on two occasions. Time spent on six different physical activity levels including sedentary, light (LPA), moderate (MPA), and vigorous (VPA) as well as additional combined categories of sedentary-to-light and moderate-to-vigorous (MVPA) physical activity was assessed. Validity of Active-Q was determined using Spearman correlation coefficients with 95% confidence intervals (CI) and the Bland-Altman method. Reproducibility was assessed using intraclass correlation coefficients (ICCs) comparing two admissions of the questionnaire.

Results: The validity correlation coefficients were statistically significant for time spent at all activity levels; sedentary (r=0.19, 95% CI: 0.04-0.34), LPA (r=0.15, 95% CI: 0.00-0.31), sedentary-to-light (r=0.35, 95% CI: 0.19-0.51), MPA (r=0.27, 95% CI: 0.12-0.42), VPA (r=0.54, 95% CI: 0.42-0.67), and MVPA (r=0.35, 95% CI: 0.21-0.48). The Bland-Altman plots showed a negative mean difference for time in LPA and positive mean differences for time spent in MPA, VPA and MVPA. The ICCs of test-retest reliability ranged between r=0.51-0.80 for the different activity levels in Active-Q.

Conclusions: More moderate and vigorous activities and less light activities were reported in Active-Q compared to accelerometer measurements. Active-Q shows comparable validity and reproducibility to other physical activity questionnaires used today.

Introduction

Physical activity is a modifiable lifestyle factor, and while high activity levels are associated with decreased risks of non communicable diseases [1], inactivity is a leading global risk factor for mortality [2]. Both behaviors are important, yet complex to measure, as different types and intensities of activities may affect health differently. Valid assessment of

physical activity in large epidemiological studies, as well as in intervention research, is therefore essential to study the associations with various health outcomes and to accurately measure physical activity, and changes in such, at different time points.

During the past decade, the use of Web-based instead of paper questionnaires has simplified data collection and improved data quality in large epidemiological studies [3]. Web-based data collection is also cost efficient due to such advantages as the use of automated data management systems for distribution of questionnaires and reminders and rapid return of high quality data obtained through implementation of, for example, automatic checks for erroneous or missing data at the time of response [4]. Selection bias has been of concern in Web-based data collection, but with increasing access to the Internet among populations worldwide, this problem has decreased substantially during the recent years [4]. Although physical activity questionnaires are feasible to use in large studies, they are prone to errors due to difficulties of recalling information, social desirability in answers and an inability to assess the complete spectrum of physical activity [5,6]. The validity of physical activity questionnaires used today varies, with most showing only moderate validity [7]. We have previously described and validated the Web-based physical activity questionnaire Active-Q with regards to total energy expenditure against doubly labeled water with good results (Spearman correlation coefficient: r=0.52, P<.001) [8]. However, another important aspect of physical activity behavior is time spent in different intensity levels, which the total energy expenditure does not convey.

Using accelerometers, movement can be objectively quantified and activities performed at different activity levels (eg light, moderate or vigorous) can be assessed. The devices are commonly worn around the waist or wrist, but wrist worn accelerometers have been shown to increase wear compliance and may thus decrease selection bias due to burden on study participants [9,10]. Therefore, to assess the validity of time spent at different intensity levels assessed with the Active-Q questionnaire, we collected accelerometer data using the wrist worn GENEA (gravity estimator of normal everyday activity) monitor [11], from 167 men. The primary aim of this study was to assess the validity of Active-Q against the GENEA with regards to time spent at sedentary, light, sedentary-to-light, moderate, vigorous and moderate-to-vigorous physical activity levels. The secondary aim was to assess the reproducibility of Active-Q by comparing results from two admissions of the questionnaire.

Methods

Study Design

Study participants were recruited from a large ongoing cohort study of men who underwent PSA (Prostate Specific Antigen) testing in Stockholm County, Sweden, from 2010 to 2012. All study participants enrolled in the cohort between March and May 2012 who had agreed to be contacted regarding additional studies, were eligible for and invited to participate in the VALTER study (VALidation against acceleromeTER).

In September 2012, 1348 men were emailed an invitation to participate in the VALTER study. Of these, 31 emails did not reach the recipient due to an invalid email address. Men who replied to the invitation were sent more detailed information about the study and were scheduled for an introductory meeting at Karolinska Institutet, Stockholm, Sweden. In total, 167 men agreed to participate. All participants were given both written and oral information about the study and signed an informed consent prior to participation.

The study design is shown in Figure 1. Participants were enrolled in the study for a total of four weeks. On the first day of the study, the participants attended an introductory meeting at which they received the first GENEA accelerometer to wear during the following seven consecutive days. Participants also received the first Active-Q physical activity questionnaire via email on the evening of the same day. The questionnaire also included background questions on height, weight, birth year, education level and handedness. Individual user names and passwords served as identifiers for the questionnaire. After seven days, the accelerometer was returned to the research group via regular mail in a padded envelope with prepaid postage received during the introductory meeting. Three weeks later, on day 21 of the study, participants once again attended a meeting at a study site and were given a new GENEA accelerometer to wear for the following seven days before returning it via mail. They also received the second Active-Q questionnaire to respond to via email. All accelerometers were returned to study personnel at the end of each measurement period. An email reminder about the questionnaire was sent to participants who had not responded within a few days. Nevertheless, 84% responded the day of admission and a total of 96% had responded the following day.

Among the 167 men who agreed to participate, only participants with complete data from both questionnaire and accelerometer measurements were included in analysis. Participants were excluded due to drop out of the study (n=2) or due to erroneous accelerometer data from the first (n=3) or second (n=3) week of measurements. Further, men who reported to be left handed (n=11) were excluded from analysis as the accelerometer was worn on the left wrist. In total, data from 148 men were included in further analyses. As an incentive, all participating men received feedback from their accelerometer measurements approximately one month after the data collection was finished.

A subgroup of participants (n=22) partook in a calibration of the accelerometers. There were no differences in age, weight, height or BMI (body mass index) (P=.10 to .37) between men included in this subgroup and the whole study population. In the calibration, each participant wore two accelerometers on the same wrist while performing five predefined activities including: sitting, standing, and walking at a pace of 2, 3 and 4 mph. Each activity was performed for five minutes under the supervision of study personnel. Activities performed, and corresponding MET (metabolic equivalent task) values were retrieved from the Ainsworth Compendium of Physical Activities [12].

The study was approved by the Research Ethics Committee at Karolinska Institutet, Stockholm, Sweden.

Figure 1. Timeline showing participants' responses to the first and second Active-Q questionnaire and when the first and second GENEA accelerometers were worn.
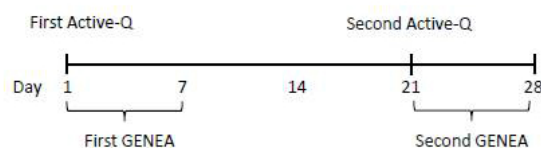
Active-Q

Active-Q is a Web-based, interactive physical activity questionnaire assessing habitual activity in adults (see Multimedia Appendix 1). It has previously been validated against doubly labeled water and has been described elsewhere [8]. Briefly, respondents report their usual activity during the past months within four different domains; daily occupation, transportation to and from daily occupation, leisure time activities, and regular sporting activities. The initial question to the means of transportation, leisure time activities and sporting activities are screening questions listing all the activities included in each domain. Only those activities selected by the participant in the screening are followed up with questions regarding frequency and duration, thereby, reducing the total number of questions each respondent needs to answer. An additional question on sleeping hours was also included, thus the questionnaire comprised 9 to 47 questions depending on previous answers and follow-up patterns. A screening question assessing working status (yes/no) preceded the questions of daily occupation and transportation. Participants reporting that they were not working did not get the questions concerning physical activity at work. All questions had predefined answers regarding frequency and duration. The additional question on sleeping hours, an addition of yoga and squash to the sporting activities, as these were frequently reported in an open response alternative to sporting activities in the previous study, and the screening question of working status were modifications made to the Active-Q after the previously published validation study [8].

All activities in Active-Q are linked to a corresponding MET value [12]. Activities with a MET value <1.5 are classified as sedentary, activities with a MET between 1.5 and <3 as light physical activity (LPA), activities with a MET of 3-6 as moderate physical activity (MPA) and activities with a MET >6 are classified as vigorous physical activity (VPA). Additional combined categories of activities classified as sedentary and light (sedentary-to-light activity) or moderate and vigorous physical activity (MVPA) were also created and included all activities with a MET <3 and ≥3, respectively. The total time reported in each category was calculated from Active-Q. An additional variable of total MET-h (reported time in hours for each specific activity multiplied by the activity's MET-value) adjusted to a 24 hour period was also created by adding missing time or subtracting over-reported time to reach a total of 24 hours. Each hour added or subtracted was assumed to have a MET value of 2.0 as this was assumed to correspond to an average intensity of sitting, eating etc. (MET=1.5) and self caring, walking at home etc. (MET=2.5).

GENEA Accelerometer

The GENEA accelerometer was developed by Unilever discover, UK and is manufactured and distributed by Activinsights Ltd., UK. It is a small (36 mm long x 30 mm wide x 12mm high, 16 gram) tri-axial accelerometer measuring vertical, anteroposterior and mediolateral movement at a rate of up to 80 Hz with a dynamic range of ±6g [11]. In the present study, acceleration was sampled at 40 Hz to decrease the amount of raw data while keeping a high enough sampling frequency to maintain accuracy. Study participants wore the accelerometer on their left wrist and were instructed to wear it continuously, but to remove it during water-based activities as this version of the accelerometer was not waterproof. Participants were provided with a diary to record all non-wear time (ie when the accelerometer was removed, for example during water activities). All recording of activities with a corresponding MET value >1.5 were corrected for in further analysis, including activities like swimming laps and water aerobics. For analysis in the present study, data from six complete days were extracted from each week of accelerometer measurements starting at midnight on the first day the accelerometer was worn. Only participants with complete data from six days of each measurement week were included in analysis. Results from the two measurement periods were thereafter combined and average daily times spent at different intensity levels were calculated using information from the total of 12 days.

Using the same methods as Esliger et al. [11], the GENEA post processing software (version 1.2.1) was used to summarize the raw 40 Hz tri-axial data into a signal vector magnitude (SVM) (gravity subtracted) (SVM_{gs}) and expressed as 1-minute epochs. Technically, for every minute the GENEA outputs SVM_{gs} defined by the equation given in Figure 2. The 1-minute epoch was obtained by multiplying each SVM_{gs} value with 60. Each SVM_{gs} value was further multiplied with 2 in order to make our SVM_{gs} values comparable to those reported by Esliger et al. [11], who used sampling frequency $K=2 \times 40 = 80$ (K is the number of samples per second).

Figure 2. Equation of GENEA output per minute using the post processing software. K is the number of samples per second (K=40 in our study), and x_ij, y_ij, and z_ij is the acceleration along the three dimensions, respectively, at the j:th sample of the i:th second of the particular minute. g is set to 1.00 by default.

$$SVM_{gs} = \sum_{i=1}^{60} \sum_{j=1}^{K} \left| \sqrt{x_{ij}^2 + y_{ij}^2 + z_{ij}^2} - g \right| / 60$$

Using data from the calibration of the accelerometers (Table 1), cut points specifically developed for the present study population of middle aged and older men were used to convert

each SVM_{gs} value from the accelerometer into an activity level (sedentary, LPA, MPA or VPA). From each 5-minute interval of accelerometer measurements during the calibration, counts from the middle three minutes were extracted for analysis. The SVM_{gs} value for each participant and activity was then calculated and plotted against the corresponding MET value of the activity (Figure 3). We fitted a simple linear regression to these data, obtaining the fitted regression line $SVM_{gs} = 529 \times MET\ -627$ ($y=529x - 627$). The equation was thereafter

used to determine cut points for SVM_{gs} corresponding to MET values 1.5, 3 and 6, for further classification of GENEA SVM_{gs} into sedentary (<1.5 MET), light (<3 MET), moderate (3-6 MET) or vigorous (>6 MET) activity levels. Combined categories of sedentary-to-light activity and MVPA were also created. Non-wear time recordings of activities with a MET value >1.5 were corrected for by subtracting time from the sedentary category and adding time to the LPA, MPA or VPA categories depending on the MET value of the reported activity.

Table 1. Mean GENEA SVM_{gs} (g·min) output for the five activities included in the calibration study.

Activity	MET Value	SVM_{gs} Mean[a] (SD)
Sitting	1.5	105.2 (77.5)
Standing	1.8	167.1 (146.3)
Walking 3.2 km/h	2.5	826.0 (236.1)
Walking 4.8 km/h	3.3	1353.3 (246.2)
Walking 6.4 km/h	5.0	1875.3 (438.4)

[a] Mean values are based on output from a total of 44 GENEA accelerometers.

Figure 3. Scatter plot displaying MET-values of activities performed during the calibration (x-axis) and average GENEA-output in SVMgs (y-axis) for each specific activity, n=22 (44 measuring points).
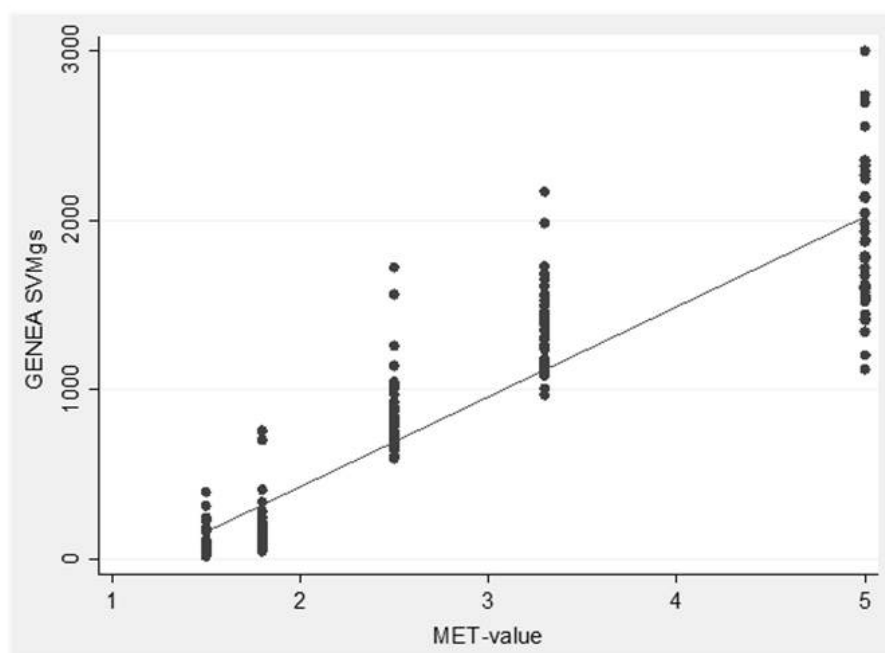
Statistical Analysis

Characteristics of study participants are presented as numbers and percentage, median or mean values with specified standard deviation (SD), total range and interquartile range (IQR). Differences between groups with regards to continuous and categorical variables were tested for using t-tests and chi-square tests, respectively.

Spearman correlation coefficients were used to assess the degree of association between time spent at sedentary, light, sedentary-to-light, moderate, vigorous or moderate-to-vigorous activity levels assessed with Active-Q and the accelerometers.

Confidence intervals (CIs) for correlation coefficients were obtained using the bootstrap method [13]. In addition, Bland-Altman plots were used to assess systematic differences between the methods and as a graphical evaluation of the associations. The difference in time reported spent in each Activity category in Active-Q and measured with the accelerometer was plotted on the y-axis while the mean of the two methods was plotted on the x-axis. The limits of agreement, ±2 SD of the difference, provide a measure of variation. Weighted kappa statistics were estimated for quartiles of MPA, VPA and MVPA measured with Active-Q and GENEA.

For the reproducibility of Active-Q and GENEA, comparing results from the first and second measurements, intraclass correlation coefficients (ICCs) were computed using the ANOVA estimator. ICCs >70 and >90 were considered as moderate and strong, respectively, in line with the definitions used in a recent review of physical activity questionnaires [7]. Analyses were performed using STATA 12.1 (STATA Corporation, College Station, TX). The significance level was set to $\alpha = 0.05$.

Results

Overview

Among the 148 men included in analyses, the mean age was 65.4 (SD 8.7) years and the mean BMI 25.7 (SD 2.9) kg/m^2. Characteristics of study participants are presented in Table 2. The majority of men (57 %) reported that they were working full- or part-time. Participants were well educated and half of the men reported having studied at university level. The median response time of the first Active-Q responded to was 7 min and 19 sec.

Time spent at different activity levels estimated from the GENEA and Active-Q measurements are summarized in Table 3. The mean time spent sedentary and in LPA according to Active-Q was underestimated compared to GENEA, with a smaller difference between the methods for the combined category of sedentary-to-light activity. Correspondingly, the mean time spent in MPA, VPA and MVPA were overestimated in Active-Q compared to GENEA. While the average time spent in MPA was overestimated by approximately 70 minutes in Active-Q, the average time spent in VPA was overestimated by approximately 20 minutes, together corresponding well with the underestimation of time spent in LPA.

Spearman correlation coefficients with 95% confidence intervals (95% CI) for time at different activity levels are shown in Table 4. Bland-Altman plots comparing results between GENEA and Active-Q are displayed in Figure 4. Statistically significant, but modest, correlations were found between estimates of time spent sedentary ($r=0.19$, 95% CI 0.04-0.34), in LPA ($r=0.35$, 95% CI 0.19-0.51), in sedentary-to-light activity ($r=0.15$, 95% CI 0.00-0.31), MPA ($r=0.27$, 95% CI 0.12-0.42) and MVPA ($r=0.35$, 95% CI 0.21-0.48) while the correlation for VPA was

higher ($r=0.54$, 95% CI 0.42-0.67). The Bland-Altman plots illustrating the differences in time estimated with GENEA and Active-Q showed a negative mean difference for sedentary time and time in LPA and sedentary-to-light activity. Positive mean differences were seen for time spent in MPA, VPA and MVPA. The limits of agreement were wide for all activity levels. While no clear trend was seen for sedentary time or time spent in LPA, decreased accuracy at low levels of activity was seen for sedentary-to-light activity, and clear trends of decreased accuracy with increasing levels of time spent in MPA, VPA and MVPA were seen. A major contributing factor to the discrepancy in time spent in MVPA, as measured by Active-Q versus GENEA, was having reported working ≥20 h/week at a moderate or higher activity level. This was seen in all participants with a difference of >300 minutes between the methods (n=12). Among participants in the 75th percentile of time spent in MVPA in Active-Q (>159 minutes), a high activity level at work, or performing household work, were the most common activities contributing time. Bicycling, spinning and/or skiing were reported by all participants having reported >100 min of VPA per day.

When dividing study participants into quartiles of time spent in MPA, VPA and MVPA assessed with GENEA and Active-Q, 32%, 46% and 33%, respectively, of participants were classified into the same quartile using both methods while 71%, 77% and 75%, respectively, were classified into the same or adjacent quartile. Results from weighted kappa statistics between the methods showed modest agreement, κ=0.16 (P=.004), κ=0.39 (P<.001) and κ=0.22 (P<.001) for MPA, VPA and MVPA, respectively.

ICCs comparing the first and second measurements of GENEA and Active-Q, respectively, are shown in Table 4. Overall, the GENEA accelerometer showed higher reproducibility compared to Active-Q for sedentary-to-light activity, MPA, VPA and MVPA. However, ICCs for sedentary time and LPA were low for the GENEA while high using Active-Q. The ICCs between different activity levels ranged from $r=0.51$-0.80 for Active-Q. Results for the two GENEA measurements showed higher ICCs for sedentary-to-light activity, MPA, VPA and MVPA ranging from $r=0.76$-0.78. The lowest ICC was found for sedentary time and LPA using the GENEA ($r=0.25$).

Table 2. Characteristics of study participants (n=148).

	Mean (SD)	Median	Min-Max	IQR[a]
Height, cm	179.2 (6.4)	179	165-198	175-183
Weight, kg	82.5 (11.0)	82	58-122	75-89
Age, years	65.4 (8.7)	66	33-86	61-71
BMI, kg/m^2	25.7 (2.9)	25.4	19.6-35.6	23.5-27.5

[a]Interquartile range

Table 3. Results of time in minutes per day spent at light (LPA, <3 MET), moderate (MPA, 3-6 MET), vigorous (VPA, >6 MET), and moderate-to-vigorous (MVPA, ≥3 MET) physical activity levels assessed by GENEA and Active-Q (n=148).

	Mean (SD)	Median	Min-Max	IQR[a]
First GENEA				
Sedentary	773 (234)	834	43-1107	708-926
LPA	617 (234)	540	299-1340	468-664
Sedentary + LPA	1390 (29)	1393	1269-1437	1379-1408
MPA	47 (27)	46	3-165	30-59
VPA	3 (6)	0	0-27	0-2
MVPA	50 (29)	47	3-171	32-62
Second GENEA				
Sedentary	804 (236)	853	83-1135	741-974
LPA	589 (234)	533	268-1347	436-630
Sedentary + LPA	1394 (31)	1399	1240-1438	1379-1415
MPA	44 (29)	40	3-198	26-56
VPA	3 (7)	0	0-61	0-3
MVPA	47 (31)	42	3-201	26-62
Average GENEA				
Sedentary	789 (186)	817	107-1116	676-941
LPA	603 (185)	566	297-1286	463-696
Sedentary + LPA	1392 (28)	1393	1255-1437	1380-1409
MPA	46 (27)	44	3-182	31-56
VPA	3 (6)	1	0-43	0-3
MVPA	48 (28)	47	3-186	32-60
First Active-Q				
Sedentary	611 (143)	579	360-1291	523-691
LPA	690 (172)	708	83-1028	582-807
Sedentary + LPA	1301 (123)	1339	849-1440	1281-1382
MPA	121 (120)	84	0-555	51-135
VPA	18 (26)	6	0-130	0-29
MVPA	139 (123)	101	0-591	58-159
Second Active-Q				
Sedentary	601 (142)	582	213-1351	516-683
LPA	700 (191)	737	6-1109	596-826
Sedentary + LPA	1301 (139)	1355	680-1428	1275-1390
MPA	116 (123)	69	0-557	41-148
VPA	22 (42)	9	0-289	0-29
MVPA	139 (139)	85	12-760	50-165
Average Active-Q				
Sedentary	606 (136)	578	338-1321	513-578
LPA	695 (166)	716	73-1003	613-810
Sedentary + LPA	1301 (120)	1346	872-1425	1265-1383
MPA	119 (112)	72	11-527	72-160
VPA	20 (31)	10	0-176	0-29

	Mean (SD)	Median	Min-Max	IQR[a]
MVPA	139 (120)	94	15-568	57-175

[a]Interquartile range

Table 4. Spearman correlation coefficients between time at different intensity levels and total MET-h in the first Active-Q questionnaire and time and total SVMgs from GENEA measurements during 12 days (n=148) and Intraclass correlation coefficients between the two Active-Q questionniares administered and between the two weeks of GENEA measurements (n=148).

	Spearman correlations		Intraclass correlations			
	Active-Q vs GENEA		Active-Q		GENEA	
	r	(95% CI)	r	(95% CI)	r	(95% CI)
Minutes/Day Sedentary	.19	(0.04-0.34)	.80	(0.74-0.86)	.25	(0.10-0.41)
Minutes/Day LPA	.15	(0.00-0.31)	.66	(0.57-0.75)	.25	(0.10-0.41)
Minutes/Day Sedentary + LPA	.35	(0.19-0.51)	.67	(0.58-0.76)	.78	(0.71-0.84)
Minutes/Day MPA	.27	(0.12-0.42)	.69	(0.60-0.77)	.76	(0.70-0.83)
Minutes/Day VPA	.54	(0.42-0.67)	.51	(0.39-0.63)	.77	(0.71-0.84)
Minutes/Day MVPA	.35	(0.21-0.48)	.67	(0.58-0.76)	.78	(0.71-0.84)

Figure 4. Bland-Altman plots illustrating differences in time spent sedentary, in light (LPA), sedentary-to-light, moderate (MPA), vigorous (VPA), and moderate-to-vigorous (MVPA) physical activity assessed with Active-Q and GENEA (y-axis) relative to the mean of the two methods (x-axis). Each point represents one study participant (n=148).
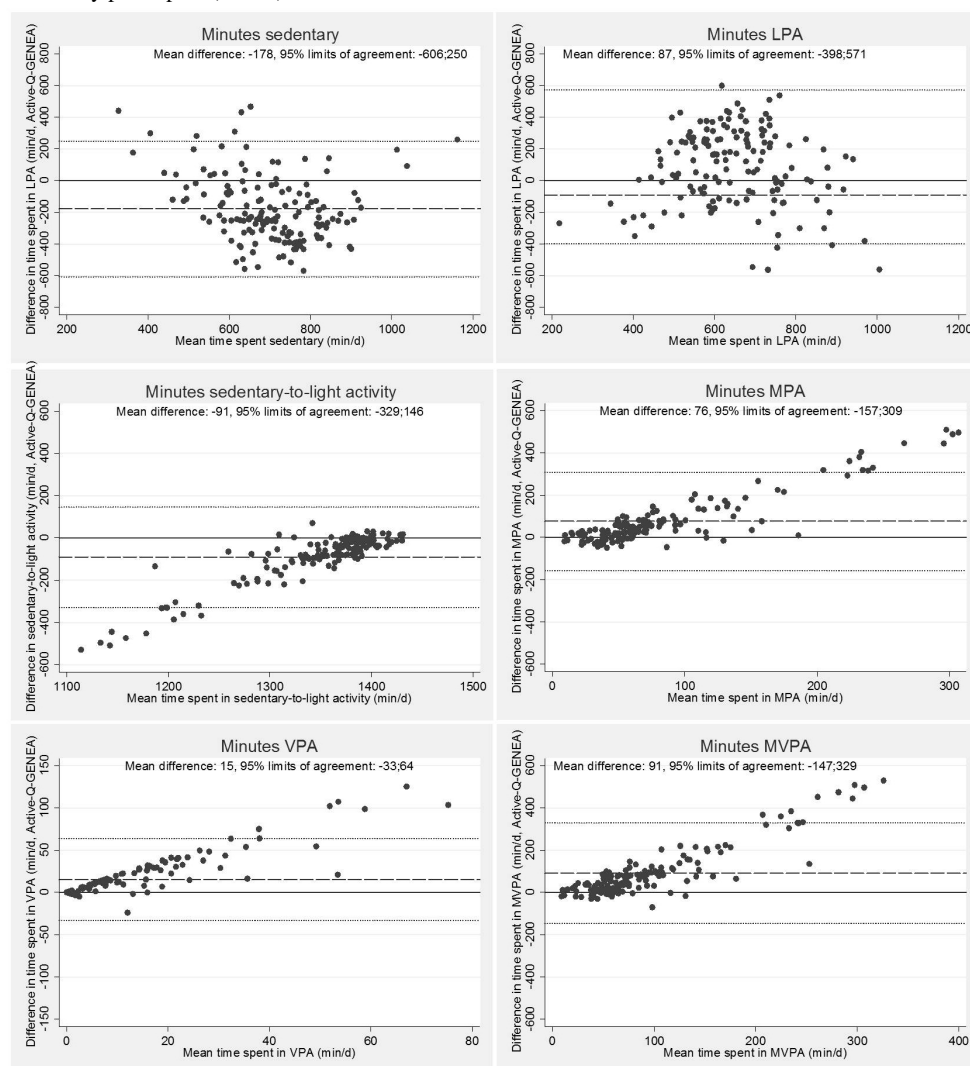
Discussion

Principal Findings

Our results from comparisons of Active-Q and the GENEA accelerometer show that Active-Q provides valid estimates of moderate and vigorous intensity activity although more time being active was reported in the questionnaire than assessed by the accelerometer. Active-Q showed acceptable reproducibility when comparing two admissions of the questionnaire.

Comparison to Other Studies

Compared to accelerometer measurements, time spent at moderate and vigorous activity levels was overestimated in Active-Q. Over-reporting of physical activity is often due to misreporting of frequency, intensity and/or duration of activities [14]. Additional factors contributing to misreporting in general are social desirability [15] and memory bias, the latter particularly affecting older individuals who may have cognitive difficulties in recalling performed activities [16]. Although accuracy is important for determining clinically relevant levels of physical activity, the ranking ability of a questionnaire is often more important than the absolute measures in large epidemiological association studies. The observed correlations between Active-Q and the GENEA accelerometer are in line with previous studies of other physical activity questionnaires when compared to accelerometer measurements. In a recent systematic review [7], over 100 physical activity questionnaires were identified and the validity against objective criterion measures was moderate at best, with median correlation coefficients ranging from 0.25 to 0.41.

A commonly used physical activity questionnaire is the IPAQ (International Physical Activity Questionnaire) [17]. A recent review [18] summarized 23 validation studies of the short form of the IPAQ (IPAQ-SF) and showed that most studies presented weak correlations as compared to objective reference methods. Correlation coefficients between IPAQ-SF and accelerometer data ranged between 0.09 and 0.39 for total physical activity, with somewhat higher correlations for MPA and VPA. Similar to Active-Q, IPAQ-SF overestimated physical activity. In a more recent validation study of IPAQ, correlations between 0.50 and 0.61 were shown for time spent in MPA, VPA or MVPA when comparing questionnaire and accelerometer measurements [19]. However, the high correlations found may be explained by the fact that IPAQ was administered by telephone, and that participants reporting activities not captured by accelerometers (eg swimming and bicycling) were excluded. Dyrstad et al. [20], found correlations similar to the present study when comparing a self reported questionnaire and accelerometer measurements of time spent in MPA. Another recent publication of the validity of RPAQ (Recent Physical Activity Questionnaire) in ten European countries [21], showed similar correlation coefficients when comparing self reported and objectively measured MVPA among men. In the same study, also in line with the results of this study, time spent in MVPA was overestimated.

In addition to comparisons of validity with other existing questionnaires, it is important to remember the population for which the questionnaire is developed. Active-Q was originally developed for adults 18-45 years for use in a large cohort study [22], and has previously been validated with regard to energy expenditure, in a younger population than the present [8]. However, Active-Q is also in use in the cohort from which study participants for the present study, men with a median age of 66 years, were recruited. It is important to validate the questionnaire in a population that is representative of the cohort being studied, although this may limit the generalizability of results to the general population. A systematic review focusing on physical activity questionnaires validated in study populations with an average age >55 years showed diverging results [23]. However, the studies included covered different constructs than the present, such as physical activity level, energy expenditure or walking, making comparisons difficult. Nevertheless, in a recent study comparing questionnaire and accelerometer results, correlation coefficients for time spent in three different MET levels corresponding to LPA, MPA and VPA, were poor (r=0.05, 0.27 and 0.01, respectively) [24].

Results from the Bland-Altman plots, reflecting absolute differences between Active-Q and the GENEA accelerometer, showed that the difference between Active-Q and GENEA increased with increasing time spent in MPA, VPA and MVPA, similar to what has been seen in other studies [20]. Correspondingly for time spent in sedentary-to-light activity, the difference between the methods decreased with increasing time while no clear trends were seen for sedentary time and LPA, respectively. The difference between the methods could have several explanations including the inability of accelerometers to capture activities such as bicycling, spinning and swimming, which may contribute to lower levels of higher intensity activities being measured [25]. Further, static and non-ambulatory activities, such as carrying heavy loads and walking uphill, are not correctly captured by accelerometers [26]. Another explanation could be the different time periods assessed in Active-Q and with the GENEA accelerometer. Ideally, the reference method should reflect the same time period as the questionnaire under validation. However, while Active-Q assessed habitual physical activity during the past months prior to being filled out, the two weeks of accelerometer measurements were made after responding to the questionnaire, thus, not reflecting the same time period. The more long term recall in Active-Q, in contrast to the current accelerometer assessment, also limits the comparison since seasonal variability is not controlled for. That seasonal variability had an effect was indicated by the fact that winter sports contributed to the time in MVPA reported in Active-Q, although the data collection was made during the fall when these activities are unlikely to be performed and captured in accelerometer measurements. Therefore, our results of validity may be underestimated due to the study design. Preferably, the Active-Q should have been administered a few weeks after accelerometer measurements to reflect the same time period.

While our results show moderate reproducibility of Active-Q, few previous studies have reported test-retest reliability of time spent at different intensity levels, making comparisons difficult [7]. One study did nevertheless show ICCs of around 0.80 for a self-reported questionnaire developed for older adults [27]. However, the time between admissions of the questionnaires

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was only 1-2 weeks and shorter time periods between questionnaire assessments have been associated with higher reliability coefficients [7]. In the present study, the time between questionnaire assessments was three weeks in order to minimize differences due to true variation (eg seasonal changes) while still maintaining a long enough interval to decrease the risk of recalling the previous answers.

Although considered to be one of the best methods to objectively assess free living physical activity, accelerometers are not without limitations [25]. They are usually worn around the waist or wrist, both placements with their own strengths and limitations [28]. However, wrist worn accelerometers, as used in the present study, have been shown to increase wear compliance [9,10]. Although hip worn accelerometers have been shown to better classify activities into different intensity categories than wrist worn [29], the wrist worn GENEA has shown excellent validity [11]. A validation of the cut points developed by Esliger et al. [11] for GENEA worn on the left wrist found a modest accuracy of the intensity classification across a broad range of activities [30]. Another study has shown high accuracy in identifying specific activities [31]. The accelerometer output may differ between different populations and our calibration study resulted in higher cut points than those previously developed. Nevertheless, our cut points were developed using a small sample and a limited number of activities.

Strengths and Limitations

In addition to the points of discussion raised in previous paragraphs, the present study has several strengths and limitations worth mentioning. First, the large sample size and the high compliance among participating men are important strengths. With some exceptions, most previous validation studies summarized in the review by Helmerhorst et al. [7] included fewer than 100 study participants in validity analysis while our study comprised almost 150 men. The high compliance and motivated study participants are further strengths to our study and made it possible to include 12 days of accelerometer measurements per individual. The number of days measured far exceeds the 3-5 days required to assess a daily estimate of the individual's habitual activity, resulting in a valid ranking of participants [32]. It also exceeds the number of days commonly assessed in other validation studies using accelerometers [7]. Further, using an objective criterion measure with a different error structure compared to Active-Q also decreases the chance of correlated errors which otherwise may affect results [33].

Conclusions

The present study shows that more moderate and vigorous time and fewer light activities are reported in Active-Q compared to the accelerometer measurements. Nevertheless, the questionnaire shows good ranking ability, and validity and reproducibility comparable to other physical activity questionnaires.

Multimedia Appendix 1

The Active-Q physical activity questionnaire.

[PDF File (Adobe PDF File), 304KB - resprot_v4i3e86_app1.pdf]

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Abbreviations

BMI: body mass index
GENEA: gravity estimator of normal everyday activity
ICC: intraclass correlation coefficient
IPAQ: International Physical Activity Questionnaire
IPAQ-SF: International Physical Activity Questionnaire (Short Form)
LPA: light physical activity
MET: metabolic equivalent task
MET-h: metabolic equivalent task x hours reported for each specific activity
MPA: moderate physical activity
MVPA: moderate and vigorous physical activity
PSA: prostate specific antigen
RPAQ: Recent Physical Activity Questionnaire
SVMgs: signal vector magnitude (gravity subtracted)
VALTER: VALidation against acceleromeTER
VPA: vigorous physical activity

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Protocol

Web-Based Study of Risk Factors for Pain Exacerbation in Osteoarthritis of the Knee (SPARK-Web): Design and Rationale

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Abstract

Background: Knee osteoarthritis (OA) is the most frequent cause of limited mobility and diminished quality of life. Pain is the main symptom that drives individuals with knee OA to seek medical care and a recognized antecedent to disability and eventually joint replacement. Many persons with symptomatic knee OA experience recurrent pain exacerbations. Knowledge and clarification of risk factors for pain exacerbation may allow those affected to minimize reoccurrence of these episodes.

Objective: The aim of this study is to use a Web-based case-crossover design to identify risk factors for knee pain exacerbations in persons with symptomatic knee OA.

Methods: Web-based case-crossover design is used to study persons with symptomatic knee OA. Participants with knee pain and radiographic knee OA will be recruited and followed for 90 days. Participants will complete an online questionnaire at the baseline and every 10 days thereafter (totaling up to 10 control-period questionnaires); participants will also be asked to report online when they experience an episode of increased knee pain. Pain exacerbation will be defined as an increase in knee pain severity of two points from baseline on a numeric rating scale (NRS 0-10). Physical activity, footwear, knee injury, medication use, climate, psychological factors, and their possible interactions will be assessed as potential triggers for pain exacerbation using conditional logistic regression models.

Results: This project has been funded by the National Health and Medical Research Council (NHMRC). The enrollment for the study has started. So far, 343 participants have been enrolled. The study is expected to be finished in October 2015.

Conclusions: This study will identify risk factors for pain exacerbations in knee OA. The identification and possible modification/elimination of such risk factors will help to prevent the reoccurrence of pain exacerbation episodes and therefore improve knee OA management.

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KEYWORDS

knee osteoarthritis; Internet-based study; case-crossover design study; pain exacerbation; risk factors

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Introduction

Osteoarthritis (OA) is the most common joint disorder with more than 50% of people aged 65 years and older having radiological evidence of OA [1,2]. It is the leading cause of chronic disability in older adults with the risk of disability due to knee OA, the most commonly affected lower limb joint, greater than the disability due to any other medical condition [3,4]. It is anticipated that as the population ages and rates of obesity rise, the prevalence of OA will increase with some predictions suggesting that the number of people who suffer from OA will double by as early as 2020 [5].

Pain is the main symptom that drives individuals with knee OA to seek medical care and is a recognized antecedent to disability and eventually joint replacement [6-11]. The determinants of pain in OA are not well understood and are best considered in a complex framework of biopsychosocial factors [12,13]. The majority of persons with symptomatic knee OA experience recurrent pain exacerbations [14-16]. Factors or "triggers" that cause such exacerbations are not clearly identified, making it difficult to minimize reoccurrence of these episodes. A potential solution to managing this problem is to identify and control modifiable risk factors associated with knee OA pain exacerbations. Based on the aetiopathogenesis of knee OA [17], it is reasonable to speculate that factors that lead to either micro-structural joint damage or that decrease the pain threshold may exacerbate knee pain experienced by persons with knee OA.

Numerous studies have assessed the relationship of physical activity to the risk of developing radiographic knee OA with little or no attention paid to the relationship between physical activity and knee OA symptoms [18,19]. Different activities may pose varying degrees of risk for symptoms in knee OA. Some activities that are potentially of interest include prolonged standing [20,21], walking up and down stairs, and getting out of a chair. At present, there is a paucity of epidemiological data to explain which particular activities may contribute to increased pain severity.

Appropriate supportive footwear is recommended in treatment guidelines for the management of knee OA symptoms, although there is little trial evidence to support this [22]. Footwear can influence load through the lower limb [23-25] and potentially lead to pain in persons with knee OA. High-heeled shoes may be particularly problematic for women given that they increase compressive forces across the knee joint [26-29].

Among both genders, a history of injury to the stabilizing or load-bearing structures of the knee renders the joint highly vulnerable to radiographic OA in subsequent years [30]. Knee injury/trauma has been identified as the most important modifiable risk factor for knee OA in men, and is second only after obesity in women [31]; however, its relationship to increased pain in those with established OA has not been revealed.

Analgesic medication adherence is a known source of variation in pain control [32]. The absence of a cure and the chronicity of knee OA warrant continued adherence to prescribed therapy to maintain efficacy. The most widely used symptomatic agents for OA, the nonsteroidal anti-inflammatory drugs (NSAIDs) and COX-2 inhibitors, are associated with high rates of adverse events [33] and rarely relieve symptoms completely [34] which may contribute to poor long-term adherence. In turn, lack of consistent analgesic medication use may be associated with pain exacerbation.

Many believe that weather conditions can influence joint pain, but science offers little proof [35]. If the phenomenon were real, cause-and-effect mechanisms might provide clues aiding treatment of joint pain. Factors include ambient temperature, barometric pressure, relative humidity, sunshine, wind speed and precipitation; although the literature on the subject is sparse, conflicting, and vulnerable to bias [36]. While the biological mechanisms may not be fully understood, for patients who believe that weather can influence their pain, the effect seems to be real.

Pain is a highly subjective phenomenon, with a complex physiological and psychological basis [37]. A full understanding of pain requires consideration of psychological and social environmental processes mediating a patient's response to their disease [38]. Helplessness, depression, stress, poor pain coping, self-efficacy, and the social context of arthritis are important considerations in understanding how people respond to their disease and pain management [39,40].

The Internet is a powerful platform that is increasingly being used in medical research [41,42]. Over the past few decades the Internet has had a major impact on research activities in various areas of health science [42-48]. The Internet can facilitate real time data capture at convenient times for participants without the practical limitations of traditional study methods. Online questionnaires have also been a useful recruitment tool for medical research projects through online social media network [47,49].

The scientific method best suited to identify a set of modifiable risk factors associated with knee OA pain exacerbations is the case-crossover design as it uses each case as its own control and is ideal for assessing the effects of triggers on recurrent episodic events [48,50-53].

We will therefore use a Web-based case-crossover design to evaluate a set of putative modifiable risk factors for pain exacerbation in people with symptomatic knee OA, including physical activity, footwear change, trauma and injury, medication use, climatic, and psychological factors.

Methods

Ethical Approval

Ethical approval has been obtained from the University of Sydney Human Ethics Committee (Protocol No: 14435), University of Melbourne Human Research Ethics Committee (HREC No. 0709220) and Radiation Safety Committee. All participants will provide either written or electronic informed consent.

Design

This will be a Web-based case-crossover study. The case-crossover study [50,51] is a scientific method to answer the question, "What happened just before an event?". In this study the event is a pain exacerbation in the context of symptomatic knee OA. The case-crossover design is analogous to a matched retrospective case-control design in which only matched pairs that are discordant for exposure contribute meaningful information. The information about possible triggers for pain exacerbation will be collected on a secure password-protected study website which will be located on a secure server. The website will display a consent form and administer the risk factor assessment questionnaires. Participants will be asked to complete these online questionnaires at the baseline and every 10 days for 90 days (control-periods) —a total of 10 questionnaires. They will be prompted to fill out these online assessments by means of automated reminder emails. The participants will also go to the website and complete pain exacerbation questionnaires when they experience an isolated incident of knee pain exacerbation (case-periods).

Control-period questionnaires will obtain the frequency and levels of potential risk factors during the control-periods (no painful episode occurred).

Case-period (pain exacerbation) questionnaires will be completed by the participants when they experience what they believe to be a knee pain exacerbation during the three months of the study. Information about the frequency and levels of potential risk factors prior to the onset of knee pain exacerbation will be obtained. Risk factor assessment questionnaires will be the same for case-period and control-period online visits. The case-period questionnaires will only be available for those individuals who qualified as having a pain exacerbation based on the difference in knee pain level compared to the mildest intensity level reported previously at the baseline visit (≥2 point increase on the numeric rating scale [NRS]).

The frequency/severity of each potential trigger/risk factor recorded during the case-periods will be compared with those that were reported during the control-periods within each participant (Figure 1).

Figure 1. Case-crossover study design and timing of exposure measurements in relation to knee OA Pain Exacerbation.
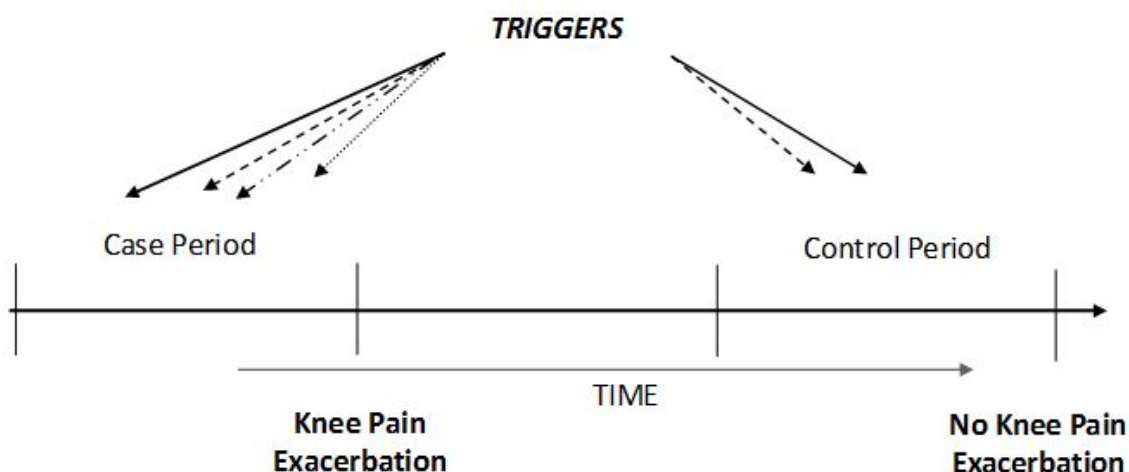
Participants

An online screening survey tool will be engaged for recruitment of eligible study participants. This tool will identify participants that qualify for the study based on their answers to eligibility questions. We will advertise the study on the official websites of Arthritis Australia, MyJointPain, Institute of Bone and Joint Research (University of Sydney), The Centre for Health, Exercise and Sports Medicine (University of Melbourne), and through Facebook.

We will email study information to the individuals from previous OA studies that have given their consent to be contacted for

future research projects. We also will put the study advertisement in some Northern Sydney district local newspapers. When a potential study candidate registers his/her interest in participation through the screening survey tool, their contact details will be emailed to a study coordinator. The study coordinator will then contact the person for further assessment and enrollment if eligible. Prospective participants will also need to provide their most recent knee x-rays or their permission to access those at the imaging facility where they were taken. Once qualified based on the knee x-ray assessment by the study physician, the person will be enrolled and provided access to the study website.

Participants will need to provide their informed consent before accessing the study questionnaires. A choice of electronic or paper consent will be available. The electronic patient information page will appear on the study website when it is accessed for the first time. At the end of this website page participants will need to acknowledge that they have read and understood the study information and agree to participate by clicking on "I agree" button to proceed to study questionnaires.

To be eligible to enter the study, participants must be aged 40 years and over; have an active email address and access to a computer with the Internet; experience pain that fluctuates in intensity in at least one knee on most days in the past month; have x-ray evidence of knee OA (defined as presence of at least one area of definite tibiofemoral (Kellgren and Lawrence grade≥ 2) or patellofemoral osteoarthritis documented on a radiograph); have not had a knee joint replacement in the most painful knee or plan to have one in the next year and have never been diagnosed with rheumatoid arthritis or fibromyalgia.

Risk Factors to be Assessed

Physical Activity

Physical activity (both recreational and occupational) will be assessed using the Seven-Day Physical Activity Recall (PAR) questionnaire; a standard, validated, and widely used measure of physical activity [54-57]. The PAR estimates an individual's time spent on physical activity, strength, and flexibility activities for the last seven days. Physical activity will be grouped into three categories: (1)"moderate" intensity activities that produce feelings similar to those accompanying brisk or fast walking; (2) "very hard" activities that produce feelings similar to those of running or jogging; and (3) "hard" activities that produce feelings that are between the feelings that go with moderate and very hard activities.

Footwear

Images of shoes/inserts, including shoes with heels > 5cm will be posted on the study website. Participants will report which type(s) of shoes they have worn during the last 48 hours and how long they were worn for. This questionnaire was used successfully in the large Framingham Foot Study [58].

Trauma and Injury

We will ask questions on whether any fall, injury, buckling or trauma occurred in or around the knee during the preceding 48 hours. These self-reported instruments have been widely used and validated in prior studies of buckling [59], injury/trauma [60], and falls [61].

Medication Use

Participants will report medication use for each of the case and control-periods by choosing medication names from the list provided in the study questionnaires. The list includes oral, topical, and injection medications for pain (including nonsteroidal anti-inflammatory drug (NSAID), opioids, other analgesics, and steroid and hyaluronic acid injections), and medications taken for other medical conditions that previously have been reported as related to OA pain. We will ask questions about the dose and frequency of these medications for yesterday, the day before yesterday, and 3-7 days ago. The information about the use of natural remedies and complementary therapies will also be collected based on the same time frame.

Weather

Specific climatic data (ie, barometric pressure, ambient temperature, and humidity)will be downloaded from the Australian Bureau of Meteorology website for the geographical location provided by the participant. We will ask participants about their location in each of the last two days. We will collect information about the time they spent in the air-conditioned environment and outside. The information about participant's travel destinations and time spent on a commercial jet in the last two days will also be recorded.

Psychological Factors

We will assess the following psychological factors using validated questionnaires: positive and negative effect/mood and catastrophizing every 10 days, and coping strategies, coping efficacy, perceived stress, and social support every 30 days. Participants will complete the Positive and Negative Affect Schedule (PANAS) Questionnaire [62] for positive and negative effect/mood measurements. Pain catastrophizing will be measured using the pain catastrophizing scale [63]. To assess the use of coping strategies, participants will complete Stone and Neale's Daily Coping Inventory (DCI) [64-66] adapted for chronic pain coping. Coping efficacy will be assessed on a scale from the coping strategies questionnaire [67,68]. The perceived stress scale will be used to measure the degree to which situations in participant's life are appraised as stressful [69]. We will assess the amount of support that participants receive from their friends and family using the Lubben social support questionnaires [70,71].

Study questionnaires for the baseline, the control-period, and case-period are shown in Table 1.

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Table 1. Study website questionnaires.

Questionnaires	Baseline	Control-period	Case-period
Demographics	x		
Comorbidities	x		
Perceived risk factors	x		
Baseline pain characterization -Index knee	x		
Baseline pain characterization -Contralateral knee	x		
Medications	x	x	x
Lubben social support	x	x	x
Knee injury and Osteoarthritis Outcome Score (KOOS) - Index knee	x	x	x
Knee Injury and Osteoarthritis Outcome Score (KOOS) - Contralateral knee	x	x	x
Intermittent and Constant Osteoarthritis Pain (ICOAP)	x	x	x
Physical activity	x	x	x
Footwear change and heel height	x	x	x
Trauma/injury/knee buckling	x	x	x
Climate	x	x	x
Pain Coping Inventory (PCI)	x	x	x
Perceived Stress Scale (PSS-10)	x	x	x
Daily mood measured by using Positive and Negative Affect Scale (PANAS)	x	x	x
Pain flare			x

Pain Outcome Measures and Exacerbation Definition

The primary outcome measure is the level of knee pain. We will assess pain level using the numeric rating scale (NRS) for pain, which is a commonly used, valid, and reliable measure [72-74]. The pain NRS is a single 11-point numeric scale ranging from 0 - "no pain" to 10 - "the worst pain possible" [72,73]. At the baseline we will ask the participants to indicate how severe their knee pain is at its mildest, usual, and worst times of their current everyday life. A pain exacerbation will be operationally defined as occurring if the pain measure is 2 points higher than it was at its mildest intensity reported at the baseline visit. Participants are instructed to provide the information about every episode when they have a disabling increase in their knee symptoms that lasts for longer than 8 hours without settling. When participants log onto the study website to report these episodes they will be asked what level of pain they are experiencing "right now". The online questionnaire will automatically determine if the current episode is a pain exacerbation based on the difference in pain level on the NRS from the previously collected NRS data. Participants will be given instruction to report any episode when they have a disabling increase in their knee symptoms that lasts for longer than 8 hours without settling. To avoid subjectivity they will not be aware of how the pain exacerbation is evaluated.

Sample Size Calculations

Study sample size was calculated based on case-crossover study design. A sample size of 146 participants will have 80% power at 95% confidence level to detect an OR of 2 for knee pain exacerbation in the case-period relative to control-period if the probability of exposure (trigger/risk factor) among control-periods is at least 0.1 and the correlation coefficient for the exposure between matched case-periods and control-periods is not more than 0.3. We will recruit over 300 participants allowing for approximately 30% of participants who may not experience a pain exacerbation due to natural course of the disease or early withdraw from the study. The sample size estimation is conservative because we assume that each participant only provides exposure information for one case and one control-period whereas in reality participants will provide data from multiple case-periods and multiple control-periods. Given the different risk factors being measured, we will not combine these in the analysis and will treat them as independent predictors.

Statistical Analysis

We will assess the relation of risk factors to the risk of knee pain exacerbation by conditional logistic regression analysis for matching model (m:n matching —as each selected participant could have multiple case and multiple control-periods) by using SAS software version 9.4. Only participants with both case and control-periods will be included in the regression analysis. Descriptive statistics such as total number, mean (standard deviation), median (range or interquartiles) or proportions will be used to summarize the data. For categorical exposure variables we will keep the original categories. For continuous exposure variables we will classify responses into categories based on predetermined cut-points. We will initially use narrow exposure categories to identify patterns of association between the risk factor and pain exacerbation; although it may be necessary later to collapse some of these categories to obtain stable estimates. Odds ratios

(OR) and 95% confidence intervals (CI) for the risk factors will be reported using the Mantel-Haenszel method [75]. We will also evaluate the joint effects of several risk factors on pain exacerbation by either comparing OR in subgroups, defined by different levels of the potential effect modifier or using multiple conditional logistic regression models. Subgroups will be compared with the chi-square test for homogeneity, or test for interaction of various risk factors.

While few data are available on the likely effect-period for each risk factor for pain exacerbation, the actual duration of the effect-period can be inferred empirically by examining the change in magnitude of the OR under different assumptions about duration. Thus, we will calculate the OR by assuming the effect-time period to be one day and then two days. The better estimate of duration is the one with minimal nondifferential misclassification (ie, one that maximizes the OR estimates) [50,52]. Self-matching of cases eliminates the threat of control-selection bias and increases efficiency.

As with any study conducted on human participants those with missing values would not contribute, or contribute less data to the effect estimates. We will take various approaches to minimize loss to follow-up, including comparison of the characteristics of those who provide the complete follow-up data with those who only provided part of the data, performing stratified analysis among those who have completed data points and among those who do not have complete data points, to see if the effect estimates vary.

Results

This project has been funded by the National Health and Medical Research Council (NHMRC). The enrollment for the study has started. So far, 343 participants have been enrolled. The study is expected to be finished in October 2015.

The data obtained during the course of the study will be presented in separate manuscripts for each of the studied knee OA pain exacerbation risk factors and their possible interactions.

Discussion

This study will use an Internet-based case-crossover design to identify potential risk factors or "triggers" for pain exacerbation episodes in people with knee OA, including physical activity, footwear change, trauma and injury, medication use, climatic, and psychological factors. This study design is best suited to answer these questions as it uses each case as its control and is ideal for assessing effects of triggers on recurrent episodic events, such as knee OA pain exacerbations [51].

The completion of this study will identify risk factors for pain exacerbations in knee OA. The identification and possible modification/elimination of such risk factors will help to prevent the reoccurrence of pain exacerbation episodes in the future and therefore improve knee OA management.

Possible limitations of the study include incomplete data in questionnaires, in addition to some potential for recall bias and participant fatigue. Every participant will be followed regularly for 90 days and it is possible that they may not report every pain exacerbation that they experience during that time. Another possible limitation is that the study cohort will include Internet-users only and the results may not be generalizable to all people with OA.

A notable strength of this study includes the real time capture of data prior to pain exacerbation and an Internet-based case-crossover study design.

The findings from this study will contribute to better understanding of the pathophysiology of pain exacerbation in knee OA, and guide the development of rational management strategies to prevent its occurrence. Identifying modifiable risk factors for pain and avoiding these factors could improve the quality of life for millions of people with knee OA and have great public health importance. If practitioners are armed with information about appropriate shoe wear, adverse physical activities, regular medication compliance amongst other factors that will be assessed in our study, this information will be important to counsel patients about during typical clinical encounters. It could also be used to direct self-management strategies and target appropriate treatments including psychological interventions. Thus, this work has immediate clinical applicability.

Authors' Contributions

DJH, YZ, KB and LM conceived and designed the study protocol and procured the project funding. JM and BM participated in its design and coordination. All authors contributed to construction and implementation of statistical analyses. JM and DJH drafted the manuscript and all authors contributed to the manuscript. All authors read and approved the final manuscript.

Conflicts of Interest

None declared.

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Multimedia Appendix 1

NHMRC Peer-review report.

[PDF File (Adobe PDF File), 92KB - resprot_v4i3e80_app1.pdf]

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Abbreviations

CI: confidence intervals
ICOAP: Intermittent and Constant Osteoarthritis
KOOS: Knee injury and Osteoarthritis Outcome Score
NHMRC: National Health and Medical Research Council
NRS: numeric rating scale
NSAIDs: nonsteroidal anti-inflammatory drugs
OA: osteoarthritis
PainPCI: Pain Coping Inventory
PSS: Perceived Stress Scale
PANAS: Positive and Negative Affect Scale
OR: odds ratios

Viewpoint

Lessons Learned From Using Focus Groups to Refine Digital Interventions

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Abstract

There is growing interest in applying novel eHealth approaches for the prevention and management of various health conditions, with the ultimate goal of increasing positive patient outcomes and improving the effectiveness and efficiency of health services delivery. Coupled with the use of innovative approaches is the possibility for adverse outcomes, highlighting the need to strategically refine digital practices prior to implementation with patients. One appropriate method for modification purposes includes focus groups. Although it is a well-established method in qualitative research, there is a lack of guidance regarding the use of focus groups for digital intervention refinement. To address this gap, the purpose of our paper is to highlight several lessons our research team has learned in using focus groups to help refine digital interventions prior to use with patients.

Introduction

Background

Digital interventions have an important role to play in promoting health and well-being among patients. However, this mode of delivering information and interaction is not without pitfalls [1]; a reality that highlights the importance of developing and refining interventions in a thoughtful, systematic manner prior to implementation [2]. One available method for refining digital interventions is focus groups, an approach used traditionally in the fields of marketing and advertising research to solicit consumer feedback on concepts and products [3]. Focus groups, now a frequently used method in qualitative research, are unique in that they enable the collection and analysis of three complementary forms of data -individual and group level data, and data generated based on participant interaction [4]. This feature is valuable because the researcher can explore multiple units of analysis to understand the research question. Additionally, focus groups are advantageous as they often allow for the spontaneous discussion of topics (eg, Butler, 1996 [5]) that may otherwise go unvoiced in other methods of data collection, such as individual interviews.

Focus groups have been used to assess individuals' perceptions of and refinements for changes to the structure, content, and utility of digital interventions. For example, focus groups have been applied to study single, standalone interventions [6,7], educational resources for patients [8,9], and the usability of several comparable tools [10]. Despite these examples, there

remains a lack of guidance for using focus groups in the context of digital health, and specifically, digital intervention refinement. To date, most recommendations have emphasized the use of focus groups for nondigital interventions [11] and recruiting participants into focus groups [12]. To address this gap, our purpose was to highlight several lessons that we learned from our collective experience [13-15] in using focus groups to help develop and refine digital interventions.

Lessons Learned

In a recent study that has been registered with ClinicalTrials.gov (NCT02330588) [13], our research team used focus groups to refine a newly developed online screening, brief intervention, and referral to treatment program designed to enhance parents' awareness of and motivation to change children's healthy lifestyle behaviors. The following are practical lessons learned from conducting these focus groups.

1. Use a Checklist to Plan, Track, and Report Aspects of the Focus Group

As qualitative research involves the exploration of complex phenomena, explicit and comprehensive reporting can be a challenge. An additional hurdle is clearly articulating the research team's background, study design, coding process, and key findings, which may be particularly important when researchers acting as focus group moderators are intellectually and potentially financially invested in the digital intervention under study. For transparency and to enhance methodological rigor, a checklist can help to organize and articulate all of the relevant processes and procedures the research team undertook in their research with focus groups. For example, the Consolidated Criteria for Reporting Qualitative Research (COREQ) [16] is a 32-item checklist that can be used to report criteria in three domains: research team and reflexivity (eg, researchers' credentials, relationship(s) with participants); study design (eg, theoretical framework, participant selection); and analysis and findings (eg, methodology, use of verification strategies).

2. Have a Helper

Participants can perceive focus groups for refining digital interventions as opportunities to share their thoughts and opinions about the intervention as well as query the rationale for different intervention elements. However, the focus group moderator has a demanding position to facilitate the flow of discussion and strategically channel participant's feedback, often within a predetermined time period. Therefore, he/she needs to strike a balance between respectfully allowing participants to "tell their stories" and contribute meaningfully while adhering to their interview guide that is typically designed to solicit feedback on a range of issues related to the intervention. With this in mind, the inclusion of an assistant or collaborator in the focus group can help to keep everyone on time and on task, as well as alleviate the moderator of distracting and time-consuming tasks, such as note-taking. For instance, if the discussion is running long or the group tends to get side-tracked by one or two individuals, the assistant or collaborator might say: "Unfortunately we are running short of time; could we follow up with you regarding your thoughts at

a later point?" This strategy allows the moderator to maintain their emphasis on the interview questions and process as well as complete the focus group in a timely manner.

3. Prepare for Constructive Feedback

In contrast to many traditional focus groups, which are often used to explore and solicit perspectives related to abstract and conceptual phenomena, focus groups for refining digital interventions are more targeted, querying participants' opinions on a tangible product in which the researchers (often including the focus group facilitator) may have painstakingly developed. It is not unusual for research team members to have an emotional response to criticism when blood, sweat, and tears have been generated through the intervention development phase. It is essential to prepare oneself for unexpected remarks as the moderator's negative expressions and/or feedback may unduly sway participants from communicating their true thoughts and feelings, which may compromise the credibility and usefulness of the data.

4. Tailor Questions to Participants

It is valuable to obtain perspectives from a diverse group of stakeholders when developing a new intervention. For instance, if developers plan to target substance abuse behaviors in adolescents, it makes sense to solicit feedback from adolescents themselves (the target audience), but also other relevant stakeholders (eg, health care professionals, parents, teachers) who may have a keen interest in the tool or who may play a role in referring or recommending the intervention to adolescents. Depending on the degree of homogeneity in each focus group, moderating questions and facilitating probes may need to be tailored for language and content. In our experience, we tailored discussion questions to groups of parents and health care professionals who were more interested in practical issues (eg, diversity of information and health services to promote healthy nutrition in families) versus researchers who showed a greater affinity for academic elements (eg, assessing parents' motivation constructs that can predict behavior change) of the intervention.

5. Preserve Context When Capturing Data

Unlike focus groups in which participants are encouraged to discuss intangible concepts (eg, an experience or process), focus groups for refining digital interventions typically query participants' views on concrete elements (eg, aesthetics, ease, and logic of navigation). Given this difference, capturing the discussion of focus group participants with a digital audio recorder and subsequent transcription may not preserve the context of intervention details to which participants refer (eg, "I like the font and images you used on this page"). To improve the accuracy of data capture in focus groups, Scott et al (2009) [17] proposed real-time data transcription using certified court reporters that include transcribing focus group discussions into text, similar to processes used in court hearings and depositions. We have used this approach and realized several benefits, including (1) the transcription is highly accurate; (2) additional context can be included into transcripts if desired; (3) turnaround is quick (3-4 business days), enabling concurrent data collection and analysis, an important tenet of qualitative research [18] even if several focus groups are planned over a short period of

time; and (4) the moderator can focus his/her full attention on facilitating the group discussion without concern for data collection.

6. Assess the Current Intervention–Do Not Create a New One

Developing or white-boarding unique concepts for digital interventions can be exciting and it is not atypical for focus group members who are highly-engaged to suggest the addition of digital elements outside the scope of the current intervention (eg, incorporation of avatars, chat rooms, and other social media components). An important task of the moderator is to manage and concentrate participants' feedback to the task at hand. Particularly when refining an intervention, as much of the design, structure, and functional elements have already been established, it is important to stay focused on more proximal aspects of refinement (eg, likability, feasibility, and utility) of the *current* intervention. It may also be helpful for the moderator to explicitly discuss the objectives of the focus group and the kinds of modifications that are possible before the group discussion begins in order for participants to have clear expectations.

7. Leverage the "Digital Expert"

In our experience, focus groups often contain at least one "digital expert", a member with personal or professional experience in design, information architecture, or computer programming. Depending on the nature of the contributions and how the moderator manages the discussion, the digital expert can exert a positive or negative influence on the group discussion. An attentive moderator can leverage the digital expert to help channel the group discussion on intervention attributes; acknowledging the individual's experience and expertise as well as utilizing probes to draw out information and insights relevant to the current intervention can engender rapport, respect, and openness throughout the group. Issues that arise beyond the scope of the focus group can be respectfully deferred to a later date, which allows the digital expert to contribute additional information while not detracting from the goal at hand.

Conclusions

Refining digital interventions using focus groups presents unique challenges and opportunities. Based on our experience to date, we have learned a number of lessons, including (1) transparency of the research process can be facilitated through the use of a checklist to plan, track, and report important aspects of the focus group; (2) some participants may misperceive focus groups as an unimpeded opportunity to discuss the intervention and efforts should be employed to optimize use of time; (3) the moderator may be heavily invested (emotionally and/or financially) in the intervention and should be prepared for critical comments from participants; (4) the refinement process may benefit from a number of different perspectives, so tailoring the discussion questions and probing follow-up questions is advised; (5) special consideration for capturing data is required so that the context of the discussion remains clear and accurate at the data analysis phase; (6) the moderator should specify the purpose, which includes refining the existing intervention rather than developing a new one; and (7) a "digital expert" may be present within the group, so the moderator should plan accordingly to manage individual contributions in order to effectively facilitate the group discussion. These practical lessons may be particularly relevant for clinicians and researchers working to refine new digital interventions. Such a process is likely to increase in frequency as health care delivery evolves to adopt novel interventions designed to optimize patient outcomes and improve health care availability, accessibility, and acceptability.

Conflicts of Interest

None Declared.

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Abbreviations

COREQ: Consolidated Criteria for Reporting Qualitative Research

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