# JMIR Research Protocols

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Protocol

# An Ecological Momentary Intervention to Reduce Alcohol Consumption in Young Adults Delivered During Drinking Events: Protocol for a Pilot Randomized Controlled Trial

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## *Abstract*

**Background:** Risky drinking is a significant public health issue in young Australian adults. Brief interventions are one of few effective methods of reducing risky drinking but are time and cost intensive; innovative methods of delivery are therefore of interest. Mobile phones offer new opportunities to collect data and intervene during risky drinking events. Mobile phones have successfully been used for delivery of alcohol-related brief interventions and data collection but not in combination with or during drinking events.

**Objective:** This pilot study will investigate the efficacy of an ecological momentary intervention (EMI), with combined ecological momentary assessment (EMA) and brief intervention delivered by mobile phones to young adults during risky drinking events.

**Methods:** We will use a 3-armed randomized controlled trial to investigate the efficacy of the intervention for reducing peak single occasion drinking. Our sample is recruited from an observational cohort study of young, risky drinkers. Participants will be randomized into 1 of 3 intervention arms. On 6 nights across a 12-week study period, EMI and EMA groups will complete hourly EMA surveys on their mobile phone. EMI participants will receive tailored feedback short message service (SMS) texts corresponding to their EMA survey responses. The EMI participants will not receive feedback SMS. A third group will have no contact (no-contact control). All groups will then be contacted for a follow-up interview within 4 weeks of the 12-week study period ending.

**Results:** The primary outcome is mean reduction in standard drinks consumed during their most recent heavy drinking occasion as measured at follow-up. Secondary outcomes include alcohol consumption over the previous 6 months, experiences of alcohol-related harms, attitudes toward drinking and drunkenness, hazardous drinking and use of tobacco and illicit drugs. A random effects mixed modelling approach using maximum likelihood estimation will be used to provide estimates of differences in mean drinking levels between those receiving the intervention and control participants.

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**Conclusions:** This study is novel in that, unlike previous work, it will intervene repeatedly during single occasion drinking events. Further, it extends previous research in this area, which has applied limited tailoring of message content for SMS-based brief interventions. The findings of this study will contribute to the growing body of evidence to inform the use of mobile health interventions for reducing alcohol consumption and harms.

**Trial Registration:** Australian New Zealand Clinical Trials ACTRN12616001323415; https://www.anzctr.org.au/ Trial/Registration/TrialReview.aspx?id=369534 (Archived by WebCite at http://www.webcitation.org/ 6qDqBZV9b)

## Introduction

Risky single occasion drinking (RSOD, sometimes termed binge drinking) remains a significant public health issue in Australia for young people. The 2013 National Drug Strategy Household Survey reported that approximately two-thirds of 20- to 29-year-olds engaged in RSOD in the past year (defined as 5 or more Australian standard drinks, or 50 g alcohol in a session) [1]. In 15- to 24-year-olds, 1 in 5 hospitalizations and 1 in 7 deaths are attributable to alcohol consumption [2]. Other associated harms include physical and sexual violence, risky sexual behavior, and both short- and long-term brain impairment and cognitive deficits [3-5].

Few individually targeted strategies have been shown to effectively change young people's drinking behaviors. A notable exception is the brief intervention, which typically involves screening and assessing drinking behavior and providing tailored, personalized feedback. Although traditionally delivered in clinical settings, brief interventions have been successfully trialed in college and university settings and have shown efficacy in reducing alcohol consumption [6-9]. Brief interventions are traditionally delivered in face-to-face mode, which means that while effective, they are both time and resource intensive. Recent efforts have attempted to upscale this approach using Web-based and mobile phone delivery of brief interventions [10-16], with some success. Building on some of the works by Kypri [10,17], Voogt et al [14] developed the "What Do You Drink" Web-based brief intervention, combining weekly Internet-based screening with tailored feedback. The study found a significant reduction in weekly alcohol consumption in the experimental arm compared to the control arm at 4 points of follow-up. Newer technologies can provide opportunities to expand on this concept further and explore in-event characteristics, behavior, and intervention.

Approximately 95% of young adults in Australia own smartphones with computerized functions and Internet connections [18]. The integration of mobile phone use into young people's lives provides new opportunities for health interventions to be delivered directly to at-risk populations during risky events such as drinking occasions.

Mobile phones have also been used as remote data collection tools. This data collection functionality means that they can serve as a platform for the screening and assessment phase of brief interventions, using ecological momentary assessments (EMAs) [19], which are repeated, real-time behavioral surveys.

Previous studies have demonstrated the feasibility of collecting EMA data on specific occasions of alcohol use by young people using mobile phones [20]. Kuntsche and Labhart developed the Internet-based cell phone–optimized assessment technique (ICAT) [21] to collect alcohol consumption data from more than 200 Swiss young adults, using repeated EMAs between 5 PM and 11AM on weekend nights. They found this method to be easy and convenient and were able to record more than 10,000 questionnaires across the 5-week study period [20].

Recent studies have attempted to combine EMA with brief intervention (sometimes called ecological momentary intervention [EMI] or screening with brief intervention [SBI]). Suffoletto et al [16] used short message service (SMS) data collection with young adults reporting their intentions to drink on the coming weekend, commitment to reduce drinking, and later, their actual weekly drinking. Tailored advice was then sent to participants in response; they reported a small reduction in binge drinking within the sample of young adults. Riordan et al [12] collected alcohol consumption data and delivered brief advice by SMS message to university students in New Zealand. In that study, participants were sent 4 total EMA during orientation week (the week prior to the university semester starting, which usually involves multiple parties and other social events) and once per week during the semester. Participants in the EMA-EMI condition additionally received SMS with health consequence warnings at 7:30 PM on each night of orientation week. They found a reduction in alcohol consumption during orientation week for women but not for men [12].

However, we could find no studies which combined repeated alcohol consumption data collection with repeated SMS brief interventions delivered during single occasion drinking events. EMA captures subjects' behaviors and experiences in real time, maximizing ecological validity by assessing subjects in their natural environment [22]. Another strength of the EMA is that it can reduce recall bias (retrospective reporting is known to underreport consumption). EMI offers both of these benefits with the added advantage of intervening in a participant's natural environment while the targeted behavior is occurring.

This study uses an EMI, combining mobile Web-based EMAs (ie, surveys completed in a mobile phone Web-browser, similar to Kuntsche and Labhart's ICAT) [21] and SMS brief interventions delivered during drinking events using mobile phones. The intervention was codesigned and evaluated by young people in a development study [23]. In the development study, participants deemed the intervention content, mode of

delivery, and level of burden to be highly acceptable and feasible [23]. This research demonstrated both feasibility and acceptability; the next phase will determine whether this intervention is effective in changing behavior. This study aims to determine the impact of a tailored brief intervention delivered by mobile phone on young people's RSOD behavior.

## *Methods*

### Study Design

We will use a 3-armed repeated measures randomized controlled trial (RCT) design to generate high-quality evidence of the impact of our mobile phone intervention on peak consumption of alcohol in risky drinking events among young people. The design of the study is summarized in Figure 1.

**Figure 1.** Study design.
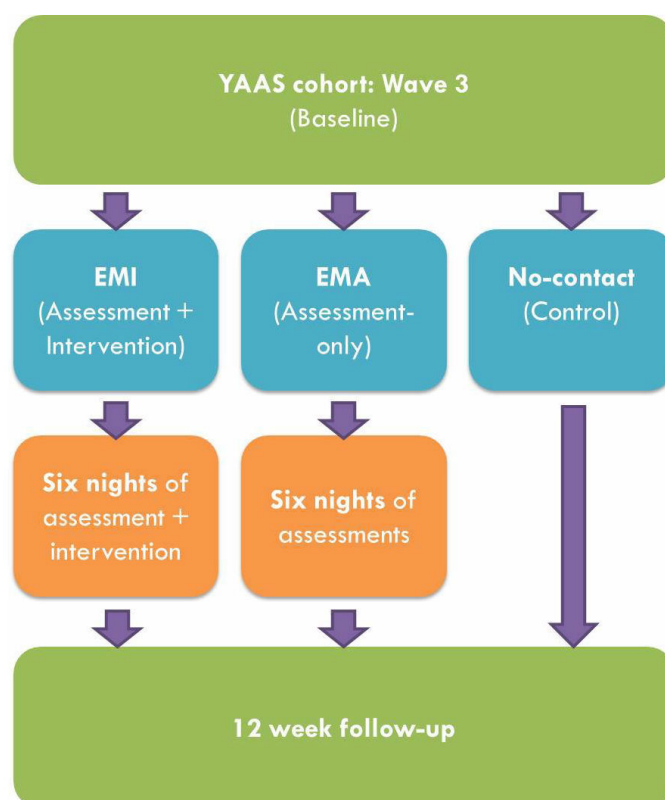


### Participants

Participants will be recruited from the ongoing Young Adults Alcohol Study (YAAS) cohort [24]. The YAAS cohort study commenced in 2012 and originally recruited a representative sample of 802 young Melburnians aged 18 to 25 years, screened for engagement in very high-risk drinking [24]. YAAS participants were recruited through random digit dialing from a sampling frame of landline telephone numbers. Eligible participants were administered a structured questionnaire using computer-assisted telephone interviews (CATIs) that included questions on demographics, past-year alcohol consumption, the Alcohol Use Disorders Identification Test (AUDIT) [25], drinking consequences and contexts [26,27], life satisfaction [28], and the most recent heavy drinking occasion [24], focusing on timing, locations, amount and types of alcohol consumed, and amount spent on alcohol at each location. Approximately half of the original sample were male (407/802, 50.7%), studying full-time (407/800, 50.9%), educated to a year 12 level (416/799, 52.1%), and had more than Aus $160 (US $118) weekly recreational spending money (416/788, 46.7%). Most were born in Australia (722/802, 90.0%), lived with parents

(736/802, 91.8%), and identified as heterosexual (738/800, 92.3%) [24].

A second wave of data collection was completed in 2013 and a third in 2015; data from the final wave will be used as the baseline for this study. In 2013, 531/802 participants (66.2%) remained from the original cohort. In 2015, a total of 373/802 (46.5%) participants remained. Participants have not previously experienced any specific interventions as part of this study other than these telephone surveys.

### Recruitment and Screening

All participants who meet eligibility criteria will be invited to receive information regarding a new study. Eligibility criteria include owning a smartphone and recent risky drinking behavior (5 or more drinks in a single session in the past 3 months).

Those who agree to receive information will be randomly allocated to 1 of 3 arms: an intervention group where participants receive a brief intervention delivered over mobile phone (EMI) or to 1 of 2 control groups where participants will either complete EMAs without brief intervention (EMA) or do not receive any contact through the trial period (no-contact

control). Participants will only receive study procedure information relating to the arm to which they have been allocated. The nature of the intervention means it will not be possible to blind participants; however, they will remain unaware of the detailed procedures of the other arms. Research personnel administering the follow-up questionnaires will be blind to the group to which participants were allocated.

Following group allocation, participants will be sent an SMS message containing a brief description of their arm of the study with a link to the participant information and consent form. Participants who do not respond will be sent 1 reminder SMS message 2 weeks later. Remaining nonrespondents will then be followed up by phone, up to a maximum of 6 phone calls each or until contact is made.

## Description of the Ecological Momentary Assessment Data Collection

Each participant from the EMI and EMA groups will be expected to choose 6 nights to complete EMA throughout the 12-week study period. We chose this number of events based on recommendations from the development study. No minimum criteria will be given to participants for amount of consumption planned; they will simply be asked to choose nights on which they are planning to drink. Participants will be provided with initial instructions on how to register for a night and will be prompted each Thursday night with a reminder to register if there are any nights over the weekend that they plan to drink. This process includes them sending a simple SMS message saying "Drink" on the day or they can register in advance by texting the name of the day of the week they intend to complete the intervention on (eg, "Saturday" for the upcoming Saturday). Participants will receive a confirmation message once they have registered.

The timing and frequency of the data collection and intervention design were informed by previous research in Switzerland [19] and Australia [23] which found that hourly surveys were perceived to have low burden. At 6 PM on chosen intervention nights, participants will receive a short SMS message asking them to complete their first survey with a link to an online questionnaire hosted by the online survey tool SurveyGizmo [29]. SurveyGizmo was chosen above other options due to mobile compatibility, visual appeal, and range of question types.

The 6 PM presurvey will ask questions relating to their intentions for the night, including how much they plan to drink, spend, and eat; a ranked list of particular adverse events they wish to avoid (eg, vomiting, not being able to get home); their planned mode of transport home; next day plans; any alcohol consumption so far; mood; and the option of writing a message to themselves to be sent back to them during the night.

At hourly intervals between 7 PM and 2 AM, respondents will be sent a shorter EMA survey that asks about current location type, alcohol consumption since last survey, spending, mood, and perceived drunkenness. Participants will also be able to opt out of the intervention at the end of each survey if they are finishing their evening.

At 11 AM the next day, participants will be sent another SMS with a mobile survey link. This survey asks for any alcohol consumption and spending occurring after the final EMA, an estimated total standard drinks and spending for the night, an estimated volume of water consumed for the night, reporting of adverse events, hangover experienced, and a fun rating of the night. Figure 2 summarizes the different data that will be collected during the drinking event at different time points.

## Intervention Group

In addition to completing EMAs, the EMI group will receive the SMS brief intervention component. Following submission of each EMA survey throughout intervention nights, they will receive a feedback SMS comprising of motivational information tailored based on their responses.

All feedback SMS during the night will be comprised of information aiming to remind the EMI group participant of their original intentions or motivations, tips to avoid adverse consequences, or feedback relating to cumulative consumption or spending. These messages will be based on a different key variable each hour (see Figure 3).

This intervention, including all questionnaires, message content, and overall study features, was codesigned with a group of 42 young people in a development study conducted in 2014 [23]. This study involved 3-hour workshops to inform the design, individual testing of the intervention on a night of drinking, and evaluation involving both in-depth interviews and a structured online survey.

**Figure 2.** Data collected during drinking event.
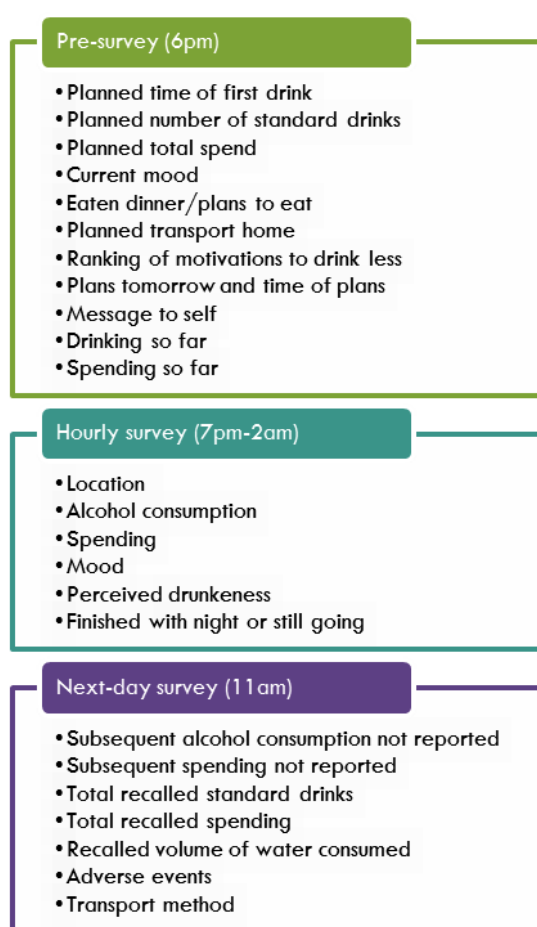


**Figure 3.** Framework for determining message tailoring.
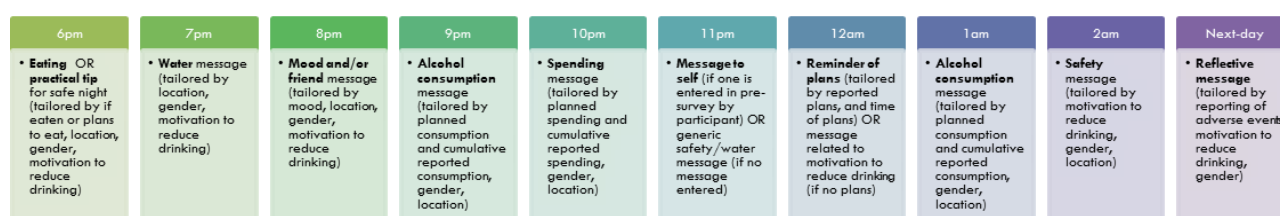


## Message Tailoring

A bank of messages has been created with over 15,000 messages contained within a matrix of key variables related to information collected about and from participants during the EMAs. Messages have been tailored to correspond with different situational contexts that participants may find themselves in throughout their drinking events. Messages were written and categorized according to gender as well as variables collected during the surveys such as varying locational contexts (ie, for a participant at a bar, as opposed to drinking at home), times of night, mood, motivations reported by participants, combinations of planned drinking versus actual drinking, and planned versus actual spending. The content, language, and framing of content was informed by the participatory codesign process used in the development study [23] with messages refined according to principles of motivational interviewing theory [30].

In order to create a feasible tailoring system, we created a framework to determine the type or topic of message sent at each hourly interval, with decision logic based on different variables collected throughout the night. Our SMS system was custom-developed by SurveySignal [31] according to our specifications. The SurveySignal system was designed so that once a participant triggered their drinking event by SMS (as described earlier), the system would generate a schedule of SMS with survey links to be sent hourly to that participant for the chosen night. If a participant opted out during the course of the night, the remaining schedule would be deleted so that no further surveys would be sent on that occasion. The SurveySignal system linked with SurveyGizmo (which we used to host our EMA surveys) using http POST so that data for the variables used in tailoring would be transmitted immediately to the SurveySignal database as soon as entered into the survey. The back end of SurveySignal has a databank of messages that were

individually written to correspond to different combinations of the tailoring variables. These combinations are described in Figure 3. For each survey filled out, algorithms are run within SurveySignal to match an individual's responses against the logic framework to determine which SMS should be sent. The system then generates and sends the matching SMS immediately to the participant. For example, at 6 PM, if the participant has indicated that they have not eaten and have not made plans to eat, they will receive a message about why it is important to eat with the particular message tailored by what they have input as something they would like to avoid that night (as a proxy for motivation to reduce drinking). A participant who reports in their presurvey that they would like to avoid feeling sick or vomiting may receive a message such as "Best way to not get sick tonight is to make sure you eat enough ASAP, and start with a big glass of water. Get on it!" In testing, most feedback SMS were received within 15 seconds of the survey completion.

## Control Groups

The first control group (EMA) will follow the EMA data collection procedure described above (including registration for 6 intervention nights and all surveys on each night) but will not receive any feedback SMS. This EMA-only group is necessary to investigate reactivity and the potential that—although unlikely [32]—completing assessments alone (without any feedback or other intervention) can affect drinking behavior. A second control group (no-contact control) will not receive any contact until follow-up, which will occur 12 to 16 weeks after the baseline assessment. The no-contact control group will be the primary control group used for comparison to the EMI group in analysis.

## Reimbursement

Participants from the EMI and EMA groups will receive reimbursements varied based on the level of participation in the study. For each event completed (up to a total of 6), participants will receive Aus $10 (US $7). If all 6 are completed, a bonus Aus $20 (US $15) is applied. Participation in the follow-up survey is valued at Aus $20 (US $15). Therefore, participants who complete all 6 events and the follow-up interview will receive Aus $100 (US $74) in cash or voucher. Participants from the no-contact control group will receive Aus $20 (US $15) for participating in the follow-up phone survey.

## Ethics

Ethics approval for the RCT has been obtained from the Monash University Human Research Ethics Committee. Ethics approval for the YAAS cohort study has been obtained from the Alfred Health Research Ethics Committee.

## Primary Outcome Measure

All measures were defined a priori. The primary outcome measure will be change in the mean peak number of drinks consumed in a single night over the 3-month intervention period between those receiving the intervention (EMI group) and control participants (no-contact control group). Our focus on heavy drinking from an occasional or binge perspective is because this is the main risky drinking pattern in our target age group [33,34]. We will assess this by asking participants about the number of drinks consumed in their last heavy drinking occasion in the past 3 months at both baseline and immediately following the intervention period. We expect to see a greater reduction in mean peak drinking in the EMI group compared to no-contact control group. In the first wave of YAAS [33], the mean number of drinks consumed on the most recent heavy drinking occasion was 13.1 (SD 5.2) Australian Standard Drinks. We estimate that reducing this by a mean of 2.5 standard drinks ($d$=0.48) would halve the odds of serious injury [35,36]; this forms the basis of our target effect size.

## Secondary Outcome Measures

Secondary outcomes of interest will also be collected at both baseline and follow-up interviews and include:

- Alcohol consumption (graduated quantity frequency)
- Alcohol-related harm (derived from the Gender, Alcohol, and Culture: An International Study [GenACIS] [27] and Victorian Youth Alcohol and Drug Survey questionnaires [37])
- Attitudes toward drinking and drunkenness (derived from GenACIS [27])
- Hazardous drinking (derived from World Health Organization AUDIT [25])
- Use of tobacco, illicit drugs, and nonmedical use of pharmaceuticals (derived from GenACIS [27])
- Life satisfaction (Personal Wellbeing Index [28])

Feasibility and acceptability will be assessed in the follow-up survey among both EMI and EMA groups using 5-point Likert scales asking participants to rate a series of individual statements pertaining to their experience of undertaking the intervention (eg, "The assessments were easy to complete" and "The feedback provided was relevant to me"). Additional process evaluation measures such as participant levels of response, refusal, and timeliness of response will be explored to assess feasibility and acceptability.

## Randomization

Using the Stata statistical software package version 13.1 (StataCorp LLC), block randomization will be conducted to ensure balanced randomization to each of the 3 study arms. Randomization will be completed by a researcher with no involvement in the trial.

## Sample Size

Study sample size is based on this primary aim to reduce mean peak consumption by 2.5 drinks in the intervention group (EMI) compared to controls (EMA and no-contact control). Assuming a standard deviation of peak drinking of 5.2, conservative 67% endpoint participation, 90% power, and 5% significance, it was estimated that a sample of 127 participants per group was required. The sample size estimate has been calculated to test for a group by time interaction from a mixed repeated measures design and a moderate correlation between subject measurements ($r$=0.45, estimated from wave 1 and 2 of YAAS cohort data).

## Statistical Analyses

Given the randomized design, dependency on repeated participant observations, and potential bias from study attrition, a random effects mixed modeling approach using maximum

likelihood estimation will be used to provide unbiased estimates (assuming a missing at random missing data process) of differences in mean drinking levels between those receiving the intervention (EMI group) and control participants (no-contact control group). Study subjects and treatment will be modeled as random and fixed factors respectively in these mixed model analyses. The interaction between intervention and study time (baseline versus 12-week follow-up) is the primary focus of analysis. Distributional assumptions of models will be tested in the data and appropriate transformations applied where these are not reasonably met. These analyses will be repeated as secondary analyses to determine the impact of the assessments alone (ie, comparison of EMA and no-contact control groups) using participant observations from EMA assessment. Further analyses may also be undertaken to investigate associations between particular types of messages and alcohol consumption.

## Results

Enrollment for this study was completed in April 2016. Data analysis is currently being undertaken, and we expect to submit our results for publication in mid-2017.

## Discussion

### Summary

This study is novel in that, unlike previous work [12,15,16,20], it is designed to intervene repeatedly during single occasion drinking events. Further, it extends previous research in this area [12,38], which has applied limited tailoring of message content for SMS-based brief interventions. Participants in this trial have been screened multiple times for risky drinking behavior, and as such, are an ideal cohort to target with an intervention. A further strength of the study is the rich data collected through multiple sources (CATI interviews and EMA data).

### Limitations

A number of limitations also exist. While the intervention has been developed and tested through participatory methods, the development study [23] only tested the intervention on one night for each participant. Adherence may be affected by requiring multiple testing occasions.

Recruitment and adherence may also be affected by the nature of the sample. Participants have already completed multiple waves of data collection across 4 years, and it is possible that participants will be less inclined to participate in another, more extensive, study. The sample consenting to participate in the RCT may end up being comprised of those more motivated to participate in research or change their behavior. Analyses of nonrespondents and refusals will be undertaken in order to investigate this possibility.

The study relies on self-reported data, which has the potential for reporting bias; participants may either intentionally or unintentionally report inaccurate data through either EMAs or the telephone surveys. Participants will be given flexibility with choice of intervention nights and are not incentivized for actual consumption in any way to minimize the risks of either encouraging drinking or falsely reporting consumption. Further, a key challenge of collecting data during a drinking event is that participants will be consuming alcohol while reporting. This will not affect our assessment of the intervention's efficacy because the primary outcome measure does not use EMA data. However, any future use of this data will be affected by this limitation, and we have implemented some measures to minimize this bias. For example, the surveys were designed to be as easy to complete as possible, in case of physical incoordination. Secondly, the surveys were hourly to give participants a shorter (and hence more easy to recall) reporting period. However, it is not entirely possible to eliminate this bias given the nature of in-event intervention. While validation with observational methods is beyond the scope of this study, data from EMAs during the night will be compared to next-day recall of alcohol consumption. There is also the possibility that intoxication may reduce the intervention message salience; however, this is yet to be tested. Another limitation of our approach is that complex tailored interventions do require more participant involvement than nontailored interventions. While our development study showed very high response rates (90% of all EMA surveys were completed), adherence in the current and other samples will not be known until tested. Finally, as with all incentivized intervention studies, adherence may not be able to be replicated outside of research settings.

### Conclusion

This study aims to investigate the efficacy of a mobile EMA and brief intervention for reducing risky drinking in young Australians. The findings of this study will contribute to the growing body of evidence [12,16,19] to inform the use of mobile health interventions for reducing alcohol consumption and harms.

## Conflicts of Interest

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## Abbreviations

**AUDIT:** Alcohol Use Disorders Identification Test
**CATI:** computer-assisted telephone interviews
**EMA:** ecological momentary assessment
**EMI:** ecological momentary intervention
**GenACIS:** Gender, Alcohol, and Culture: An International Study
**ICAT:** Internet-based cell phone–optimized assessment technique
**NHMRC:** National Health and Medical Research Council
**RCT:** randomized controlled trial
**RSOD:** risky single occasion drinking
**SBI:** screening with brief intervention
**SMS:** short message service
**YAAS:** Young Adults Alcohol Study

Protocol

# Home-Based HIV Testing and Counseling for Male Couples (Project Nexus): A Protocol for a Randomized Controlled Trial

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## Abstract

**Background:** HIV prevalence remains high among men who have sex with men (MSM) in the United States, yet the majority of research has focused on MSM as individuals, not as dyads, and has discussed HIV risks primarily in the context of casual sex. Nexus is an online prevention program that combines home-based HIV testing and couples HIV testing and counseling (CHTC). It allows partners in dyadic MSM relationships to receive HIV testing and care in the comfort of their designated residence, via video-based chat. By using video-based technologies (eg, VSee video chat), male couples receive counseling and support from a remote online counselor, while testing for HIV at home.

**Objective:** This randomized control trial (RCT) aims to examine the effects of video-based counseling combined with home-based HIV testing on couples' management of HIV risk, formation and adherence to explicit sexual agreements, and sexual risk-taking.

**Methods:** The research implements a prospective RCT of 400 online-recruited male couples: 200 self-reported concordant-negative couples and 200 self-reported discordant couples. Couples in the control arm will receive one or two home-based HIV self-testing kits and will be asked to report their results via the study's website. Couples in the experimental arm will receive one or two home-based HIV self-testing kits and will conduct these tests together under the facilitation of a remotely located counselor during a prescheduled VSee-based video CHTC session. Study assessments are taken at baseline, as well as at 3- and 6-month follow-up sessions.

**Results:** Project Nexus was launched in April 2016 and is ongoing. To date, 219 eligible couples have been enrolled and randomized.

**Conclusions:** Combining home-based HIV testing with video-based counseling creates an opportunity to expand CHTC to male couples who (1) live outside metro areas, (2) live in rural areas without access to testing services or LGBTQ resources, or (3) feel that current clinic-based testing is not for them (eg, due to fears of discrimination associated with HIV and/or sexuality).

**Trial Registration:** ClinicalTrials.gov NCT02335138; https://clinicaltrials.gov/ct2/show/NCT02335138 (Archived by WebCite at http://www.webcitation.org/6qHxtNIdW)

**KEYWORDS**

HIV; telemedicine; male couples

## Introduction

HIV prevalence remains high among men who have sex with men (MSM) in the United States [1]. Recent research has drawn attention to the role of male dyads in the US HIV epidemic, with primary partners identified as the source of approximately one-third [2] to two-thirds [3] of new HIV infections. Given these estimates, a significant paradigm shift in HIV prevention is needed. Efforts have traditionally focused on MSM, in particular gay-identifying men, (1) as individuals versus dyads and (2) as having been the focus of messages about HIV risks, primarily in the context of casual sex. Recent research findings have illustrated high rates of sexual risk behavior for HIV with primary and casual partners, low rates of disclosure of potentially risky episodes with casual partners to primary partners, and reduced frequency of HIV testing among male couples [4-10]. In addition, relationships may convey a misplaced sense of protection [11,12], to some degree created by the historical prevention focus on reducing numbers of sexual partners among MSM [13]. The Office of the US Global AIDS Coordinator, through dissemination of prevention guidelines for MSM in the President's Emergency Plan for AIDS Relief-supported countries, now recommends couples HIV testing and counseling (CHTC) for male couples [14].

CHTC has been used as an HIV prevention intervention for heterosexual couples in Africa for over 20 years [15]. Labeled as a "high leverage HIV prevention intervention" by the US Centers for Disease Control and Prevention (CDC) [16], CHTC is considered an effective approach to HIV prevention among male couples. The difference between CHTC and individual HIV testing and counseling is that both partners of the male couple receive counseling and testing together at the same time [17]. During the CHTC session, the counselor learns about the couple's relationship and provides tailored counseling and HIV prevention recommendations based on the characteristics of the couple's relationship and their joint HIV status [17]. Through the adaptation of CHTC and the high acceptability among MSM [15,18], preliminary data from MSM in three US cities—Atlanta, Chicago, and Seattle—demonstrate the readiness of US MSM to receive and use CHTC [19,20]. Preliminary data also suggests that male couples receiving CHTC do not report increased levels of intimate partner violence (IPV) or relationship dissolution [21]. CHTC is now considered by the CDC to be an effective public health strategy and is currently being implemented in over 40 US states [17,22].

A critical aspect of CHTC involves discussing a couple's sexual agreement. Sexual agreements refer to mutually understood rules between two partners that describe the kinds of sexual behavior that are allowed within and outside of their relationship [23]. Sexual agreements are common among male couples [5,23-30]. In CHTC, male couples discuss their sexual agreements, role-play with the counselor about how they would communicate about breaking their sexual agreement to their partner, and develop an HIV prevention plan based on their sexual agreement and couple HIV serostatus. Research regarding male couples' sexual agreements has shown that men are less likely to practice concurrent condomless anal intercourse (CAI) if they value and commit to their agreement and if they perceive their main partner to be dependable and investing in the relationship [29,31-33]. Additionally, promoting positive relationship dynamics has the potential to reduce couples' risk for HIV, as increased trust, communication, commitment, and social support are shown to be associated with lower odds of breaking a sexual agreement, which can ultimately reduce unique HIV risks (eg, CAI) for the couple [4].

In addition to CHTC, another HIV testing option is home-based HIV testing, which was approved by the US Food and Drug Administration in 2012 [34]. Some have argued that the lack of direct counseling with home-based testing may prevent MSM from (1) fully understanding the results, (2) adopting safer preventive strategies, and/or (3) successfully linking to care if newly HIV positive [35]. One way to address the lack of counseling for home-based HIV testing may be through the use of remote online counseling delivered through video-chat software. Online counseling offers a convenient, confidential, and user-controlled opportunity to provide support and information to individuals who otherwise may not be willing or able to access services in person. Telemedicine modalities, such as email, instant messaging, chat rooms, video conferences, and interactive media, have provided online counseling services for people suffering from disabilities, depression, and anxiety; for survivors of trauma; and for cancer treatment [36]. Although the use of telemedicine to address HIV is a fairly recent development, evidence from diverse settings suggests it is feasible, acceptable, and effective [36-38]. A number of HIV prevention interventions have been designed to deliver messages and counseling through use of the Internet [39-42]; the results indicate that increases in knowledge, self-efficacy, and motivation for behavior change can be achieved with the participant sitting remotely at their computer. Few online services, however, have been developed to facilitate HIV testing and none have been tailored for couples. Furthermore, the majority of interventions have been delivered through text-based communication, which fails to capture important verbal and visual cues (eg, tone of voice and body language) of clients.

A vital cornerstone to prevention and linkage to care is HIV testing [43]. This paper describes the protocol for a new randomized controlled trial (RCT) that combines the CDC-recommended prevention strategy of CHTC with home-based testing for male couples via video-based counseling and testing. By using video-based technologies (eg, VSee video chat), male couples receive counseling and support from a remote online counselor, while testing for HIV at home. This combination of HIV testing efforts is needed and timely because few interventions exist for male couples, especially those who live in rural areas and areas with few LGBTQ resources. This

RCT aims to examine and compare the intervention's effects on the relationship's ability to manage HIV risk, formation and adherence to explicit sexual agreements, and sexual risk-taking between self-reported concordant-negative and self-reported discordant male couples. Participants complete surveys at baseline, 3 months, and 6 months. It is hypothesized that couples exposed to the intervention will learn communication skills and receive psychoeducation that allows them to work together on HIV prevention planning. As a result, it is hypothesized that couples exposed to the intervention will be more likely to report discussing and forming sexual agreements and be more likely to adhere to agreements, yet also more likely to disclose if they break their agreements.

The theoretical basis for intervention is the Couple's Interdependence Theory (CIT) [44], a framework that combines both interdependence theory and communal coping perspectives and captures constructs central to the intervention. The framework guides the selection of measures of behavior change within the couple's relationships. Through interdependence, both members of the couple will rely on themselves and on each other to reach individual- and/or couple-positive and/or couple-negative healthy behaviors. These outcomes will either improve or detract from the quality of the couple's relationship. With this in mind, communal coping assists couples in achieving positive healthy behaviors that benefit both members of the couple as they cooperatively communicate to reach their desired goals [44]. These measures relate to the intervention in two ways. First, some aspects of communication and decision making within the partnership may influence the efficacy of the intervention; couples with more constructive communication styles may benefit from CHTC than would couples with less constructive communication styles. Second, some aspects of partnerships, such as efficacy around implementing behavioral change, may benefit more from CHTC. In this way, changes in key characteristics of the partnerships may be in the causal pathway between the intervention and the adoption of greater health-enhancing behaviors (ie, reduction in CAI outside of the relationship) within the partnership. The causal pathways are conceptualized as follows: couples exposed to the intervention package will receive opportunities to talk together about HIV, sexual health, and sexual agreements within their relationship through the assistance of a trained CHTC counselor and will have the ability to self-test for HIV as a couple at home. This may in turn impact communal coping, use of coping, and transformation of motivation. This may lead to initiation and maintenance of health-enhancing behaviors, which is conceptualized as reduction in sexual risk-taking (eg, CAI) within and outside of the relationship relative to couples who self-test for HIV at home without the presence of a counselor. In the research design, predisposing factors, outcome efficacy—the shared desire for the same outcome (ie, HIV prevention strategies)—and couple efficacy are collected separately from each member of the male couple before the HIV testing intervention is delivered, and will again be collected at 3-month and 6-month follow-up assessments.

## Methods

### Description of Trial and Intervention

#### Design

The research activities involved a blind prospective RCT of approximately 400 online-recruited male couples—200 self-reported concordant-negative couples and 200 self-reported discordant couples. Couples in the control arm will receive one or two home-based HIV self-testing kits and will be asked to report their results via the study's website. One kit will be provided for each person who reports to have previously tested HIV-negative or unknown status; partners in serodiscordant couples who report living with HIV will not be retested. Couples in the experimental arm will receive one or two home-based HIV self-testing kits and will conduct these tests together under the facilitation of a remotely located counselor during a prescheduled VSee-based video CHTC session.

#### Participants

Participants for each male couple must meet the following eligibility criteria: (1) two men who have been in a sexual relationship with each other for more than 6 months; (2) >18 years of age; (3) both participants not having been tested for HIV in the last 3 months, or for serodiscordant couples, the negative partner not having tested for HIV in the last 6 months; (4) reporting no IPV or coercion within the last 12 months; (5) willing to have HIV test kits delivered to an address they provide; (6) have access to the Internet within their home, or the home of at least one partner; and (7) be either self-reported concordant HIV negative or self-reported HIV serodiscordant. Participants for the trial are being recruited from across the United States, with recruitment via online advertisements placed on key social media websites (eg, Facebook and Instagram) and social media sites aimed specifically at MSM (eg, Grindr and Scruff). When men click on the advertisement, they are taken to a page containing basic study information, including a short description of study activities. If they express an interest in participation, they are then taken to the study consent form and if they consent, they are directed to a short eligibility screener. Men who (1) do not consent, (2) do not meet the eligibility criteria, or (3) do not provide an email for a main partner—defined as a sexual relationship with "a man who you feel committed to above all others"—are taken to a screen thanking them for their interest. Men who are eligible to participate must provide an email address for their main partner so that they can be enrolled in the study together. Further, eligible men able to participate and that provide their partner's email address are directed to a registration process. During the registration process, both partners provide their contact information, including an email address, a mobile phone number, and a mailing address; they are also asked to provide a nickname or preferred name of choice. Once both partners have (1) completed the consent forms, (2) completed the screening questionnaire, (3) proven eligible for the study, and (4) registered on the study website, a joint email is sent to both partners asking them to complete the baseline questionnaire, individually.

## Randomization

Upon individual completion of the baseline survey by both partners, couples are randomized to either the home-based HIV testing arm or video-based CHTC with home-based HIV testing arm using a stratified 1:1 treatment allocation. The strata are based on two levels of serostatus: seroconcordant negative and serodiscordant. The treatment assignments are generated with the use of a pseudo-random number generator with permutated blocks that are used to ensure balance within stratum between the numbers of couples assigned to each treatment. The randomization process generates one of two emails to both study participants for the enrolled male couple, indicating whether they will be receiving home-based HIV testing or video-based CHTC with home-based HIV testing.

## Intervention

The proposed intervention is a combination of home-based HIV testing and CHTC offered remotely via VSee video chat. In the control arm, couples receive one or two home-based HIV testing kits based on the couple's serostatus; the partner living with HIV in a serodiscordant couple does not repeat HIV testing. These kits sent to couples in the control arm contain one or two HIV testing kits as well as instructions on how to use the kits and how to report their test results in the study portal. In the experimental arm, couples receive one or two home-based HIV testing kits and complete the testing while undergoing a remote, VSee video-based CHTC session. Individual participants testing positive in either the experimental or the control condition are linked to their preference of local HIV care-specific resources within 48 hours. They will receive another HIV test at their preferred local HIV care-specific resource to validate the preliminary positive test result. These participants will receive follow-up from the CHTC counselor at 1-week, 1-month, and 3-month postresult of HIV-positive status to assess their engagement in care.

For couples randomized to the experimental arm, an email informs them that they have the opportunity to receive one or two home-based HIV testing kits and to take part in a video-based counseling session. The email provides details on the expected content of a CHTC session, the expectation that both partners will need to conduct their individual HIV tests and receive their results together in the presence of a remote counselor, as well as further logistical information (ie, length of the counseling session). From this email, couples are instructed to log on to the study website to order their HIV testing kits, with the same options as the control arm. Figure 1 shows the log-in page that users see when logging on to the Project Nexus website. For those randomized to receive HIV home testing with CHTC, they are asked to select a CHTC appointment time via an electronic calendar, which is shown in Figure 2. To allow intent-to-treat analysis, couples who do not complete the CHTC session and do not schedule an appointment, as well as couples in the control arm who do not report their HIV test results, are able to move on to take the 3-month and 6-month surveys.

The CHTC session is conducted via video chat using VSee. Figure 3 is an example of the VSee interface that participants see when waiting for their prescheduled counseling session to begin. The session is conducted by a counselor who is trained in CHTC and will last approximately 30-45 minutes. Pretest counseling focuses on the couple's relationship, their perceived HIV risk factors, and focuses on their sexual agreement. Both partners individually conduct their own HIV test and read their individual results together, as instructed by the counselor. Participants are asked to show the counselor their test result; the counselor then confirms the test result for accuracy of interpretation. Figure 4 is the interface the participant sees when entering their HIV testing result to the Nexus website. Posttest counseling focuses on dyadic prevention messages and revisits the couple's HIV risk concerns and sexual agreements in light of their test results. The counselor records the couple's HIV test results in the couple's study file. The counselor is trained to keep focus on the couple in the event that an HIV-positive result is given during a CHTC session. While a focus on the immediate needs of the HIV-positive partner is required, the discussion remains focused on how the couple can work together to keep the positive partner healthy and to keep the risk of HIV within, and not outside of, the relationship with other partners, while also meeting the needs of both partners within the male couple. If both couples are seroconcordant negative, the counselor discusses strategies that will minimize the risk of HIV transmission within and/or outside the relationship. The prevention-counseling element of the CHTC session focuses on talking the couple through prevention options and asking them to consider which prevention options may work best based on their relationship needs, context, and unique risk profile.

**Figure 1.** Project Nexus website log-in page.



**Figure 2.** Calendar function for selecting a couples HIV testing and counseling (CHTC) appointment.
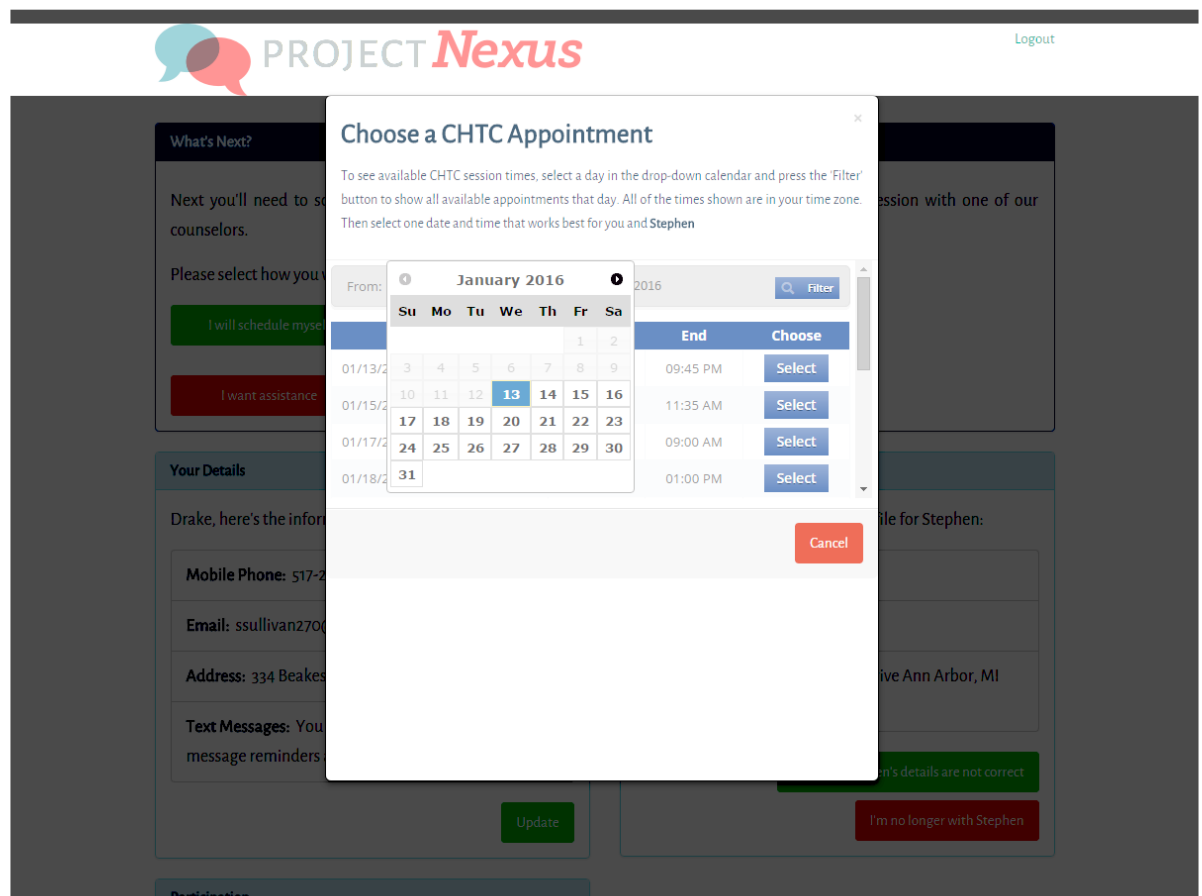
**Figure 3.** VSee session interface.
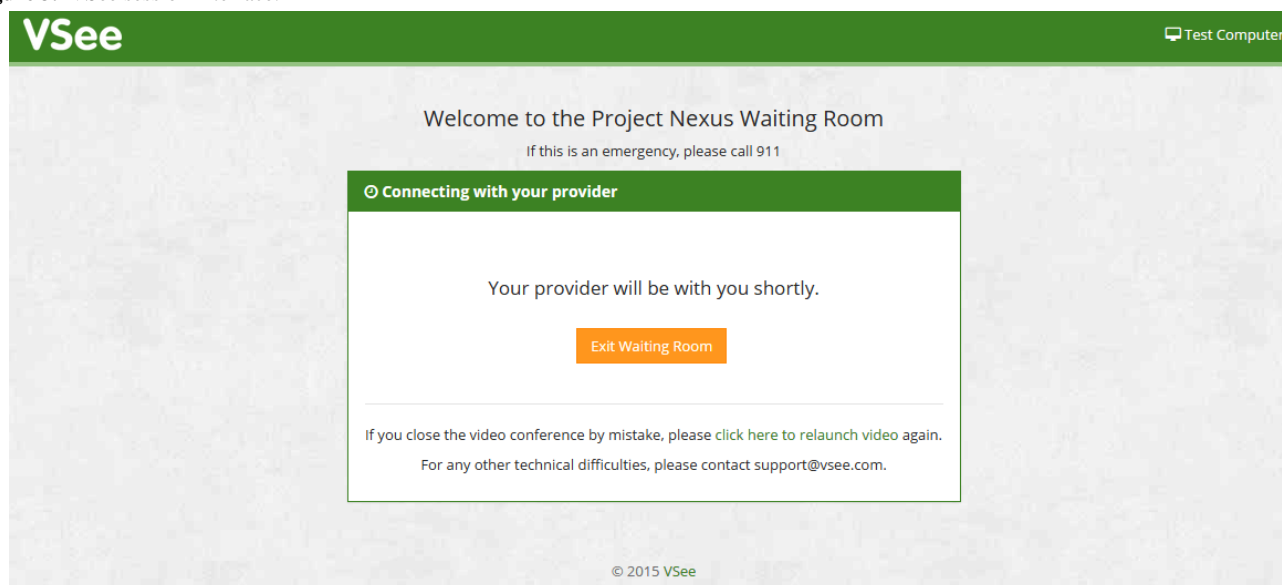


**Figure 4.** HIV test results reporting page on Nexus website.



## Preliminary Data

An online survey of 1285 MSM from across the United States was conducted to examine willingness to use the proposed intervention (unpublished data). Respondents were recruited through targeted advertisements on Facebook over 10 days from October to November 2012. Of the 907 men who self-reported a negative HIV serostatus and provided complete data, 72.0% (653/907) reported they would be likely to use a home-based HIV test, 69.0% (626/907) reported they would be likely to use CHTC, and 75.0% (680/907) reported that they would be likely to use a home-based HIV test together with a VSee video-based

CHTC session. The willingness to use the proposed intervention did not vary by age ($P$=.60), race ($P$=.91), recent (ie, <12 months) HIV testing behavior ($P$=.43), or recent CAI ($P$=.39). Among those with main partners (510/907, 56.2%), 82.0% (418/510) reported they would likely use the intervention. Among those who reported recent physical violence from an intimate partner (55/502, 11.0%), 67% (37/55) reported they would likely use the intervention. Emory University Center for AIDS Research also funded a trial of Skype-based counseling with 15 male couples from Atlanta to examine feasibility and acceptability of the video-chat counseling session. Although the trial did not incorporate HIV testing, 15 male couples were

recruited using the same online recruitment methods as proposed in this intervention. Couples completed a baseline survey describing recent sexual risks and sexual agreements in their relationships; then each couple underwent an approximately 45-minute counseling session via Skype video-based chat. During the session, the Emory-based counselor talked to the couple about their sexual agreements and their management of HIV risks, and then referred them to local services. Approximately half of the couples were in monogamous relationships; the mean relationship duration was 17 months. A total of 10 couples had formalized agreements around sex outside of the relationship, which ranged from monogamy to allowing sex with outside partners under certain conditions. Couples then completed an online survey about their experiences with the Skype video-based counseling session. Satisfaction was universally high—mean satisfaction was 4.8 out of 5 and 100% of participants said they would recommend the service to other male couples. Crucially, 100% of couples stated that they would be willing to include HIV testing in the video-based counseling session, with the main reasons being "convenience" and "having access to counseling while testing at home."

## Outcomes: Overview

The study outcomes are based on the conceptual model of CIT [44]. All measures are collected via the baseline, 3-month, and 6-month online surveys. Primary outcomes are the initiation and maintenance of health-enhancing behaviors. Secondary outcomes measure relationship characteristics.

## Primary Outcomes

Initiation and maintenance of health-enhancing behaviors are conceptualized as including two sets of outcomes: sexual agreements and sexual risk-taking as well as linkage and retention to HIV care.

### Sexual Agreements

All surveys include questions taken from previous studies of male couples' sexual agreements [45]. Participants are asked which of the following best describes their current sexual agreement with their main partner: "neither of us can have sex with outside partners," "we can have sex with outside partners, without any conditions or restrictions," "we can have sex with outside partners, but with conditions or restrictions," or "we do not have an agreement." Additional items about agreements will further assess whether couples permit (or do not permit) that certain sexual behaviors, mainly CAI and oral sex, can occur with outside partners. In follow-up surveys, participants are asked whether their agreement had been broken in the previous 3 months, if they disclosed the agreement breakage to their partner, whether they have changed their agreement, and, if relevant, how their agreement had changed.

### Sexual Risk-Taking

Behavioral measures adapted from the National HIV Behavioral Surveillance behavioral inventory, as well as from studies using behavioral measures among thousands of MSM [46,47], will collect information both on sexual behaviors with the main sex partner in the 3 months before the interview and on sexual behaviors with all sex partners outside the relationship that may exist. For sex with the main partner, men are asked to estimate

the number of anal sex acts with the main partner and the number of those acts that were condom protected. For outside the relationship, men are asked a series of questions about each outside partner. Questions include HIV status of that partner (if known), whether the sex outside the relationship was disclosed to the main partner, the number and type of sex acts (ie, oral, anal, both, etc) with each outside partner, and the proportion of those sex acts that were protected by condoms. Data on use of and adherence to preexposure prophylaxis (PrEP) are collected.

### Linkage to HIV Care

The following outcomes as indicators of linkage to care, per the recent recommendations of the Institute of Medicine [48], are measured within 3 months of HIV diagnosis via self-report [49,50]: (1) attending at least one clinical care appointment, (2) having at least one CD4 test performed, and (3) having at least one viral load test performed.

## Secondary Outcomes: Dyadic Characteristics

### Overview

The four elements of Lewis' model [44]—Predisposing factors of couple, Partner's transformation of motivation, Process of communal coping, and Use of communal coping—are referred to as dyadic characteristics. In a recent RCT of CHTC, scales were developed to capture these constructs; all scales showed strong reliability and evidence for construct validity was obtained for all scales [51]. In this intervention, each of the scales is collected in the baseline and follow-up surveys.

### Predisposing Factors of Couple

Several scales are used to measure this element. The Perceived Severity of HIV Scale involves the perception of the personal, psychosocial, and physical consequences of a particular health threat. A total of 13 items were developed that crossed the three pertinent consequences of a particular health threat: personal, psychosocial, and physical. The Preferences for General Lifestyle Outcomes Scale is defined as the degree to which interacting partners agree about the shared or joint outcomes in their relationship and is composed of two subscales: the Preferences for General Lifestyle Scale and the Preferences for Sexual Health Outcomes Scale. The Preferences for General Lifestyle Scale includes six outcomes, including diet, nutrition, and social activities. The Preferences for Sexual Health Outcomes Scale relates to sexual health, for example, reducing one's risk for HIV. In addition, scales to measure other predisposing factors of couples are proposed for inclusion. Conflict style determines how respondents typically handle conflict in their relationships, so the Conflict Style Inventory will be included [52]. Communication style will be measured with the Communication Patterns Questionnaire Constructive Communication subscale [53]. Finally, problem-solving skills are measured with the Adherence Problem Solving/Readiness Scale [54].

### Partner's Transformation of Motivation

In a recent RCT of CHTC, two measures were developed: ability of the participants to respond (1) cognitively and (2) emotionally to the health threat [21]. The scale for emotional response includes whether the respondent reports being fearful, nervous,

or anxious about HIV. The scale for cognitive response includes whether the respondent reports understanding the risks of HIV transmission associated with being in a serodiscordant relationship and the risks associated with outside sex partners.

### Process and Use of Communal Coping

Several scales are also used to measure this element. The Outcome Efficacy to Reduce HIV Threat Scale discusses how communal coping involves couples working together and making decisions together to reduce the health threat. Three subscales were created to capture the full range of outcome efficacy related to these three processes of communal coping. For the first subscale, Joint Effort, the stem "My partner and I believe that 'working together' versus on our own is an effective strategy" is used. For the second subscale, Communication, the stem "Communicating with my partner is an effective strategy for..." is used. For the third subscale, Planning and Decision Making, the stem "My partner and I making decisions together rather than separately is an effective strategy" is used. The items for each of the three subscales were the same as the items used for the Preference for Sexual Health Outcomes Scale. The Couple Efficacy to Reduce HIV Threat Scale defines couple efficacy as a couple's confidence that together they can engage in communal coping efforts.

In addition to the outcomes tied to Lewis' framework [44], we also include two additional outcomes: violence and relationship dissolution. The Conflict Tactics Scale Revised [55] assesses both perpetration and experience of IPV. Relationship dissolution is assessed using an item that asks each partner in the couple to report the current status of their relationship and reason for dissolution at follow-ups.

## Statistical Analysis: Dyadic Characteristics

### Overview

Dyadic characteristics will be analyzed within and between couples over time by HIV status and study arm (control vs experimental). Simple *t* tests and chi-square tests will be used to investigate systematic differences among average scales between experimental and control arms and between serodiscordant and seroconcordant-negative couples. Next, regression, generalized linear mixed models, and marginal models via generalized estimating equations (GEE) will be used to model longitudinal item and scale measures. In general, participants will be nested within couples, so the participant is regarded as the experimental unit; outcomes within couples and over time are potentially correlated. Initially, an unstructured serial correlation structure for the within-subject covariance and a single correlation parameter to describe the within-couple correlation will be assumed. If the unstructured covariance structure is too weak leading to nonconvergence issues and weak identification, more structure will be placed on the residuals and stronger models will be considered, such as an exchangeable or autoregressive correlation structure. Statistical inference will be likelihood based for the mixed models while generalized score and Wald tests will be used for statistical inference in the marginal models. In the presence of missing data, both mixed and marginal models accommodate missing

data (eg, dropout), although the former under a weaker (missing at random) assumption.

### Sexual Risk-Taking

The definition of at-risk sex will be serostatus specific. For serodiscordant couples, at-risk sex will be CAI with either their main or outside partners. For seroconcordant-negative and seroconcordant-positive couples, at-risk sex will be CAI with outside sex partners. While data on PrEP use and adherence will be collected, the definition of at-risk sex focuses on condom use given the CDC recommendation for continued condom use for those adopting PrEP. The incidence of at-risk sex acts will be calculated as an incidence density, with the numerator being the number of individual at-risk sex acts and the denominator being person-years of follow-up time. Comparisons of the incidence of at-risk sex acts will be made by comparing incidence densities between the two arms. Incidence rates per couple-year of follow-up will be estimated and compared using exact methods based on the Poisson distribution by using the GEE approach. Baseline covariates include race, age, and duration of relationship. Period incidence rates—6-monthly incidence density rates—of at-risk sex will be estimated by performing a GEE Poisson regression analysis of the 6-monthly counts. This will be implemented using the PROC GENMOD procedure by SAS (SAS Institute Inc) [56] and using an exchangeable correlation structure for the repeated observations of couples. The incidence density ratio, or incidence rate ratio (IRR), is the ratio of the incidence density in one treatment group (intervention arm) to that of another group (control arm). Results by each baseline covariate will be summarized as the IRR and the 95% confidence interval. These analyses will be descriptive and include analyses stratified by race/ethnicity. Prevalence of each outcome will be calculated and prevalence of outcomes will be compared in the control and intervention groups using chi-square tests or Fisher's exact tests, as appropriate.

### Sexual Agreements

Separately tabulated data about disclosure of sex outside the relationship and percentage of couples with agreements involving sex outside the primary relationship will be developed. These analyses will be descriptive and include analyses stratified by race/ethnicity, study arm, and couple serostatus. These analyses will also characterize the prevalence of agreements about sex outside relationships, the extent to which those agreements are adhered, and any shift of adopting safer sexual behaviors with outside partners, again stratified by race/ethnicity and study arm. A focus of the analysis will be identifying differences across the study arms in the percentages of couples who report a shift to safer sexual agreements at follow-up. In addition, the Actor-Partner Interdependence Model (APIM), which uses the dyad (eg, couple) as the unit of analysis, will be used to predict how an individual and his partner's reports of dyadic characteristics—described within Lewis' model [44]—affect whether the individual formed, changed, and kept the sexual agreement he had with his main partner [31]. Procedures for using SAS to calculate actor-partner effects with dichotomous outcomes with male couples (eg, indistinguishable

dyads) have previously been reported in detail [31] and will be used for the proposed RCT.

### Linkage to Care

The percentage of HIV-positive respondents who receive a timely (<3 months) comprehensive visit—a visit including a CD4 count, viral load count, and the date of their first care visit—will be tested for significance across the two study arms. The percentages of couples who are seroconcordant negative, seroconcordant positive, and serodiscordant, as part of the description of the analysis samples, will be recorded. To assess whether the concordancy of the couple modifies the intervention effects, formal statistical tests—likelihood ratio tests in mixed models and generalized score tests in marginal models—of the null hypothesis will be conducted. The null hypothesis is that the two-way interaction effect for the aforementioned items and scales between intervention and concordancy is zero. If the statistical test does not reject the null hypothesis, the concordancy main effect in the model will be retained, removing the two-way interaction, and conclude that there is not sufficient evidence to suggest that concordancy modifies the intervention effect.

The safety of the intervention at both the individual and couple levels will be evaluated by examining reported IPV within the relationship and relationship dissolution. At the individual level, prevalence of each individual adverse outcome or any adverse outcome will be calculated. Prevalence of outcomes will be compared across the control and intervention arms, by serostatus of the couple, and by relationship duration using chi-square tests or Fisher's exact tests, as appropriate. At the couple level, the APIM will be used to predict how an individual and his partner's reports of dyadic characteristics affect the individual's experience of IPV and reported relationship dissolution.

### Feasibility

In addition to the outcomes, the study will assess feasibility by examining (1) time to recruit 400 couples to the intervention and (2) rate of recruitment per 100 men expressing interest in participation. Acceptability of the intervention will be determined by analysis of data from the satisfaction survey on the intervention's acceptability to couples. In addition, the percentages of male couples who do not complete the home-testing profile and the percentage of those not returning test results via the study website will be analyzed.

### Cost Analysis

To examine the cost of the proposed intervention, cost data are collected by input type and by activity, using an activity-based costing matrix. Input types include study personnel salaries and benefits, supplies, equipment, HIV testing kits, and training materials. Activities include training (ie, counselors and crisis counseling), recruitment of participants, VSee video-based chat, follow-up, and linkage to care. For the experimental arm, counselors record the time spent per session of the counselor because these are the only additional (ie, incremental) costs incurred relative to the control arm.

### Incentives

Individual participants each receive US $50 for completing each of the main three surveys: the baseline, the 3-month follow-up, and the 6-month follow-up. If all surveys are completed by both members of the male couple, the total incentive amount is US $300 per couple (US $150 per individual participant).

### Sample Size

The goal is to enroll and maintain a sample of 400 male couples: 200 serodiscordant and 200 seroconcordant couples, 100 of each couple per arm (experimental vs control). To achieve this, the intervention aims to screen approximately 1000 male couples—500 serodiscordant and 500 seroconcordant male couples—and will exclude those with a recent (<12 months) history of IPV. Assuming 15% of male couples have a recent history of IPV, this will produce approximately 850 couples for randomization, 425 per arm. Allowing for 20% loss to follow-up and additional 20% relationship dissolution, this will produce a sample of 400 male couples who are expected to complete the prospective RCT. The sample size is calculated based on the detection of significant changes in each of the main outcomes (ie, changes in sexual risk-taking, such as CAI), formation and adherence to explicit sexual agreements, and relationship functioning for the management of HIV risk. As an example, we will assume that about 25% of male couples change agreement status after couples counseling and we will use a two-sample test of binomial proportions with type I error rate at 5%. Using these assumptions, it is determined that 52%, 67%, and 85% statistical power is necessary to detect a difference of 10%, 12%, and 15%, respectively, in a change-of-agreement status between the two arms within seroconcordant or serodiscordant groups (ie, comparing 150 male couples per arm). In other words, under the same conditions, the probability is .52, .67, and .85 that the lower bound of the confidence interval for the proportion change in agreement status in the intervention arm is at least 3%, 5%, and 8% different than the proportion in the control arm, respectively, when the alternative hypothesis is true. If data is pooled across seroconcordant and serodiscordant couples, assuming that combining data makes sense in terms of the magnitude and direction of the intervention effect, then 81%, 92%, and 99% statistical power is necessary to observe differences of 10%, 12%, and 15%, respectively (ie, comparing 300 male couples per arm). In this case, at least 80% statistical power will be necessary to detect as little as a 5% difference between the lower bound of the confidence interval for the proportion in the intervention versus the control arm. Based on discussions with participant advocates and partnered community-based organizations, it is projected that any difference exceeding 5% would be scientifically meaningful and would have public health impact. The analysis also considers differences in linkage to HIV care among HIV-positive individuals in each arm, but it is not powered to detect significant differences, given the small number of incident positive cases.

### Trial Registration, Ethics, Consent, and Institutional Board Approval

The research and ethics presented in this study have been reviewed and approved by the University of Michigan

Institutional Review Board (HUM00102906), in addition to the Data Safety Monitoring Board. The study is also registered on ClinicalTrials.gov (NCT02335138).

## Results

Project Nexus was launched in April 2016 and is ongoing. To date, 219 couples have been enrolled and randomized, with 219 couples remaining eligible for continued study participation, as they have reportedly not experienced IPV, ended a relationship, falsified information, or any other criteria that would make them ineligible for study participation. Of all eligible couples, 95% have taken the baseline survey; the remaining couples are all within the time between enrollment and taking the survey. The 3- and 6-month follow-up surveys have maintained high retention rates at over 90%. Of couples randomized to the control arm, 88.0% (95/108) have reported their home HIV testing results. Of couples randomized to the intervention arm, 76.6% (85/111) have scheduled and completed the video-chat-based counseling session. In total, 5.9% (26/438) of participants have tested preliminarily as HIV positive, of which 73% (19/26) were actively linked to care.

## Discussion

Online CHTC via video chat provides an opportunity to expand CHTC to male couples who (1) live outside metro areas, (2) live in rural areas without access to testing services or LGBTQ resources, or (3) feel that current clinic-based testing is not for them (eg, due to fears of discrimination associated with HIV and sexuality). Although home-based HIV testing is now a reality, many still question the lack of counseling available to those who are undergoing testing in the individual household. A video-chat-based CHTC session potentially provides an inexpensive way to remedy this problem and provides an opportunity for those receiving an HIV-positive result to receive assistance in linkage to care. The proposed activities not only have the potential to expand CHTC to male couples who currently do not have access, but may provide opportunities to improve the utility of home-based testing for couples by providing them a forum to discuss prevention planning with a counselor. It is true that some individuals use home-based HIV testing because they do not want counseling and the proposed intervention would probably not be adopted by those people. However, for couples who desire and/or need counseling and do not have access due to physical or sociocultural barriers, a low-cost, video-based counseling session provides the opportunity to reach them, create HIV prevention planning, and locate linkage to care in a safe and comfortable environment.

## Conflicts of Interest

None declared.

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## Abbreviations

**APIM:** Actor-Partner Interdependence Model
**CAI:** condomless anal intercourse
**CDC:** US Centers for Disease Control and Prevention
**CHTC:** couples HIV testing and counseling
**CIT:** Couple's Interdependence Theory
**GEE:** generalized estimating equations
**IPV:** intimate partner violence
**IRR:** incidence rate ratio
**MSM:** men who have sex with men
**PrEP:** preexposure prophylaxis
**RCT:** randomized controlled trial

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Protocol

# Simple Wound Irrigation in the Postoperative Treatment for Surgically Drained Spontaneous Soft Tissue Abscesses: Study Protocol for a Prospective, Single-Blinded, Randomized Controlled Trial

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## *Abstract*

**Background:** Skin abscesses are a frequent encountered health care problem and lead to a significant source of morbidity. They consequently have an essential impact on the quality of life and work. To date, the type of aftercare for surgically drained abscesses remains under debate. This leads to undesirable practice variations. Many clinical standard protocols include sterile wound dressings twice a day by a home-care service to reduce the chance of a recurrent wound infection. It is unknown, however, whether reinfection rates are comparable to adequate wound irrigation with a nonsterile solution performed by the patient. Our hypothesis is that simple wound irrigation with nonsterile water for postoperative wound care after an abscess is surgically drained is feasible. We assume that in terms of reinfection and reintervention rates unsterile wound irrigation is equal to sterile wound irrigation.

**Objective:** The primary aim of this study is therefore to investigate if there is a need for sterile wound irrigation after surgically drained spontaneous skin abscesses.

**Methods:** In a prospective, randomized controlled, single-blinded, single-center trial based on a noninferiority design, we will enroll 128 patients randomized to either the control or the intervention group. The control group will be treated according to our current, standard protocol in which all patients receive a sterile wound irrigation performed by a home-care service twice a day. Patients randomized to the intervention group will be treated with a nonsterile wound irrigation (shower) twice a day. All patients will have a routine clinical control visit after 1, 3, 6, and 12 weeks in the outpatient clinic. Primary outcome is the reinfection and reoperation rate due to insufficient wound healing diagnosed either at the outpatient control visit or during general practitioner visits. Secondary outcome measures include a Short Form Health Survey, Visual Analog Scale, Patient and Observer Scar Assessment Scale, Vancouver Scar Scale, and the EurolQol 5-Dimension Questionnaire. Those questionnaires will be completed at the outpatient control visits.

**Results:** The trial was started in June 2016 and enrolled 50 patients by article publication. Regarding the adherence to our protocol, we found 10% of loss to follow-up until now. Only 2 patients needed reoperation and only 1 patient needed a change of treatment (antiseptic therapy). Most patients are happy with their randomized treatment but as expected some patients in the sterile group complained about timing problems with their working hours and home-care service appointments. Most patients in the nonsterile group are satisfied being able to take care of their wounds independently although some patients still depend on the home-care service for the wound dressing. We are hoping to have enrolled enough patients by summer 2017. The follow-up will take until autumn 2017, and study results are expected to be published by the end of 2017. This trial is solely supported by the cantonal hospital of Lucerne.

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**Conclusions:**  Nonsterile wound irrigation is more likely to be carried out independently by the patient than sterile wound irrigation. Therefore, if nonsterile wound care shows comparable results in terms of reinfection and reintervention rates, patient independence in the aftercare of surgically drained abscesses will increase, patients can return to work earlier, and health care costs can be reduced. In a preliminary, conservative estimation of health care costs, an annual savings of 300,000 CHF will be achieved in our hospital.

**Trial Registration:**    German Clinical Trials Register DRKS00010418; https://drks-neu.uniklinik-freiburg.de/ drks_web/navigate.do?navigationId=trial.HTML&TRIAL_ID=DRKS00010418    (Archived    by    WebCite    at http://www.webcitation.org/6q0AXp5EX)

**KEYWORDS**

skin and soft-tissue infections; recurrent infection; wound irrigation; surgical draining of abscesses; aftercare

## Introduction

Skin abscesses are frequent health care problems that often affect young and vital patients. Abscesses can be a significant source of morbidity and can mean an essential limitation of quality of life as well as an incapacity to work [1]. Therefore, timely and sufficient surgical drainage and aftercare is an essential part of care, not only to prevent potential life-threatening complications due to inappropriate therapy (eg, necrotizing fasciitis, toxic shock syndrome, Ludwig's angina) but also to enable a normal social life and a return to work as soon as possible.

The current literature shows great national and international variability of the surgical method, with incision, excision, or spindle-shaped opening and without essential evidence for the superiority of one of the methods [2,3]. Furthermore some surgeons prefer a primary wound closure with or without antibiotic therapy [4-7].

Regarding the aftercare for open wound treatment, the diversity continues and literature can be found on wound irrigation with sterile fluids, unsterile fluids [8], and antiseptic fluids [9]; antibiotic therapy [5,6]; and use of different wound dressings such as silver-containing hydrofiber [10], hyaluronate hydrogel [11], and essential oils [12]. These different treatment options are combined in various ways, and so far the results regarding reinfection rates and failure of therapy seem to be comparable.

For superficial perianal abscesses, a German consensus grade S3 (evidence- and consensus-based) guideline is available [13] suggesting surgical drainage without specifying the type of drainage (excision, incision, or spindle-shaped opening) due to limited data. For the aftercare, prospective randomized trials are lacking but the consensus recommends periodic wound irrigation with antiseptic fluid or subsequent antibiotic therapy only being necessary in individual cases [14]. Patients are often instructed to change the dressing twice a day and irrigate the wound with a sterile solution. For sterile treatment, the assistance of a home-care service is often needed, which can impair the social life due to frequent appointments. Therefore, the question arises if an alternative method could at least support the independence of the patient and lead to sufficient wound treatment without regular appointments and sterile wound irrigations.

Considering a trend toward cost-effective medicine and a reasonable use of medical infrastructure, it is questionable whether every wound needs to be irrigated with a sterile solution twice a day by a special home-care service. We consider the nonsterile wound irrigation (carried out in the shower) as a potential treatment option that offers independence for the patient. It is expected that patients can carry it out independently or with the help of a family member. Additionally, this could lead to an earlier return to work [8].

We hypothesize that simple wound irrigation with nonsterile water for postoperative wound care is feasible after surgical draining of abscesses. Moreover, we postulate that wound irrigation in the shower (simple wound irrigation) is equal to sterile wound irrigation accomplished by special home-care service teams in terms of reinfection and reintervention rates. Additionally, we claim that patients who irrigate the wound using nonsterile water (shower irrigation) will be more independent and that the overall costs are less compared to sterile water irrigation due to less frequent consultations of the home-care services.

To our knowledge, this is the first prospective randomized trial evaluating the value of postoperative wound irrigation using nonsterile solution in surgically drained abscesses.

## Methods

### Study Design

Based on a noninferiority design, we designed a prospective, randomized, controlled, single-blinded, single-center trial. We present the study protocol in accordance with the Standard Protocol Items: Recommendations for Interventional Trials guidelines [15].

### Study Population

The study includes patients treated for spontaneous soft tissue abscesses in the largest nonuniversity hospital in Switzerland.

Patients with a primary superficial abscess presenting at the emergency department will be eligible for the inclusion if they fulfill all of the followed criteria:

- Soft tissue abscess with an indication for surgical drainage
- 18 years or older
- Sufficient understanding of spoken and written German
- Signed informed consent

- Hospitalization of at least one night to ensure sufficient teaching from the nurse concerning wound management (according to the study protocol)

We will exclude patients if they meet at least one of the following exclusion criteria:

- Patients presenting with residual abscesses, abscesses located on the head, or abscesses with a confirmed fistula
- Patients suffering from immunodeficiency (eg, HIV infection, leukemia)
- Patients taking autoimmune therapy
- Patients not willing or able to sign the informed consent
- Patients with psychiatric conditions
- Patients not able to return for appointments at 1, 3, 6, and 12 weeks

## Preliminary

Essential prestudy preparations are needed to ensure proper inclusion of patients and correct documentation of the preoperative situation.

### Defining Period

Standard preoperative documentation of the abscess and its surrounding is necessary to ensure sufficient surgical drainage and to enable comparability between both groups. An abscess was defined as an enclosed collection of liquefied tissue, known as pus, affecting the subcutaneous tissue and representing the immune defense reaction of the body against foreign material or bacteria. As seen in Figure 1, the abscess consists of (1) the area of fluctuation caused by the collection of liquefied tissue, (2) the area of cellulitis caused by hyperemia due to an immune reaction of the body, and (3) the area of induration caused by the hardening of the soft tissue due to the inflammation.

We also defined provisions that needed to be followed to ensure proper surgical drainage during our trial: (1) the incision of the skin has to be at least as long as the fluctuation, (2) the incision of the skin has to be spindle-shaped to ensure a wide opening of the abscess cavity, and (3) the spindle-shaped incision has to include at least two-thirds of the width of the fluctuation.

### Implementation Period

An educational period teaching basic facts about abscesses will be initiated before the inclusion period starts. All surgeons treating the above mentioned conditions will participate in a special lecture about the pathophysiology, diagnosis, and management of abscesses. We defined the necessity for documentation of the following parameters (see Figure 1): the diameter of the fluctuation and hyperemia and photo documentation with a scale. Finally, everyone involved received handouts containing all relevant information.

## Randomization

Prior to the operation, patients are being randomized either to the control or the intervention group using sealed envelopes. The randomization will be carried out after the signed informed consent is obtained.

**Figure 1.** Definition of the area of hyperemia (red) and fluctuation (central frame) with a ruler to indicate the size of the areas.
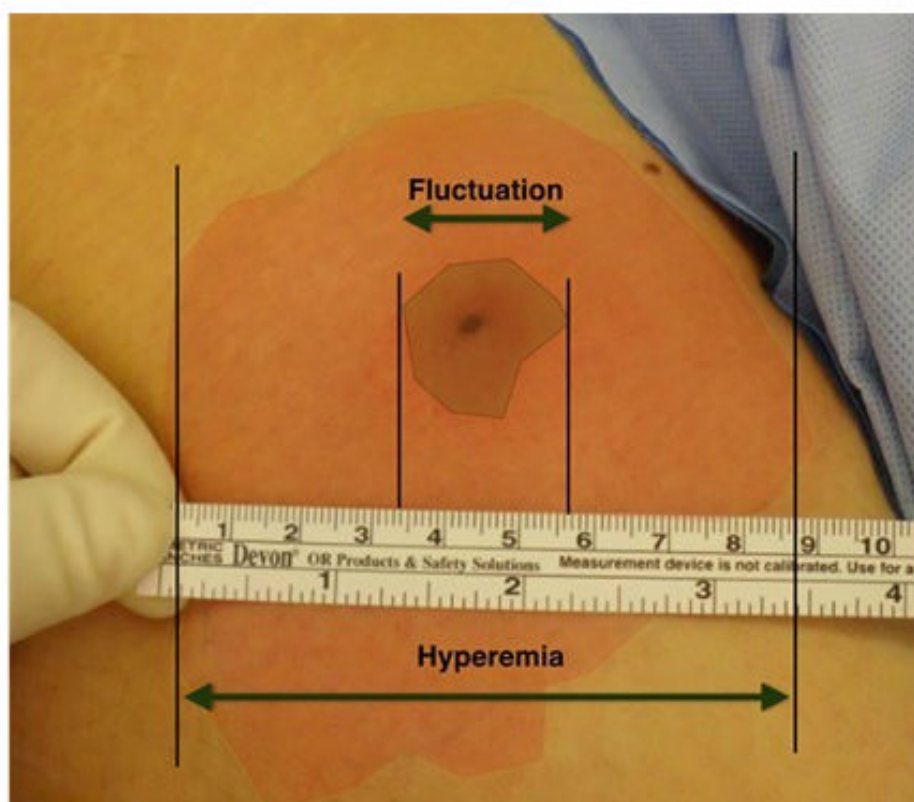
### Control Group (Group I)

Patients belonging to the control group will be treated according to our current protocol, including sterile wound treatment supported by a home-care service. We recommend a standard of sterile wound irrigation twice a day using either Ringer's lactate or normal saline solution. The wound, including the whole cavity, should be irrigated 3 to 5 times with a 20 mL syringe, treating the whole wound surface with gentle pressure. Thereafter, a moist and unfolded gauze is inserted in the cavity. The unfolded gauze develops a bigger osmotic pressure and therefore ameliorates the suction effect on the cavity. Subsequently the wound should be dressed in a sterile way using gauze and tape to fix the dressing. The home-care service is informed with a standard form.

### Intervention Group (Group II)

Patients belonging to the intervention group are treated according to a modified aftercare protocol. We recommend shower irrigation for the nonsterile treatment twice a day. The patient is recommended to use a shower with room temperature water and irrigate the entire wound cavity with gentle pressure for 1 to 2 minutes using water only. The use of shower gel, soap, or shampoo is forbidden. After wound irrigation, the dressing of the wound with a moist and unfolded gauze followed by a dry nonsterile gauze and tape is carried out similar to the control group.

The first postoperative wound dressing is changed by the nurse and surgeon on the ward. The patient and/or family members are trained to adequately manage the wound and change the dressings. In case the patient is unable to change the dressing alone, the same home-care service is requested to support the patient. The home-care service is informed with a standard form.

## Outcome

As we present a noninferiority approach, the purpose of this analysis is to show comparable results in the intervention group in terms of reinfection and reoperation rates.

### Primary Outcome

We defined the primary endpoint as a reinfection or a reoperation after an abscess is surgically drained. A reinfection was defined as a persisting or new reddened wound with signs of induration and fluctuation. If there were any signs of purulent exudation with the above-mentioned signs, we considered the wound to be reinfected, and a reoperation was performed. A reoperation was defined as any operation performed in the same region within the time frame of the study control (12 weeks postoperative).

### Secondary Outcome

Secondary outcomes are measured using specific scar scores as well as nonspecific outcome tools as shown in Table 1.

#### Specific Scar Tools

The Vancouver Scar Scale (VSS) [16], first described by Sullivan in 1990, assesses 4 variables: vascularity, height/thickness, pliability, and pigmentation. These variables are assessed by the surgeon without the perception of the patient concerning his or her scars.

The Patient and Observer Scar Assessment Scale (POSAS) includes subjective symptoms of pain and pruritus of the scar. It consists of 2 numerical scales: the patient scar assessment scale and the observer scar assessment scale. It assesses vascularity, pigmentation, thickness, relief, pliability, and surface area, and it incorporates patient assessments of pain, itching, color, stiffness, thickness, and relief [17].

#### Nonspecific Tools

Health status measurement will be performed using the Short Form Health Survey (SF-36) in all patients. The SF-36 is a 36-item, patient-reported survey of patient health. The questionnaire includes 8 sections (vitality, physical functioning, bodily pain, general health perceptions, physical role functioning, emotional role functioning, social role functioning, and mental health) and in each a score ranges between 0 and 100. The score is proportional to the outcome, with the best possible result of 100 [18,19].

The EQ-5D is a standardized measure of health status developed by the EuroQol Group. The 5-dimension, 5-level questionnaire consists of 2 pages: the EQ-5D descriptive system and the Visual Analog Scale (VAS). The descriptive system comprises 5 dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) and each dimension has 5 levels (no problems, slight problems, moderate problems, severe problems, and extreme problems). Additionally, the VAS records the respondent's self-rated health on a 20 cm vertical visual analog scale with endpoints labeled "the best health you can imagine" and "the worst health you can imagine."

A self-designed questionnaire was made to investigate the expenditure during the home-care service visits. Questions concerning the time each home-care service person has spent with wound dressing, type of material (gauze, tape, solution, syringes), and amount of time spent are being recorded. In addition, questions concerning time and frequency of family doctor visits and duration of inability to work will be documented.

A medical questionnaire answered by the surgeon in the outpatient clinic documents the size of the wound cavity. Additionally, the surgeon needs to comment on whether there are signs of cellulitis (defined as flushed tissue with signs of induration), the quality of the wound (cavity and edges), any exudation from the wound or signs of persisting fluctuation (liquid-filled cavities).

## Outpatient Control Visits

All patients receive a standard postoperative outpatient control visit after 1, 3, 6, and 12 weeks. All questionnaires except the VSS and the POSAS will be answered during each visit as shown in Table 1. The VSS and POSAS will be used at the 12-week control visit as definite wound healing is needed to answer these questionnaires. As this is a single-blinded trial, it is essential to ensure blinding of the investigator at the outpatient control visit. All outpatient follow-ups will be carried out by two blinded surgeons investigating the wound and filling out the questionnaire.

**Table 1.** Timeline of outcome measurements.

| | | Study period | | | | | |
| | | Enrollment | Allocation | Outpatient control | | | |
| | | ED[a] | Operation | Week 1 | Week 3 | Week 6 | Week 12 |
|---|---|---|---|---|---|---|---|
| Enrollment | | | | | | | |
| | Inclusion criteria | X | | | | | |
| | Informed consent | X | | | | | |
| | Randomization | X | | | | | |
| | Patient baseline characteristics | X | | | | | X |
| Interventions | | | | | | | |
| | Control group | X | X | X | X | X[b] | X |
| | Intervention group | X | X | X | X | X[b] | X |
| Assessments | | | | | | | |
| | SF-36[c] | X | | X | X | X[b] | X |
| | VAS[d] | X | | X | X | X[b] | X |
| | EQ-5D[e] | X | | X | X | X[b] | X |
| | Medical questionnaire | X | | X | X | X[b] | X |
| | VSS | | | | | | X |
| | POSAS | | | | | | X |

[a]Emergency department.

[b]Optional outpatient control, only necessary if wound still open at 3 weeks control.

[c]SF-36: Short Form Health Survey.

[d]VAS: Visual Analog Scale.

[e]EQ-5D: EuroQol 5-Dimension Questionnaire.

[f]VSS: Vancouver Scar Scale.

[g]POSAS: Patient and Observer Scar Assessment Scale.

## Statistical Analysis

Statistical analysis will be performed using SPSS version 21 (IBM Corp). The mean and standard deviation will be calculated and reported for basic patient-related data. Primary analysis will be carried out comparing frequency of reintervention between the intervention and control groups. Moreover, we will try to identify risk factors as basic patient-related data or surgery-associated factors (time of surgery, operation time, experience of the surgeon) using regression models.

Secondary clinical outcome measures will be presented in means with the corresponding standard deviation. The intervention group and the control group will be compared using mean value analysis models (*t* test; multifactorial mean value analysis). We will assume that data missing will be random; therefore, missing data will not be imputed, as we will use the mixed model approach for the longitudinal analyses.

## Sample Size Calculation

Based on international publications, we estimate a 15% reinfection rate as statistically significant [20-22]. The literature remains inconsistent concerning reinfection rates in surgically drained abscesses. Based on these findings and using a power

of 0.80 and alpha failure of .05 we performed a sample size calculation. Based on a noninferiority approach, we calculated 58 patients were needed in each treatment arm. We added 10% loss of follow-up to our power calculation ($58 \times 1.10 = 64$ patients in each treatment arm) and determined 128 patients need to be included in our study.

## Calculation of Cost Savings

Since nonsterile wound care is easier to perform, we presume that patients in this group are more likely to perform their wound care without the help of a home-care service. Since the dressing in some cases cannot be performed independently and some patients may not have any family member to help, some patients in the nonsterile group may need assistance by a home-care service as well. Also, some patients or family members might feel the need for supervision in the beginning of the wound care, which will be carried out by the home-care service. We assume that on average 1 week of assistance will be enough time and therefore calculated 1 week of home-care service for the nonsterile group.

In contrast, we think that patients in the sterile group are not likely to be able to perform the wound care on their own. Also family members might not be able to provide adequate assistance

in sterile wound irrigation and therefore patients are more likely to depend on the home-care service for the entire open wound treatment period. We assume that an average treatment will last 4 weeks.

The estimated time for a proper wound treatment by the home-care service is 20 minutes. Wound treatment is carried out twice per day, totaling 280 minutes each week. The home-care service in the city of Lucerne costs 65 CHF (Swiss Francs) per hour, leading to 305 CHF per week.

If an average treatment lasts 4 weeks and patients from the nonsterile group are thought to be independent after 1 week while patients from the sterile group will need assistance for 4 weeks, a savings of 915 CHF for each patient in the nonsterile group can be assumed solely based on the health care costs. Over the last year, 320 patients with abscesses have been treated at our hospital. Changing our postoperative treatment strategy from a sterile to nonsterile aftercare would save approximately 300,000 CHF annually solely on medical expenses.

## Ethical Considerations

The study design is in accordance with the Declaration of Helsinki [23] and with the Swiss laws (Human Research Act and Human Research Ordinance). This study was approved by the medical ethics research committee Basel and registered with the Ethikkommission Nordwest- und Zentralschweiz (EKNZ) [BASEC 2016-00002] and the German Clinical Trials Register [DRKS00010418]. All forms given to patients and information obtained using the above mentioned questionnaires have been approved by the EKNZ. Essential changes in the course of the trial will be reported immediately and submitted for approval by the ethics committee.

Information and results will not be presented to the EKNZ on a regular basis, but, for data verification, authorized representatives of the project manager and the ethics committee have access at any time to the medical data relevant to the project, including the medical history of participants.

Serious adverse events must be reported immediately, and if potential life-threatening complications occur, the trial will be stopped unless the safety is proven by the ethics committee. Patients participating in this clinical trial are covered by a special hospital insurance. This insurance is free for patients and covers any damage or potential damage as well as death caused by the study.

## Results

The trial was started in June 2016 and enrolled 50 patients by article publication. Regarding the adherence to our protocol, we found 10% of loss of follow-up until now. Only 2 patients needed reoperation and only 1 patient needed a change of treatment (antiseptic therapy). Most patients are happy with their randomized treatment but as expected some patients in the sterile group complained about timing problems with their working hours and home-care service appointments. Most patients in the nonsterile group are satisfied being able to take care of their wounds independently although some patients still depend on the home-care service for the wound dressing.

We are hoping to have enrolled enough patients by summer 2017. The follow-up will take until autumn 2017, and study results are expected to be published by the end of 2017. This trial is solely supported by the cantonal hospital of Lucerne.

## Discussion

To date, the standard in postoperative aftercare for surgically drained soft tissue abscesses remains under debate. As patients are often young, it is important that they can return and participate as soon as possible in daily (working) life after an operation.

A more independent postoperative treatment plan could lead to an increase in independence during the healing process and lead, based on a more self-perceiving view of the patient, to better results in terms of quality of life during the healing process. Moreover, a more independent wound treatment could lead to more cost-effective medicine, a more reasonable use of medical infrastructure, and an earlier return to work. This prospective randomized trial is therefore important in order to investigate whether a recommendation for nonsterile and independent wound irrigation is justifiable or not for surgically drained soft tissue abscesses. Moreover, if a nonsterile after-treatment protocol is justifiable, it is expected that it would improve quality of life and lead to a significant medical cost reduction of 300,000 CHF annually in our hospital.

## Authors' Contributions

AR, FO, and FB drafted the manuscript and designed the study. FB will act as trial coordinator. LF, KB, and JM participate in the organization, control, and follow-up of the patients. Statistical analysis will be carried out by AR, FO, and FB as well as JM. All authors have read and approved the final manuscript.

## Conflicts of Interest

None declared.

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**Abbreviations**

**ED:** emergency department
**EKNZ:** Ethikkomission Nordwest- und Zentralschweiz
**EQ-5D:** EuroQol 5-Dimension Questionnaire
**POSAS:** Patient and Observer Scar Assessment Scale
**SF-36:** Short Form Health Survey
**VAS:** Visual Analog Scale
**VSS:** Vancouver Scar Scale

Protocol

# Testing the Effectiveness of a Primary Care Intervention to Improve Uptake of Colorectal Cancer Screening: A Randomized Controlled Trial Protocol

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## Abstract

**Background:**   Screening for colorectal cancer (CRC) significantly reduces mortality associated with this disease. In Australia, the National Bowel Cancer Screening Program provides regular fecal occult blood tests (FOBT) for those aged 50 to 74 years, however, participation rates in the program have plateaued at 36%. Given low uptake in the National Bowel Cancer Screening Program, it is necessary to explore alternate methods to increase CRC screening rates. Primary care is a promising adjunct setting to test methods to increase CRC screening participation. Primary care guidelines support the recommendation and provision of CRC screening to primary care patients. Those in the National Bowel Cancer Screening Program target age range frequently present to their primary care provider.

**Objective:**   This study tests the effect that a multicomponent primary care–based intervention has on CRC screening uptake when compared to usual care.

**Methods:**   Primary care patients presenting for an appointment with their primary care provider complete a touchscreen survey to determine eligibility for the trial. Those aged 50 to 74 years, at average risk of CRC, with no history of CRC or inflammatory bowel disease, who have not had an FOBT in the past 2 years or a colonoscopy in the past 5 years are eligible to participate in the trial. Trial participants are randomized to the intervention or usual care group by day of attendance at the practice. The intervention consists of provision of an FOBT, printed information sheet, and primary care provider endorsement to complete the FOBT. The usual care group receives no additional care.

**Results:**   The primary outcome is completion of CRC screening 6 weeks after recruitment. The proportion of patients completing CRC screening will be compared between trial groups using a logistic regression model.

**Conclusions:**   CRC screening rates in Australia are suboptimal and interventions to increase screening participation are urgently required. This protocol describes the process of implementing a multicomponent intervention designed to increase CRC screening uptake in a primary care setting.

**Trial Registration:**   Australian New Zealand Clinical Trials Registry ACTRN12616001299493; https://anzctr.org.au/Trial/Registration/TrialReview.aspx?id=371136&isReview=true (Archived by WebCite at http://www.webcitation.org/6pL0VYIj6). Universal Trial Number U1111-1185-6120.

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## Introduction

Globally, colorectal cancer (CRC) is the third most common cancer in men and the second most common cancer in women [1]. Overall, it is the fourth leading cause of cancer death [2]. Worldwide, 1.4 million people are diagnosed with CRC every year, and 694,000 die as a result [2]. In Australia, CRC is the second most diagnosed and second most common cause of cancer death [3]. In 2012, 14,958 Australians were diagnosed with CRC and in 2013, 4162 died as a result of CRC [3].

The effectiveness of CRC screening using a fecal occult blood test (FOBT) has been established in several large randomized controlled trials (RCTs) [4-7]. Biennial FOBT screening reduces mortality from CRC by 13% to 33% [4-8]. FOBT is an affordable, accessible form of screening that can be completed by an individual in the privacy of their own home. Studies in the United States [9] and Israel [10] have found that the majority of participants prefer FOBT compared to other screening methods such as colonoscopy. Participants report that they prefer FOBT because it is convenient, affordable, less time-consuming, less painful when compared to other screening modalities, and requires no bowel preparation [9-11]. In Australia, guidelines recommend biennial FOBT for people aged 50 years and above who are at average risk of CRC [12].

Given the benefits associated with CRC screening, many countries, including Australia, have implemented population-based screening programs [13]. Population-based screening programs can be defined as those that provide a simple test to detect early signs of disease to all individuals in a target group, usually defined by age [14]. In Australia, those aged 50 to 74 years are mailed an invitation and FOBT kit as part of the federally managed National Bowel Cancer Screening Program [13]. Briefly, the program mails individuals an immunochemical FOBT, instructions, and a reply paid envelope. Completed tests are sent to a central processing laboratory. A reminder letter is sent to those not returning a test within 8 weeks [13]. Invitees returning a completed FOBT are able to nominate their primary care provider to receive test results.

The impact of this and other population-based screening programs is dependent upon achieving high rates of initial uptake and repeat screening among invitees. However, the most recent National Bowel Cancer Screening Program monitoring report indicated that, of the 1.4 million people sent an FOBT in 2013-2014, only 36% returned a completed FOBT [13]. Given this, there is an urgent need to explore ways to improve engagement in CRC screening.

Primary care is a potential setting to increase CRC screening participation. Primary care providers have frequent contact with those in the target age group for CRC screening [15], and giving advice on preventive care is perceived by patients as a key part of the primary care provider's role [16]. Primary care guidelines [17-19] recommend that providers play a role in promoting CRC screening by assessing risk based on family history and providing screening advice and test referral. Despite this, a large proportion of primary care patients in Australia have not been screened at the recommended interval [20]. This suggests that in Australia, as in other countries, CRC screening advice is not routinely delivered in the primary care setting [21-23]. This may be due to a range of factors including limited time within the consultation [24-26], perceived lack of patient interest in conversations about CRC screening [21], and cultural barriers [27].

Systematic reviews have identified strategies that are effective for increasing CRC screening uptake in the primary care setting [28-31]. Two reviews concluded that supplying patients with free FOBT when they attended an appointment with their physician resulted in an increase in CRC screening uptake by 15% to 42% when compared to usual care [29,30]. Further, RCTs that included paper-based information on CRC screening using an FOBT also significantly increased CRC screening in the intervention group when compared to those that included no paper-based information or usual care [32,33]. RCTs have found that primary care provider endorsement (ie, recommendation to take part in screening) as part of an organized screening program invitation is associated with increased CRC screening uptake when compared to standard invitations [34,35]. Most studies, however, have evaluated primary care provider endorsement in the context of mail-based interventions [31,36]. Face-to-face endorsement within the context of a primary care consultation may have greater impact on screening uptake. While reviews have identified a number of potentially effective primary care–based strategies for increasing CRC screening, the majority of studies using opportunistic strategies have taken place in the United States [30,36]. Given that the United States has a different health care system than Australia, it is unclear how generalizable these findings are to the Australian primary care setting.

Building upon current evidence, this study incorporates effective strategies to deliver a multicomponent intervention to increase CRC screening in the Australian primary care setting. The intervention comprises a novel combination of printed information on screening, the provision of a free point-of-care FOBT, and face-to-face primary care provider endorsement of screening.

## Methods

### Hypotheses

Our first hypothesis is that compared to usual care participants, those allocated to the intervention group will report a 20% higher rate of CRC screening uptake at 6-week follow-up. Our second hypothesis is that compared to usual care participants, those in the intervention group will show a greater increase in knowledge from baseline to follow-up.

**Figure 1.** Flow of participants.
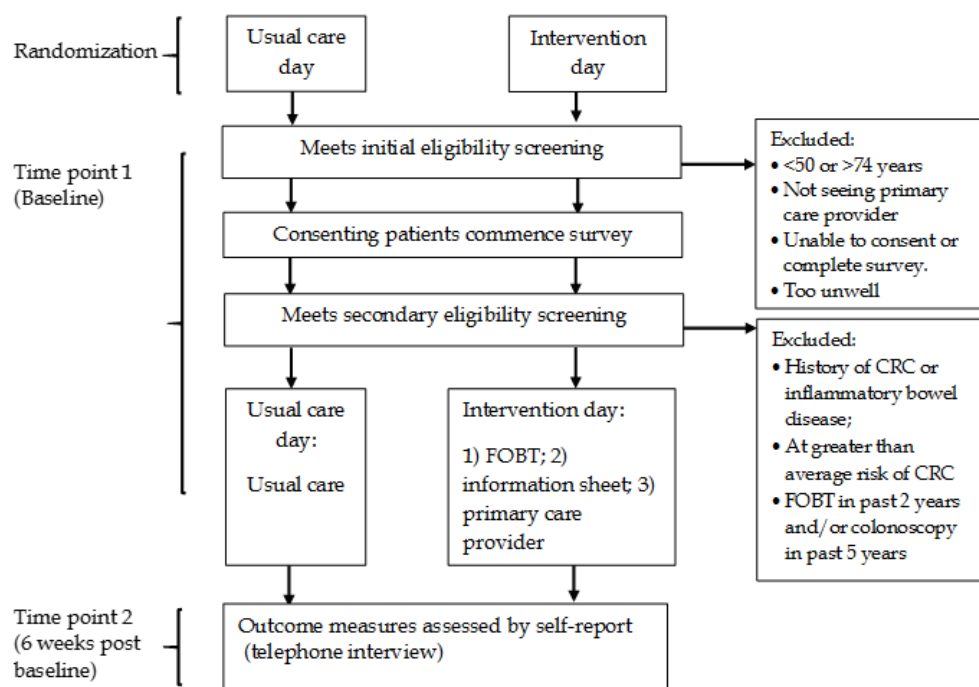


CRC: colorectal cancer; FOBT: fecal occult blood test

## Trial Design and Setting

This study is taking place in 5 primary care practices in New South Wales, Australia. A cluster RCT design is being used with consenting participants allocated to the intervention or usual care group depending on the day they attend the practice (see Figure 1).

## Practice Eligibility and Recruitment

A convenience sample of primary care clinics has been recruited for this study. To ensure adequate throughput of patients, eligible practices were required to have at least 2 full-time equivalent primary care providers. Primary care practice managers were sent an invitation and information statement via email. Nonresponding practices were followed up by telephone. Of 18 invited practices, 5 agreed to participate. Practice managers and primary care providers within each practice received an information statement and provided written informed consent.

## Randomization

Using a computer-generated randomization table with block sizes of 4, recruitment days are randomly allocated using a 1:1 ratio to intervention or usual care. Randomization by day rather than individual participant was selected to minimize potential for contamination between experimental groups. The allocation cannot be concealed from the research assistant conducting participant recruitment; however, these staff do not have access to the assignment schedule and are only made aware of allocation the day prior to attending the practice.

## Participant Eligibility Criteria

Those who (1) are aged 50 to 74 years, (2) have no personal history of bowel cancer or inflammatory bowel disease, (3) are at average risk of CRC, and (4) have not had an FOBT in the past 2 years or a colonoscopy in the past 5 years are eligible to participate in the trial.

## Exclusion Criteria

Those who are (1) not seeing a primary care provider, (2) too unwell, (3) unable to complete the touchscreen survey, or (4) unable to speak and read English sufficiently are excluded from the trial.

## Training of Staff

All training is delivered by one of the chief investigators prior to any recruitment. A training manual for research assistants developed by the research team is used for both training and as a reference during recruitment and follow-up. All research assistants receive face-to-face and on-site training in recruitment and data collection procedures. Reception staff are provided with an overview of the project as well as the process to identify eligible patients and how to refer them to the research assistant. A sign reminding reception staff to check patients for eligibility is placed at their workstation. One of the chief investigators attends a regular staff meeting at each practice to brief the primary care providers about the project and provide them with a dialogue sheet to encourage FOBT completion by patients assigned to the intervention group.

## Procedure for Assessing Eligibility

A two-stage process determines trial eligibility. Initial patient eligibility screening begins when reception staff flag patients in the target age range to the research assistant, who invites patients in the waiting room to complete a touchscreen survey to assess trial eligibility, and if eligible, to take part in the trial. Patients are provided with an information statement and allowed time to ask any questions they may have about the trial. Those providing written consent complete a 10-minute touchscreen survey in the waiting room prior to their primary care appointment. Assistance to complete the touchscreen survey is provided by the research assistance as required. Study participants do not receive compensation for their time in the study.

Second-stage patient eligibility screening is performed during the touchscreen computer survey:

1.  No personal history of bowel disease: Participants are asked whether they have ever received a diagnosis of bowel cancer or inflammatory bowel disease (yes/no). FOBT screening recommendations related to biennial FOBT are only relevant to asymptomatic individuals with no prior history of CRC. Therefore, those who respond "yes" are excluded.

2.  Average risk for CRC: Participants are asked "How many of your first-degree relatives have ever been diagnosed with bowel cancer?" (0, 1, 2 or more) and "Were any of your relatives who have had bowel cancer diagnosed before the age of 55?" (yes/no). Based on criteria in the Australian National Health and Medical Research Council guidelines [12], those who report no relatives diagnosed with CRC aged younger than 55 years and up to one first-degree relative diagnosed with CRC at any age are classified as average risk for CRC. Those classified as at higher risk of CRC are excluded, as biennial FOBT recommendations do not apply to higher risk populations for whom more intensive methods of screening may be recommended. These participants receive a sealed envelope containing information about their survey results and are advised to discuss this with their primary care provider during their appointment.

3.  Overdue for CRC screening: Average risk participants are asked to report whether they have ever had an FOBT or colonoscopy and, if so, when they had their most recent test. National Health and Medical Research Council guidelines recommend that average risk persons in the eligible age range undergo FOBT every 2 years [12]. Colonoscopy is not recommended as a routine screening test in Australia for those at average risk [12] but may be undertaken for other reasons (eg, the investigation of symptoms). Therefore, only those who report that they have not had an FOBT in the past 2 years or colonoscopy in the past 5 years are eligible for the trial.

The survey end screen contains a code that indicates to the research assistant if the participant is eligible for the trial. Eligible participants then receive the intervention if they attend the practice on an intervention day.

## Intervention

Immediately after completing the touchscreen survey, those participants identified as eligible for the trial and attending the practice on an intervention day are provided with a large envelope by the research assistant and advised to take it into their appointment with the primary care provider. This contains an FOBT kit accompanied by a referral form, instructions and a postage paid envelope addressed to a commercial pathology laboratory and a printed information sheet. The information sheet is a single-page A4 sheet using bold colored boxes to separate the information. The information encompasses topics including the type of screening test they should complete and how often they should complete this, what to do with the FOBT, what a positive FOBT result means, and credible websites where further information about bowel cancer screening can be obtained. The information sheet has a Grade 8 Flesch-Kincaid reading level.

When the participant takes the envelope into their appointment, the primary care provider explains the importance of FOBT and encourages the participant to complete the test.

## Usual Care

The usual care group receives no additional care. At the completion of the study, an information sheet similar to that provided to the intervention group is mailed to participants in the usual care group. This sheet contains additional information about how an FOBT can be sourced.

## Ethics and Dissemination

### Data Management

Baseline data is collected using QuON open source survey software [37]. QuON is a software system specifically designed for the development of scientific surveys that allows data collection and aggregation of data via a Web browser. QuON survey data is instantaneously transmitted to the University of Newcastle secure server. No data is stored on the touchscreen device. Data is downloaded from QuON as a .csv file and imported directly to Stata IC 11.2 (StataCorp LLC) for statistical analysis. This form of data collection reduces the risk of data inaccuracy. Follow-up data is collected via computer-aided telephone interview using the QuON software system. This involves a structured interview of each participant guided by a preprogrammed electronic survey. The research assistant reads each question on the electronic survey to the participants and records all responses directly into the online interface. For most questions prespecified response options are provided to the participant (eg, yes, no, not sure).

### Monitoring

Due to the size and duration of the study a formal monitoring committee and interim analysis is not required. The study is subject to the conditions of the University of Newcastle's Human Research and Ethics Committee, including a random audit procedure to ensure the study is conducted in accordance with the approved ethics submission. This study has received ethical approval from the University of Newcastle Human Research and Ethics Committee (H-2014-0198) and has been registered with the Australian New Zealand Clinical Trials

Registry (ANZCTR) [ACTRN12616001299493]. Any protocol amendments that may affect the conduct of the study, including changes of study objectives, study design, patient population, sample sizes, study procedures, or significant administrative aspects will require a formal amendment to the protocol. The modifications will be approved by the University of Newcastle Human Research Committee and updated as a new protocol version with the ANZCTR.

### Confidentiality and Access to Data

Consent forms are stored in a locked filing cabinet at the University of Newcastle and accessible by one member of the research team. Data collected via touchscreen survey is instantly uploaded to a secure University of Newcastle server accessible only by a password-protected access system. Data will be retained for at least 7 years under these conditions at the University of Newcastle. FOBT results processed by the commercial pathology laboratory are electronically conveyed to the patient's primary care provider by the password-protected online system. The pathology laboratory provides the researchers with the names of participants returning their FOBT but not individual test results. These details will be stored in a password-protected electronic file on the University of Newcastle server.

## Data Collection

### Baseline Survey

For participants meeting the trial eligibility criteria, the following measures are collected in the touchscreen computer survey:

1. Demographic characteristics: age, gender, marital status, employment situation, highest education level, current private health insurance, current health care concession card holder.
2. Primary care provider visit characteristics: Participants are asked how many times they have seen their primary care provider in the past 12 months and whether they always see the same primary care provider, usually see the same primary care provider, or see whichever primary care provider is available.
3. Perception of personal risk of bowel cancer: Australian data indicates that 1 in 10 males and 1 in 15 females will develop CRC in their lifetime [3]. Participants are asked to select a response to the following statement: "I think my chance of being diagnosed with bowel cancer in my lifetime is..." Responses are 1 in 15, 1 in 25, 1 in 50, and 1 in 100.
4. Attitudes and intentions regarding CRC screening: Participants are asked to indicate their level of agreement with the following statements: (1) "Fecal occult blood testing is an effective way to detect bowel cancer," (2) "I am confident I could complete an FOBT," (3) "Most of my family aged 50 and older screen for bowel cancer," and (4) "I intend to complete an FOBT in the next 2 years." Response options are "strongly disagree," "disagree," "neither agree nor disagree," "agree," and "strongly agree."
5. Knowledge of CRC screening recommendations: A 4-item study-specific instrument assesses knowledge of CRC screening recommendations using a multiple-choice format.

The questions are prefaced by a description of average risk: "The following knowledge questions use the term 'people at average risk of bowel cancer.' Most people are at average risk of bowel cancer as they do not have a personal or strong family history of bowel cancer." Each question has 4-6 response options. The questions were derived from National Health and Medical Research Council CRC screening guidelines [12]. The questions are (1) "At what age do you think people at average risk of bowel cancer should start screening?" (2) "What do you think is the recommended screening test for people at average risk of bowel cancer?" (3) "How often do you think a person at average risk of bowel cancer should have an FOBT?" and (4) "A positive FOBT means?" One point is awarded for each correct response.

### Follow-Up Survey

Follow-up data is collected by telephone interview 6 weeks after study enrollment. This time point was selected based on data from the National Bowel Cancer Screening Program showing that participation rates begin to plateau within 6 weeks of invitations being sent [13].

CRC screening: Participants are asked to self-report whether they have completed any form of CRC screening (FOBT, colonoscopy, other). If the patient indicates they completed an FOBT, they are asked where they obtained this.

Knowledge of CRC: The 4-item instrument to assess CRC screening knowledge at baseline is also delivered at follow-up to detect changes in CRC knowledge.

Intervention group only: Acceptability of feedback sheet is assessed by the following questions: (1) "Did you read the feedback sheet?" (yes/no), if yes, (2) "Do you have any suggestions about how the feedback sheet could be improved?" (free response), (3) "Did you access any of the websites listed on the feedback sheet?" (yes/no), if yes, (4) "Which websites did you access?" and (5) "Do you think it would be helpful to receive information sheets from your primary care provider about other health issues?" (free response). Reasons for not being screened: Participants who report no screening are asked if there was a particular reason they did not use the kit provided at their primary care provider appointment (free response).

### Process Measure

The researchers receive electronic notification of the names of participants returning an FOBT from the commercial pathology laboratory; however, no results are provided. This process measure will be used for an analysis of the sensitivity of self-reported screening.

### Analysis and Sample Size

The age and sex of consenters and nonconsenters will be compared using the chi-square test for categorical variables and the *t* test or nonparametric equivalent for continuous variables. The proportion of participants completing CRC screening at the follow-up time point will be compared using a logistic regression model, including treatment group and site as independent variables. The correlation of observations induced by the design of the study will be accounted for through cluster

robust variance estimation. A logistic regression will determine the characteristics associated with CRC screening. Differences in knowledge scores between the usual care group and the intervention group will be determined by ordinal logistic regression. For all tests, we will use 2-sided *P* values with a 5% significance level; exact *P* values will be reported. The primary analysis population will be all those who are randomized. Analysis will follow the intention-to-treat principle, with missing data imputed using multiple imputation. A sensitivity subanalysis of self-report versus pathology records in the intervention group will be conducted.

The sample size was calculated based on the primary aim. A sample size of 80 participants per arm will enable detection of a 25% increase in self-reported CRC screening for participants in the intervention group compared to 5% in the usual care group with 90% power at 5% significance. This calculation allows for a small design effect of 1.2 to allow for potential clustering by the design of the study (day of the week) and assumes on average 10 eligible participants will be available per day. Given that all participants eligible for randomization will have not participated in CRC screening via FOBT in the past 2 years or colonoscopy in the past 5 years, the underlying population prevalence of screening will not be considered in the sample size calculation.

## Results

At the time of submission, 5 primary care practices have consented to participate, with 100 participants enrolled in the study. Follow-up of participants has commenced, and it is anticipated all data collection will be complete by August 2017. Data analysis is in the preliminary stages. The authors will disseminate trial results through peer-reviewed publications and presentations at conferences.

## Discussion

### Strengths and Limitations

Previous research has demonstrated that multicomponent interventions are more likely to increase CRC screening participation than singular interventions [28]. Our study will test a multicomponent intervention using a gold standard RCT design across 5 primary care clinics. Very few intervention studies to increase colorectal cancer have been conducted in an Australian primary care setting.

### Authors' Contributions

MC, EM, and ND conceived the study, wrote the project application for funding, and developed the study protocol. CO advised on study design, sample size, and statistical methods. All authors contributed to the drafting of the manuscript or revising it critically for intellectual content.

### Conflicts of Interest

None declared.

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## Abbreviations

**ANZCTR:** Australia New Zealand Clinical Trials Registry
**CRC:** colorectal cancer
**FOBT:** fecal occult blood test
**RCT:** randomized controlled trial

Protocol

# The Effectiveness of a Computer Game-Based Rehabilitation Platform for Children With Cerebral Palsy: Protocol for a Randomized Clinical Trial

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## *Abstract*

**Background:** It is difficult to engage young children with cerebral palsy (CP) in repetitive, tedious therapy. As such, there is a need for innovative approaches and tools to motivate these children. We developed the low-cost, computer game-based rehabilitation platform CGR that combines fine manipulation and gross movement exercises with attention and planning game activities appropriate for young children with CP.

**Objective:** The objective of this study is to provide evidence of the therapeutic value of CGR to improve upper extremity (UE) motor function for children with CP.

**Methods:** This randomized controlled, single-blind, clinical trial with an active control arm will be conducted at 4 sites. Children diagnosed with CP between the ages of 4 and 10 years old with moderate UE impairments and fine motor control abnormalities will be recruited.

**Results:** We will test the difference between experimental and control groups using the Quality of Upper Extremity Skills Test (QUEST) and Peabody Developmental Motor Scales, Second Edition (PDMS-2) outcome measures. The parents of the children and the therapist experiences with the interventions and tools will be explored using semi-structured interviews using the qualitative description approach.

**Conclusions:** This research protocol, if effective, will provide evidence for the therapeutic value and feasibility of CGR in the pediatric rehabilitation of UE function.

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## KEYWORDS

## *Introduction*

### Background and Rationale

Canada and India face a growing population of children with cerebral palsy (CP), with the condition occurring in 2 to 4 of every 1000 live births in North America and India, respectively [1-3]. Children with CP have deficits in fine and gross motor skills, often with co-occurring deficits in visual-spatial processing skills [4-6]. The ability to perform functional tasks with the upper extremities (UEs) is an important predictor of success in daily activities and participation in school, leisure, and social activities [7]. Therapy programs designed to improve UE motor and visual-spatial processing skills must strive to maximize neurodevelopmental capacities and prevent secondary disabilities [8,9].

There are different approaches to therapy for children with CP [10-17]. The effectiveness of these programs is proportional to the intensity and amount of training and the task-specificity of the exercise regime [18-21]. For example, constraint-induced movement therapy (CIMT) and hand-arm bimanual intensive therapy (HABIT) are promising rehabilitation programs for restoration of hand-arm function. These treatment approaches stress that both functional demands and repetitive intensive training are important in the rehabilitation of fine motor skills and to restore functional skills. Typically CIMT needs administration of 6 hours a day and the child can use only the affected arm, making bimanual activities impossible to perform. There is growing evidence to support the idea of activity-dependent central nervous system (CNS) plasticity [22]. In addition, the notion is emerging that neural reorganization reflects learning achieved through generating real experiences, applying focused attention, simulating close-to-normal movements, and repetition [23]. However, it is difficult to engage children with CP in therapy for long periods of time and sustain motivation for the intense repetitive task practices. Thus, there is a need for innovative and cost-effective therapeutic approaches and tools that motivate children with CP to complete long-term neurorehabilitation programs and that provide opportunities to improve neurodevelopmental outcomes.

Parents and clinicians rate motivation as the most influential personal characteristic for adherence to therapy and for determining motor and functional outcomes in children with CP [24]. An emerging, promising approach to engaging children in therapy is to incorporate computer games in which a range of learning elements with interactive cognitive challenges help children to positively engage in activities. Studies have provided evidence of the benefits of video games in rehabilitation training and show that well-designed interactive games can improve players' motor skills and visual-spatial processing skills [24-30].

For this purpose, we developed the low-cost, computer-aided, game-based rehabilitation and learning platform CGR [31-37]. CGR combines fine or gross motor exercises and visual-spatial cognitive activities appropriate for children with CP in a game-based format. A motion detecting "Therapy Mouse" (Mobility Research, AZ) will be used as the computer game controller. It is a miniature and wireless plug-n-play computer interface device, which contains firmware and inertial sensors that allow physical motion, specifically instantaneous position, to be translated and interpreted as a standard motion of a Universal Serial Bus (USB) mouse, and which has high fidelity and responsiveness. Because the miniature motion mouse can be easily attached with Velcro to many objects, this approach provides a highly flexible therapy tool applied to fine or gross UE motor skills. Many objects with varied sizes, shapes, weights, surface properties, and functional demands can be used for exercise and for practicing a variety of gross or fine motor skills. Importantly, when the motion mouse is attached to the chosen object fun computer games can be played [8,28,31,36-37]. As CGR allows handling and manipulation of many objects (ie, ones commonly used in daily activities), activity goals can be imbedded in the therapy program. Many inexpensive modern games, "exergames," and brain fitness games now exist that are visually rich, fun, and engaging, include a variety of visual-spatial tasks, and require choice and other planning type activities. Performing goal-directed manipulation tasks through engaging and guided repetition creates experiences crucial to improving the brain's ability to learn [10,37].

### Study Objectives

A randomized controlled trial (RCT) with an intention-to-treat is proposed to evaluate the effectiveness of the game-based rehabilitation program on fine manual dexterity, upper limb motor skills, and visual-spatial cognitive functions in children aged 4 to 10 years old diagnosed with CP. This single-blind randomized clinical trial with an active control arm will be conducted at 4 sites. Two groups of children will be examined: one group will receive the experimental game-based program and the other group will receive usual therapy (see Multimedia Appendix 1). The first hypothesis is that an engaging, game-based UE exercise regime will result in greater improvements in hand-arm function as compared to the usual outpatient physical therapy program. The second hypothesis is that the UE exercise program, which uses computer games having a variety of visual-spatial activities, will result in greater improvements in visuospatial cognitive functions as compared to the usual outpatient physical therapy program.

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## Study Design

This study will evaluate the feasibility of the procedures such as recruitment, intervention delivery, participant retention, and measurement tools. Semi-structured interviews will be conducted with the parents of the children and with the treating therapists. The broad research questions are: "what were the experiences of the study participants with the game-based and current therapy programs, and on what context were the experiences based?" The qualitative findings of participant's and therapists' experiences will help to identify (1) perceived exercise benefits; (2) difficulties with the exercises and using the technologies; (3) engagement and motivational value of the computer games; (4) personal and environmental factors that influenced doing the exercises; and (5) recommendations and modifications for improving the exercise programs.

## *Methods*

### Study Setting

This randomized controlled, single-blind clinical trial with an active control arm will be conducted at the following 4 sites: (1) University of Manitoba and Rehabilitation Centre for Children at the Special Services for Children and Youth (SSCY) Centre (Drs Szturm, Rempel, Restall, and Mrs Kanitkar, Winnipeg, Manitoba, Canada); (2) SDM College of Physiotherapy, Dharwad in collaboration with Usha's School for Exceptional Children, Hubli (Drs Parmar, Savadatti, Kamate, and Naik, Karnataka, India); (3) Christian Medical College (Drs Sharma, Pandian, and Gandhi, Ludhiana, Punjab, India); and (4) Kasturba Medical College (Dr Narayan, Mangalore, Karnataka, India).

### Inclusion Criteria

Children diagnosed with CP (N=140) between the ages of 4 and 10 years old with moderate UE impairments and fine motor control abnormalities will be recruited. The following screening tools will be used: (1) Manual Ability Classification System (MACS), level 2 to 3 [38]; (2) Gross Motor Function Classification Scale (GMFCS), levels 2 to 4 [39]; (3) Ashworth scale of spasticity in wrist and fingers, level 0 to 1+ [40]; and (4) the pediatric version of the Mini-Mental State Examination assessment scale, level 17 and above. This will be used to the screen level of cognitive function. For each site, we will use a permuted block randomization scheme stratified by age and level of impairment as measured by the MACS and GMFCS [41].

### Exclusion Criteria

Exclusion criteria for the study will be (1) visual or auditory impairment such that they cannot see and interact with the video games; (2) secondary orthopedic complications due to neurodegenerative disease (NDD) or as a result of surgery to the upper limb that may have caused permanent changes in upper limb musculoskeletal structure; (3) recent Botulinum toxin therapy (less than 6 months); (4) seizures, or (5) complex communication disorders.

## Procedures and Interventions

Ethical approval was obtained from the health research ethics boards of each site. For each site a permuted block randomization scheme will be used and stratified by age where 4- to 6-year-olds will be one subgroup and 6- to10-year-olds will be the other subgroup. Each program will take 16 weeks, with 3 45-minute sessions per week. A workshop and uniform training program will be organized at SDM College of Physiotherapy, Dharwad, India for physiotherapists who will provide the assessment and the 2 intervention programs. This will be attended by Dr Szturm and Mrs Anuprita Kanitkar who will organize and coordinate the therapy program. The 2 intervention groups will be treated in all 4 locations limiting biases like contamination. The therapists conducting the assessments will be blinded to group assignment.

### Control Group Intervention

The control group (n=70) will receive the usual, comprehensive physical therapy for 45 minutes per session 3 times a week for 16 weeks. The therapy protocols will be individualized for every participant according to their level of impairment and preset goals, based on the principles of intensive repetitive task practice programs such as CIMT and HABIT. These consist of stretching of spastic muscles (activity-based dynamic stretching with child's active involvement to the spastic upper limb muscle, particularly muscles which are required for preparatory techniques will be involved in lengthening) and UE weight bearing exercises (ie, UE weight bearing in fundamental or functional position in the form of scapular and upper thoracic rotation and/or push and pull with a vestibular ball while maintaining corrected scapular positioning). A variety of arm and hand activities will be practiced, such as reaching for rings, removing and putting them back, ball throwing, opening a bottle cap, turning a door knob, clay activities, picking marbles from sand, and putting pellets and pegs into sockets, etc.

### Experimental Group Intervention

A typical session for the experimental group (n=70) will consist of stretching exercises followed by the game-based exercise program. Similar to the concept of "shaping," and consistent with CIMT principles, CGR takes advantage of ergonomic properties of common objects to amplify limited and small amounts of voluntary movement and then allows opportunities for an appropriate switch to objects having more demanding movement requirements or functional demands. CGR allows object properties (size, weight, texture, and surface properties) to be easily manipulated in therapy. This provides graded practice for activities that need to be repeated in daily activities and in play. An important element of the platform is the ability to incorporate movement precision. In this regard, we target finger-hand function and not just transport and/or reaching movements.

Different computer games require different levels of movement amplitude, speeds, precision levels, as well as repetition and appeal to individual preferences. Furthermore, many inexpensive "off the shelf" computer games have a broad range of visuospatial cognitive content. Knowledge of the therapeutic value (object and games activities) can allow the therapist to

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prescribe an integrated program to target specific goals, for example, speed, accuracy, endurance, visuospatial functions, and cognitive inhibition, and to exercise 2 or 3 fingers, the whole hand, and bimanual tasks tailored to individual child abilities.

In a manner similar to interval training, 6 to 8 objects selected for specific therapy goals will be used to play computer games. Objects can be selected for motor skill training of finger/wrist or elbow and shoulder motions, and also of bimanual controls. Each object manipulation exercise will be used for 2 to 4 minutes. A number of possible objects which, when instrumented with the motion mouse, can be used for the game-based exercise program is shown in Figure 1 (see also Szturm et al [31]). Many action and cognitive-type computer games are available to play; these will be selected by the treating therapist based on (1) degree of difficulty; (2) movement amplitude, speed, and accuracy; (3) visual-spatial processing requirement; and (4) personal preferences of the child. Common computer games that will be used in the game-based exercise program are shown in Textbox 1.

**Figure 1.** Descriptions of the object manipulation tasks and their respective therapy values for assessment and/or treatment. A miniature, wireless motion mouse is attached with Velcro to each object. Each object manipulation task has specific fine or gross motor skill qualities for therapeutic exercise or ergonomic properties.
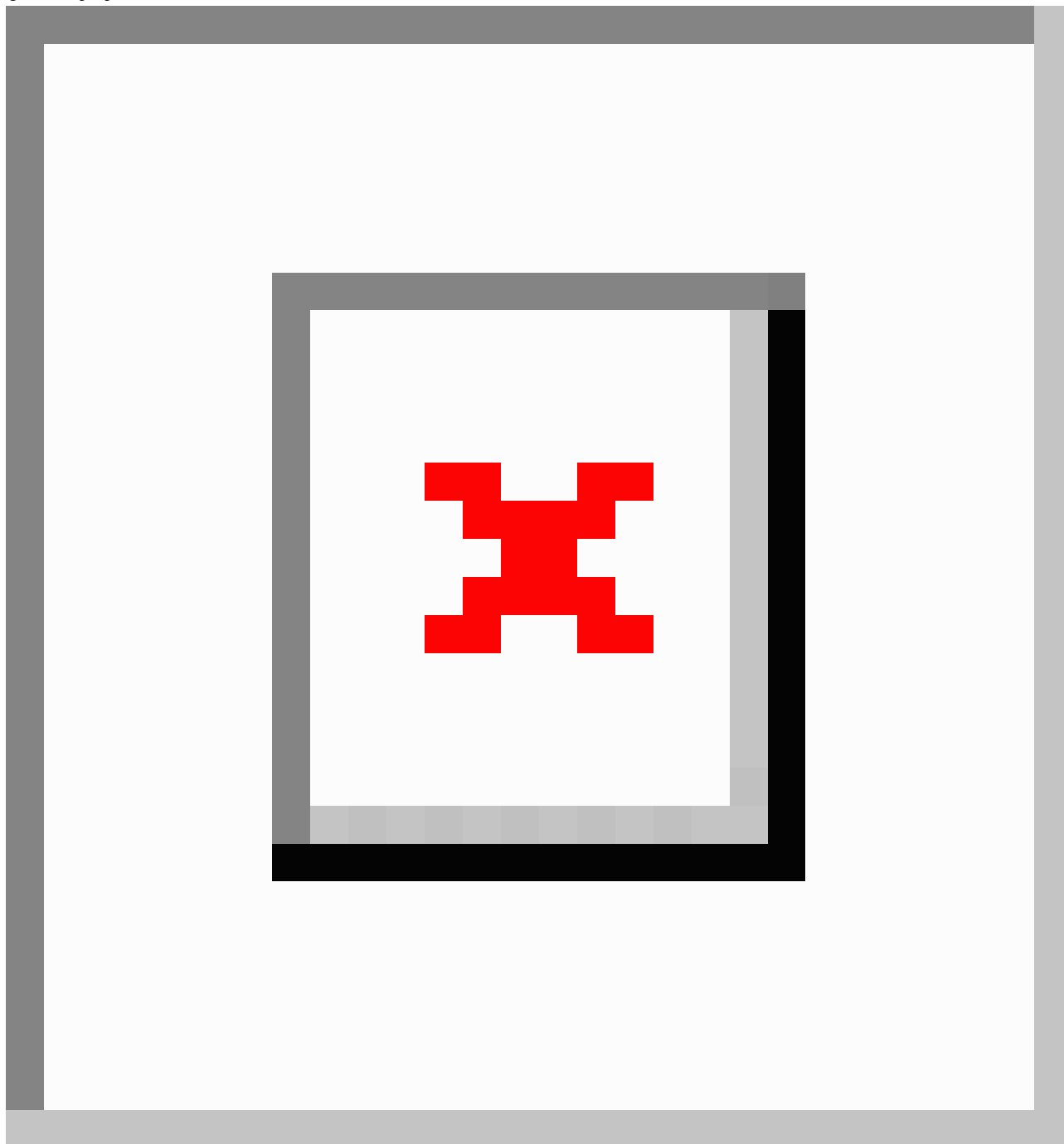
**Textbox 1.** Computer games that will be used in the exercise program.

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Computer game

1.  Aqua Ball and Action Ball.

    a.  Horizontal, single-axis brick buster with slow to moderate speed, and low to moderate movement precision.

    b.  Small to moderate number of distracters and simple to complex 2D backgrounds.

2.  Jar of marbles and butterfly escape.

    a.  Horizontal, single-axis matching colors with slow to moderate speed and low to moderate movement precision.

    b.  Small to moderate number of distracters and simple and moving backgrounds.

3.  Owls and bubbles.

    a.  A single-axis game that requires the player to move the mouse cursor on bubbles to pop them and free the owls to fly away.

4.  Hummingbird.

    a.  A single-axis game that requires the player to move the bird up and down so that it touches the flowers.

5.  Feeding frenzy.

    a.  Two-axis game play with slow motion element and low to moderate movement precision.

    b.  Moderate to large number of distracters.

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## Primary Outcome Measures

The Quality of Upper Extremity Skills Test (QUEST) is a commonly used outcome measure that evaluates quality of dissociated movements, UE gross motor function, and object manipulation in children with CP. It consists of 36 tasks evaluated in 4 domains: dissociated movement, grasp, protective extension, and weight bearing. The tool has demonstrated excellent test-retest reliability [42], and through construct validity studies, has been demonstrated as a good measure of UE motor skill [43].

The following subtests of the Peabody Developmental Motor Scale, Second Edition (PDMS-2) will be used: (1) object manipulation (24-item subtest that measures a child's ability to manipulate balls); (2) grasping (a 26-item subtest that measures a child's ability to use his or her hands [44]); and (3) Visual-Motor Integration (VMI) subtest (a 72-item subtest that measures a child's ability to use visual perceptual skills). Both the PDMS-2 fine motor composite score and the VMI subtest score have shown high test-retest reliability and have good construct validity [45,46].

Immediately following the 16-week intervention, a semi-structured interview format will be used to ask parents about the 5 most important activities their child was trying or wanted to do, but was having difficulty performing and/or difficulty in retaining.

## *Results*

We will test the difference between the experimental and control groups on the QUEST and PDMS-2 outcome measures using analysis of covariance (ANCOVA); the dependent variable will be the post-intervention measurement of the outcome and the covariates will be the pre-intervention measurement and group

membership as the between-subjects effect. Residual diagnostics will be carried out for the ANCOVA model and if their normality assumption fails to hold, appropriate transformations of the response, such as logarithmic, will be explored. Based on published data for the primary outcome measures (QUEST and PDMS-2) [37-41], a power analysis was conducted to determine the required sample size to test the difference between the experimental and control groups using the ANCOVA model. We selected the case (QUEST) which gave the largest sample size. Assuming a correlation of at least 0.6 between baseline and final outcome, then with a sample size of 128 and a standard deviation of 25 we will be adequately powered to detect a difference of 10 units with 80% power, and 5% alpha post intervention. We expect an attrition rate of 10% over the study period. Given this, we propose to recruit a sample of 140 children to participate in equal numbers to be randomized to each group. All calculations were made with PROC GLMPOWER of SAS version 9.3 (SAS Institute, Cary, NC).

Feasibility will be evaluated on the basis of the 2010 Thabane et al model [47] which evaluates 4 domains: process, resources, effectiveness, and human and data management. Process evaluates feasibility of key study processes, such as participant recruitment rates, dropout rates, eligibility criteria, and participant retention rates. Resources, such as time taken to complete study assessments and other resource problems, will be reported over the study period by the project site leads from each site and the data will be compiled.

The parents of the children and the therapist experiences with the interventions and tools will be explored using semi-structured interviews using the qualitative description approach. The following open-ended questions will be asked of the children's parents: (1) when you agreed to participate, how did you hope your child would benefit from the therapy program? (2) Were there things about the game (or exercise

therapy program) for your child you liked and things you did not like? (3) What did you think about the computer games your child was asked to play? Did your child enjoy the games? Were there games which your child did not seem to enjoy? (4) Did you feel that this therapy program helped your child? (5) If you were provided with the right setting, would you want your child to continue with these exercises?

The following open-ended questions will be asked of each treating therapist who delivered the game-based therapy program: (1) compared to usual therapy exercises how easy or difficult was it to implement the game exercise program for the children? (2) What kind of difficulties did you face, if any, regarding the use of the motion mouse or other parts of the technology? (3) What qualities did the computer game based intervention possess, if any, that made it more engaging and fun for the children than the conventional protocol? (4) Why would you like to recommend this intervention and technology to your peers, colleagues, and patients? (5) Are there any thoughts, queries, or doubts regarding this treatment method that you would like to express or discuss with us?

The responses of the parents and therapists will be analyzed with content analysis methods using the descriptive as well as interpretative approaches [48,49]. The data collected during the semi-structured interviews will be in the local language. Responses will be transcribed and translated by authorized personnel to organize the data by labelling, structuring, and familiarizing processes. Each participant's data will be reviewed and analyzed by 2 researchers. Their narrative summary will then be sent back to the parents and therapist for review and approval to ensure trustworthiness of the transcribed and summarized data. Direct quotes from parents' and physiotherapists' interviews will be used while writing the descriptive report to illustrate a range of issues faced during the study, behaviors, experiences, and opposing views of participants and strategies. These will be used to develop general statements and hypotheses, which can be tested in subsequent studies. A second order analysis will take place by creating a coding plan based on the research questions. Once the data is coded and sorted, these responses will be categorized to identify themes. The recurrent themes and response clusters are helpful to build event sequences.

## Discussion

Emerging game-based rehabilitation technologies have the potential to improve child participation in repetitive task practice, and therefore, enhance function. The purpose of the study is to provide evidence of the therapeutic value of CGR to improve UE motor function for children with CP. CGR is designed to be used with modern, common computer games, which are low-cost and easily available. Commercial games offer a wide range of levels of precision and movements that vary in speed, amplitude, direction, and accuracy. There is also a wide range of executive cognitive activities available in commercial games for children. It is important to have a large variety of exercise and cognitive activities in games to maintain high levels of motivation and interest among participating children. Knowledge of the therapeutic value (object and games) can allow the therapist to prescribe an integrated program to target specific goals.

The qualitative findings of participants and therapists will help to identify the perceived exercise benefits, any difficulties with the exercises and using the technologies, the engagement and motivational value of the computer games, personal and environmental factors that may have influenced doing the exercises, and any recommendations and modifications for improving the exercise programs.

### Conflicts of Interest

None declared.

### Multimedia Appendix 1

CONSORT flow diagram.

[PDF File (Adobe PDF File), 347KB - resprot_v6i5e93_app1.pdf ]

### Multimedia Appendix 2

CONSORT checklist.

[PDF File (Adobe PDF File), 46KB - resprot_v6i5e93_app2.pdf ]

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## Abbreviations

**ANCOVA:** analysis of covariance
**CIMT:** constraint-induced movement therapy
**CP:** cerebral palsy
**GMFCS:** Gross Motor Function Classification Scale
**HABIT:** hand-arm bimanual intensive therapy
**MACS:** Manual Ability Classification System
**PDMS-2:** Peabody Developmental Motor Scale, Second Edition
**QUEST:** Quality of Upper Extremity Skills Test
**UE:** upper extremities
**VMI:** Visual-Motor Integration

Protocol

# The Use of Text Messaging to Improve the Hospital-to-Community Transition in Acute Coronary Syndrome Patients (Txt2Prevent): Intervention Development and Pilot Randomized Controlled Trial Protocol

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## Abstract

**Background:** Acute coronary syndrome, including acute myocardial infarction (AMI), is one of the leading causes for hospitalization, with AMI 30-day readmission rates around 20%. Supporting patient information needs and increasing adherence to recommended self-management behaviors during transition from hospital to home has the potential to improve patient outcomes. Text messages have been effective in other interventions and may be suitable to provide support to patients during this transition period.

**Objective:** The goal of this study is to pilot test a text messaging intervention program (Txt2Prevent) that supports acute coronary syndrome patients for 60 days postdischarge. The primary objective is to compare self-management, as measured by the Health Education Impact Questionnaire, between patients receiving only usual care versus those who receive usual care plus the Txt2Prevent intervention. The secondary objectives are to compare medication adherence, health-related quality of life, self-efficacy, health care resource use (and associated costs), all-cause and cardiovascular disease (CVD) readmission, and all-cause and CVD

mortality rates between the 2 groups. The third objective is to assess acceptability of the text messaging intervention and feasibility of the study protocol.

**Methods:** This is a randomized controlled trial with blinding of outcome assessors. The Txt2Prevent program includes automated text messages to patients about standard follow-up care, general self-management, and healthy living. The content of the text messages was informed by and developed based on interviews with patients, discharge materials, theoretical domains of behavior, and a clinical advisory group composed of patients, clinicians, and researchers. We will recruit 76 consecutive cardiac in-patients with acute coronary syndrome who are treated with either medical management or percutaneous coronary intervention from a hospital in Vancouver, Canada.

**Results:** Assessments at baseline will include measures for demographic information, self-management, health-related quality of life, and self-efficacy. Assessments at follow-up will include medication adherence, readmissions, health care resource use, and mortality in addition to the reassessment of baseline measures. Baseline assessments are done in-person while follow-up assessments are completed through a combination of mailed packages and phone calls. Semistructured interviews with participants will also be performed to better understand participant experiences managing their condition and with the text messages.

**Conclusions:** This study will determine preliminary efficacy, feasibility, and acceptability of the Txt2Prevent program to support acute coronary syndrome patients in the transition to home following hospital discharge. The results of this study will be used to inform a larger trial.

**Trial Registration:** ClinicalTrials.gov NCT02336919; https://clinicaltrials.gov/ct2/show/NCT02336919 (Archived by WebCite at http://www.webcitation.org/6qMjEqo6O)

## *Introduction*

### Background

Cardiovascular disease (CVD) is one of the leading causes for hospitalization and death in Western countries [1,2]. Acute coronary syndrome (ACS) includes the diagnoses of acute myocardial infarction (AMI) and unstable angina. AMIs are the second most common reason for inpatient admissions in Canada (excluding giving birth), with over 60,000 cases [3] while ACS was the primary or secondary cause of over 1.1 million unique hospital admissions in the United States in 2010 [4]. Approximately 60% of these admissions were due to AMIs, making AMIs a leading cause for inpatient admissions [4,5]. The initial period following discharge is the highest risk for readmission, with 14% of AMI patients having an urgent readmission within 15 days of discharge and 20% of patients being readmitted by 30 days [6]. In the United States, Dharmarajan et al [7] found that AMI patients' daily change in risk of readmission has declined by 95% by day 38 postdischarge. In Canada, the median days until readmission in ACS patients was 23 (interquartile range: 5 to 41 days) [8]. Readmissions are of concern because of the impact on patient quality of life [9] and the cost to the health care system, which has been estimated at $1 billion in the United States in 2013 [10,11].

Patients have several challenges during the transition period after discharge that can influence readmissions, including lack of support, potentially preventable adverse events, and patient inability to perform self-management behaviors [12,13,14]. During the transition period, patients report feeling overwhelmed, uncertain, and alone with physical or mental setbacks [12,15]. Patients may be confused about the information they received in the hospital [15] and may want

more information once they are home because being informed often provides reassurance [12]. Additionally, up to 23% of patients may experience adverse events after discharge, such as adverse drug events or therapeutic error, of which half may be preventable or ameliorable [13]. Having better transitional care could help to identify or prevent these errors. Following hospital discharge, ACS patients also must become independent with new self-management responsibilities [12,16]. Self-management is the concept that people with chronic illness, such as CVD, must live with and manage their disease on a daily basis, which includes engaging in healthy behaviors to control or reduce the impact of their disease, communicating effectively with health professionals and caregivers, and managing physical and emotional challenges [17]. Meta-analyses have found chronic disease self-management programs have been associated with reduced hospital use (particularly in CVD and respiratory patients) [18], improvements in health behaviors such as aerobic exercise, cognitive symptom management, and communication with physicians [19], improvements in health outcomes such as glycemic control in diabetes patients and blood pressure reductions in hypertension patients [20,21], and increased quality of life and self-efficacy [22,20]. Self-management for ACS patients includes recommended behavioral changes (eg, smoking cessation, exercise, and adhering to a healthy diet) and taking their medications as prescribed. Despite this knowledge, research shows that many patients continue with unhealthy behaviors. In one study, 30 days after discharge, 35% of smokers continued to smoke and 29% of patients do not adhere to physical activity and diet recommendations [14]. The authors found nonadherence to smoking, diet, and exercise behavioral recommendations is associated with a 3.8-fold increased risk of myocardial infarction, stroke, or death at 6 months postdischarge [14]. Another study reported that within the first 7 days after

discharge, 23% of cardiac medication prescriptions were not filled despite the association between medication adherence and reduced mortality [23]. Therefore, providing continuing support post–hospital discharge has the potential to affect several key factors of post-ACS management, including medication adherence, lifestyle changes, and adverse events, which in turn can impact patient experiences and outcomes.

Text messaging technology presents an opportunity to help support patients during the hospital-to-home transition. Mobile phone ownership has increased from 65% in 2004 to 92% in 2015 in the United States [24]. While mobile phone ownership is higher in younger demographics, 78% of adults ages 65 and older own a mobile phone [24], and 80% of mobile phone owners send or receive text messages making it one of the most commonly used features [25]. Text messages can provide information to patients in a manageable amount at the appropriate time point in their recovery. Messages can include reminders and prompts to engage in the recommended postdischarge behaviors. Messages are inexpensive to send and receive, and automated delivery systems do not require a significant amount of staff time to maintain. Additional benefits are that messages may be stored on the device to be accessed multiple times and do not require both the sender and the receiver to be available at the same time, such as with a standard phone call. Text messages also have a wide geographic reach, ensuring that patients do not have to travel to receive the information. In previous text messaging studies with patients with or at risk for CVD, there have been improvements in self-management behaviors, such as medication adherence [26], and increased leisure, physical activity, and walking [27]. Text message interventions have also contributed to improvements in cardiac risk factors including lowering LDL cholesterol and systolic blood pressure [28]. Additionally, a systematic review of text messaging studies in diabetes patients found improved scores on measures for self-management capacity [29]. The studies in a CVD population did not target the hospital-to-community transition period, so it is worth investigating the potential for text messaging to support CVD patients as they transition from hospital to home.

## Study Objectives

The aim of this pilot study is to test a 1-way text messaging intervention program (Txt2Prevent) composed of 48 messages that supports ACS patients for 60 days after their hospital discharge in a single-blinded randomized controlled trial. The objectives are as follows:

1. To compare self-management between participants receiving usual care versus participants receiving usual care plus the Txt2Prevent program as measured by the Health

Education Impact Questionnaire (heiQ). The heiQ assesses proximal outcomes of self-management and patient education programs [30].

2. To compare health-related quality of life, medication adherence, self-efficacy, all-cause and cardiovascular-related hospital readmissions and mortality rates, and health care resource use (and associated costs) between participants receiving usual care versus those receiving usual care plus the Txt2Prevent program.

3. To assess the acceptability of the text messaging intervention program according to patient participants and the feasibility of the study protocol for study staff.

We hypothesize that the Txt2Prevent group will have improved self-management compared with usual care. This paper describes the research protocol for the pilot study [ClinicalTrials.gov NCT02336919] in accordance with the Consolidated Standards of Reporting Trials (CONSORT) eHealth checklist [31].

## *Methods*

### Overview

The Txt2Prevent project is a mixed methods, single-blinded randomized controlled trial with a parallel group design. Participants will be randomized to receive either usual care or usual care plus 1-way text messaging for the first 60 days postdischarge from the hospital (Txt2Prevent).

### Setting, Participants, and Recruitment

Participants will be recruited from the provincial heart center located in a tertiary care hospital in Vancouver, British Columbia, Canada. This hospital serves patients from across the province, including the local metropolitan area as well as urban and rural areas. Consecutive patients admitted for ACS, as identified by clinical staff, will be screened for eligibility (see Figure 1). ACS patients whose treatment is a coronary artery bypass graft will be excluded as they have different recovery guidelines than medical management or percutaneous coronary intervention patients due to the more invasive nature of the procedure. Those who are eligible and interested will provide written, informed consent. The consent process will occur in person at the hospital. If the patient is discharged before it is possible for the research assistant to complete the written consent process, the patient may provide their phone number to study staff so they can complete an oral consent process over the phone within 7 days of discharge. The research assistant will also explain and give the participant a 1-page sheet outlining the study process and study contact information while the participant is still in the hospital or over the phone (including sending a copy through email or mail).

**Figure 1.** Study design and flow (ACS: acute coronary syndrome, CVD: cardiovascular disease).
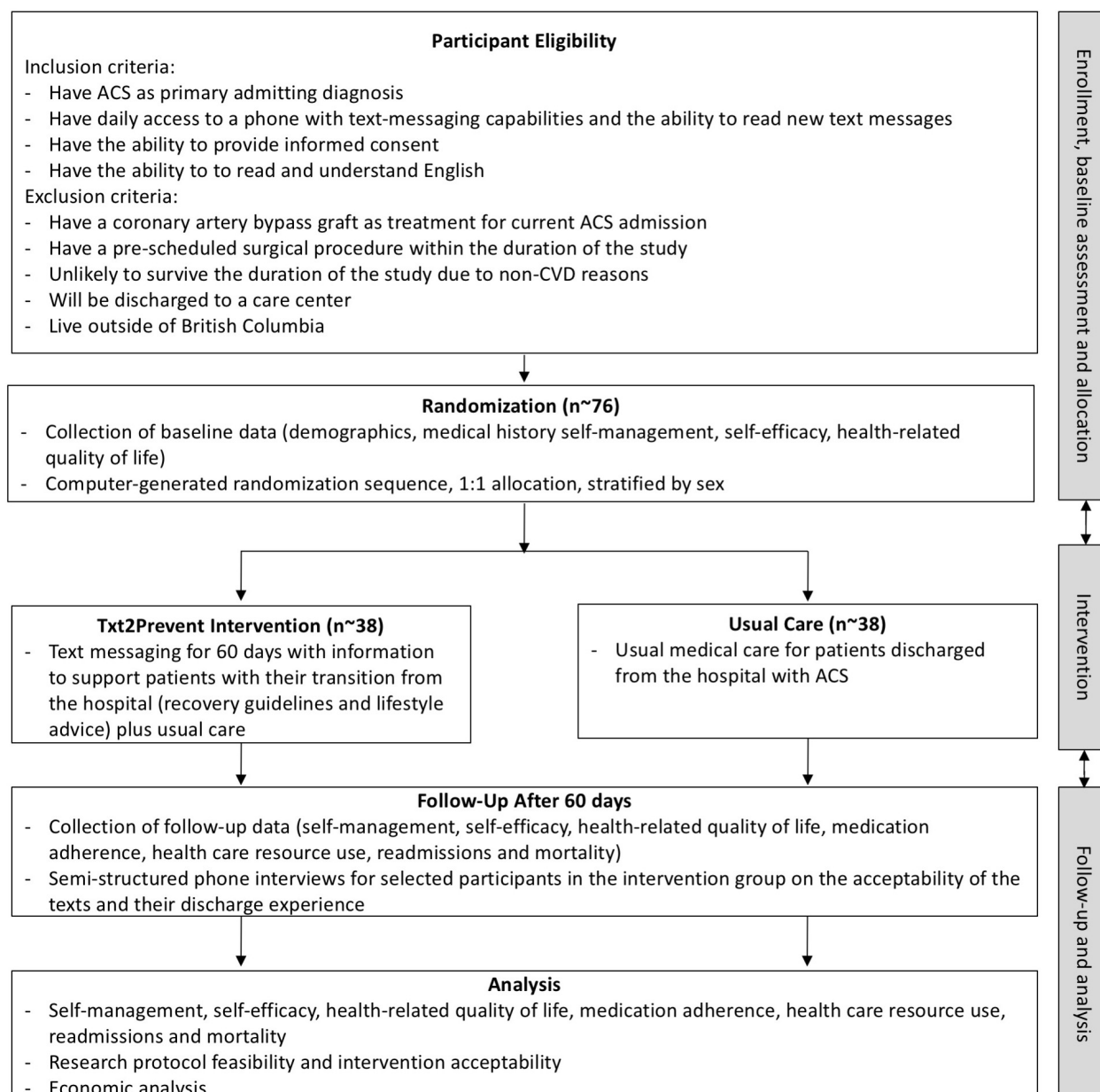


## Sample Size

A convenience sample of 76 participants will be enrolled in the study. This sample size is based on the feasibility of recruitment over a 6-month time period and is not determined in order to be able to detect between-group differences. Approximately 750 unique ACS patients were discharged from the target hospital during the 2012/2013 fiscal year. In a preliminary feasibility survey of patients, 14 of 28 had mobile phones with texting capabilities. Assuming 40% are eligible and 50% agree to participate [32], we expect approximately 76 patients will agree to participate over 6 months of recruiting.

## Randomization

After discharge and once the baseline assessment has been completed, participants will be randomized to receive either usual care or usual care plus the 60-day text messaging program (Txt2Prevent) using a 1:1 allocation ratio. To minimize bias,

randomization will be conducted by a research assistant who is not involved in either the recruitment or data collection phases. This research assistant will use a Web-based randomization service developed through an independent research center. To ensure balance between the groups, the randomization will be stratified by sex and use block randomization with variable block sizes. The randomization research assistant will register participants for the TxT2Prevent intervention, when appropriate, and then contact all participants by phone to inform them of their group assignment. The start date for participants in the Txt2Prevent program will be documented. A letter will also be sent to all study participants' primary care providers informing them that their patient has been enrolled in the study. Primary care providers will be identified by the participant. The primary care providers' addresses will be obtained online from the registry maintained by the provincial licensing and regulatory body for physicians. Participants will be told to contact the research assistant who performs the randomization during the

course of the study if they have any questions. Participants will be aware that the text messaging program is the intervention of interest as it is being compared to usual care.

## Study Design

### Intervention

The intervention group will receive a total of 48 health-related text messages: 1 per day for the first 36 days, then 1 every other day for days 37 to 60 (Table 1). The text messaging program will begin the day after the participant is discharged from the hospital or, if the participant has already been discharged, immediately after the baseline questionnaires are completed. Some of the messages are time sensitive regarding their recovery (eg, the recommended timeframe to see their primary care provider after discharge), while others are general healthy living texts. Participants randomized to the intervention group will be registered through our secured, password-protected text messaging administrative website. We will input what time of day to send the message based on the participant's preference and indicate whether they should be in the smoking ("current smoker" or "quit within the past 6 months") or nonsmoking stream. These streams have 2 different text messages where current smokers are provided with cessation information while nonsmokers are encouraged to remain smoke-free and to avoid second-hand smoke. The text message delivery will be automated, and each text message will cost $0.0075 to send.

We will be able to confirm if the text messages are delivered but not whether the text messages were opened and read. Some of the text messages contain URL links and phone numbers for resources that are accessible province-wide. The URL links are converted to a bit.ly link to make them shorter and to allow us to monitor how many times the links were accessed. After the initial sign-up, study staff involvement will only be required if the participant is readmitted to the hospital. Participants who are readmitted will have their text messages paused until discharge for all readmissions. Those participants readmitted for ACS will be restarted from the day 1 text message when discharged. Participants are instructed about the process to inform us of any readmittances at the time of consent, when we inform them of their group assignment, and in 3 text messages throughout the text messaging program. The text message is a 1-way communication; if a participant responds to the text, they will receive an automated message saying that incoming text messages are not monitored regularly. Participants receive a 1-page information sheet with instructions about the text messaging program. Participants will be able to request to stop

receiving the text messages by speaking to the randomization assistant over the phone.

An advisory committee (consisting of cardiologists, a general practitioner, a community pharmacist, a cardiac nurse specialist, patient-users, a programmer, a benefits evaluation specialist from a federally funded, nonprofit digital health organization, and academic researchers) developed the messages based on 6 guiding principles. Messages had to be (1) based on clinical evidence, (2) consistent with the hospital's current discharge instructions, (3) general enough to apply to a range of patients with the target condition, (4) within a 160-character limit to be compatible with older mobile phones, (5) at a grade 8 reading level, and (6) cocreated with patients to be acceptable. The advisory committee identified important themes to include such as the timing of the standard appointments (all ACS patients discharged from the recruitment hospital are recommended to visit their general practitioner within 2 weeks and cardiologist within 6 weeks), psychosocial needs (including depression, stress, anger, and social support), diet, physical activity, medication information, and recovery guidelines (eg, returning to work, driving, and resuming sexual activity). The intervention incorporates social marketing principles such as formative research about the target audience's perspective and emphasis on appropriate communication channels and messages [33]. Instead of conforming to a single one of the many branded theories of behavior change, the intervention reflects a set of cross-cutting theoretical domains; the themes in the messages relate to concerns about knowledge, skills, roles and identity, beliefs about capabilities (eg, self-efficacy), beliefs about consequences, motivation, attention and decision processes (eg, cues to action such as reminders), environmental context and resources, social influences, emotion, and action plans [34].

The advisory committee drafted and revised messages based on the guiding principles, identified themes, current discharge materials, and interviews conducted with 4 discharged CVD patients (1 man and 3 women; ages 36-71 years). Revisions addressed the wording, timing, and order of the messages as well as reviewing and including any absent topics that were believed to be important based on the advisory committee's experiences. After the advisory committee approved the messages, 2 focus groups (totaling 7 participants with coronary artery disease; 5 women and 2 men) were held with participants of a cardiac rehabilitation program to assess the appropriateness and acceptability of the messages. After further minor revisions to address the findings from the focus groups, the patient members of the clinical advisory committee pilot-tested the text messages by receiving them for 60 days.

**Table 1.** Examples of the text messages developed. All messages start with "T2P:" to indicate the source .

| Topic | Example text message |
| --- | --- |
| Appointment reminders | T2P: Make an appointment to see your family doctor within 2 weeks of leaving the hospital. If you need a doctor, try the tool at: http://bit.ly/findaMD. (Day 2) |
| Smoking cessation | T2P: Not smoking is one of the most important things you can do for your health. For quitting resources, check out: http://bit.ly/quitnow.bc. (Day 8) |
| Recovery guidelines | T2P: Resuming sex: a general guide is that if you can go up a flight of stairs without symptoms, it is probably safe to restart sexual activities. (Day 14) |
| Psychosocial | T2P: It is common to feel sad or depressed after a heart attack or being in the hospital. If you feel this way for 2+ weeks, contact your doctor. (Day 16) |
| Physical activity | T2P: Have you done something physically active today? If you have questions, call the Physical Activity Line at 1-877-725-1149 or talk to your doctor. (Day 21) |
| Medication reminders | T2P: Bring a list of your medications to your appointment when you see your doctor. You can get copies from your pharmacist. (Day 9) |

### Usual Care

The usual care group will not receive text messages. During hospitalization, these participants will typically receive an education session from a nurse prior to discharge as well as being provided with printed educational materials. The participant is informed that they should see their general practitioner within 2 weeks, their cardiologist within 6 weeks, and are recommended to join a cardiac rehabilitation program. The follow-up appointment with the cardiologist and the referral to cardiac rehabilitation may be scheduled while the participant is in the hospital, but they generally have to schedule the appointment with their general practitioner themselves. If they wish to join any additional programs, they must seek these out or learn about them from their health care professionals.

### Study Outcomes

The primary outcome is the change in self-management between the 2 groups as measured by the heiQ. The heiQ comprises 40 questions and measures 8 domains that are indicators of effective self-management programs: positive and active engagement in life (5 questions), health-directed behavior (4 questions), skill and technique acquisition (4 questions), constructive attitudes and approaches (5 questions), self-monitoring and insight (6 questions), health service navigation (5 questions), social integration and support (5 questions), and emotional well-being (6 questions). Items are scored on a Likert scale from 1 to 4. The heiQ was developed using item response theory and structural equation modeling and the subscales have acceptable to high internal consistency (Cronbach alphas ranging from .70-.86, depending on the domain) [30]. The heiQ has been used in a broad range of patient education programs including ehealth settings and with CVD patients [35]. The heiQ will be measured at both the baseline and follow-up sessions.

Secondary outcomes are health-related quality of life, cardiac self-efficacy, medication adherence, health care resource use, hospital readmissions, and mortality. Health-related quality of life will be measured by the EQ-5D-5L, a measure of health status developed by the EuroQol Group that comprises 5 dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression; 1 item per dimension) with each item having 5 levels of response [36]. The Canadian EQ-5D-5L

scoring algorithm will be used to value the health state descriptions reported by study participants [37]. Cardiac self-efficacy will be measured through a modified Sullivan Cardiac Self-Efficacy scale. The original scale has 13 items and is composed of 2 factors, control symptoms and maintain function. Responses are on a 5-point Likert scale where a higher number indicates more confidence. It has high internal consistency (Cronbach alphas of .90 and .87 for the 2 scales, respectively) and good convergent and discriminant validity when compared with other distress and disability scales [38]. The modified version combines 2 questions about symptoms and adds additional questions about diet and emotional distress. Medication adherence will be measured with the 8-item medication adherence scale developed by Morisky et al [39,40,41]. This medication adherence scale has good internal consistency (Cronbach alpha = .83) and reliability when assessed in a hypertensive population [39]. It has good sensitivity (93%) and moderate specificity (53%) [39]. Health care resource use over the 60-day follow-up period (ie, visits to health care practitioners, visits to a hospital, use of phone health services, cardiac rehabilitation program participation, out-of-pocket expenses, and medication use) will be self-reported by all study participants in a structured format using a questionnaire developed by the research team [42]. Self-report resource use questionnaires provide an efficient method of collecting information in the absence of routine data sources [42,43]. Although reliance on self-reported health care resource use may be regarded as a limitation, the 60-day follow-up period in this study is significantly shorter than timeframes that have been used extensively in economic evaluations performed alongside clinical trials. Hospital readmissions will be assessed through self-report and medical records. Mortality will be assessed through medical records. The EQ-5D-5L and cardiac self-efficacy scale will be measured both at baseline and follow-up while medication adherence and health care resource use will be measured only at follow-up.

The study's third objective is to assess the acceptability of the text messaging intervention program and to describe the feasibility of the study protocol. Acceptance of the text messaging intervention will be assessed by measuring participant satisfaction with the program using 2 5-point Likert items as well as through semistructured interviews with intervention

group participants about their experiences with the text messages. During the semistructured interviews, we will explore aspects of the text messaging program that were felt to be beneficial and aspects that were considered less beneficial and could be improved. To assess feasibility, we will track recruitment rates, follow-up rates, and questionnaire completion rates. We will also evaluate the randomization process, the text message delivery system, and the data collection process by asking research staff to keep a log of barriers and challenges. Study staff will be asked to document in writing their perceptions of the acceptability and feasibility of the program along with any other feedback they wish to provide.

## Statistical Analyses

As this is a pilot study, we are not statistically powered to detect the magnitude of differences we will be looking for in the full trial. Nevertheless, we will undertake similar analyses to those we will use in the full trial and regard them as exploratory in nature. First, descriptive statistics will be used to characterize the sample. All variables will be analyzed for their distribution, and relevant transformations will be applied if distributions are nonnormal. For the primary outcome, change from baseline heiQ scores will be analyzed using multiple linear regression, using the intent to treat principle. The dependent variable will be the change from baseline heiQ scores while the independent variables will be group assignment, age, sex, and any clinically relevant baseline factors identified. Change in health-related quality of life and self-efficacy questionnaire scores and differences in medication adherence scores will be modeled in the same method as the primary outcome. Predictors of hospital readmissions and mortality will be analyzed with logistic regression while a survival analysis will be used to evaluate the time until event between the 2 groups using a Cox proportional hazards regression. Group assignment, age, and sex will be a priori covariates. Clinically relevant differences in baseline factors will be included as covariates in the models. Missing values will be addressed as per the guidelines provided with the questionnaires. SPSS (IBM Corp) will be used for statistical analysis. Statistical significance will be set at $P<.05$.

An economic evaluation will also be performed alongside the pilot trial, utilizing EQ-5D-5L and health care resource use data collected during the 60-day follow-up period. A cost-consequence analysis framework will be used as the base case economic evaluation [44,45] where resource use (and associated costs) and outcomes (eg, quality-adjusted life years [QALYs] generated from EQ-5D-5L responses) within the 2 study groups are listed, separately, in a disaggregated format. This type of evaluation makes no attempt to combine costs and effects into a single outcome measure (such as a cost-per-QALY ratio) and has particular value in aiding transparency. Canadian guidelines for the conduct and reporting of economic evaluations will be followed; publication of updated Canadian guidelines is expected in early 2017 [46].

## Assessments

### Baseline Assessment

When possible, the baseline assessment will be done as a face-to-face session prior to hospital discharge. In situations

where the baseline assessment cannot be completed prior to discharge, it will be completed by phone or through an online survey within 7 days of discharge. The assessment will consist of the heiQ, EQ-5D-5L, and Cardiac Self-Efficacy questionnaires. Participants will also be asked demographic questions (age, sex, marital status, geographic location, employment status, education, and household income) and questions about their mobile phone (frequency of use, texting frequency, need for help or support, confidence in using, type of mobile phone, and ownership). Medical history (reason for admission, comorbidities, previous cardiac events, and smoking status) will also be obtained through a combination of self-report and medical record review. Trained assessors will be blinded as randomization will not occur until after the baseline assessment.

### Follow-up Assessment

At 60 days following randomization, all participants will be contacted to complete a follow-up assessment. The assessment will consist of the readministration of the heiQ, EQ-5D-5L, and modified Cardiac Self-Efficacy Scale. Additionally, the Morisky Medication Adherence Scale (MMAS), health care resource use and smoking status questionnaire, and the readmissions and mortality assessment will be completed. All readmission events per participant will be recorded. The health care resource use questionnaire will be administered over the phone, while the other questionnaires (heiQ, EQ-5D-5L, Cardiac Self-Efficacy Scale, and MMAS) will be sent by surface mail, along with a $20 gift card. If the participant is unable or unwilling to complete the questionnaires by mail or phone or is unresponsive to our attempts at mail or phone contact, they will have the option to complete the questionnaires via an online survey. An approved online version of the EQ-5D-5L will be used (approval from the EuroQol Group), while the other outcome measures will be adapted to an online survey format and tested for user friendliness. The method for assessment will be documented in the study database. If the participant cannot be contacted, we will attempt to recontact every 3 to 5 days by using phone, mail, and email contact information. Participants will be considered lost to follow-up if the follow-up session is not completed within 6 weeks after the 60 days following randomization.

Participants who are randomized to the Txt2Prevent group will also be invited to participate in a semistructured phone interview after completion of the 60-day follow-up. Interviews are expected to be approximately 30 minutes and will be done at a different time than the follow-up assessments in order to avoid a lengthy phone call. Interview participants will be selected to cover a range of characteristics to represent the sample of study participants (eg, male/female, rural/urban, and different age groups). Participants will be asked to share their experiences of living with and managing their condition as well as their views on the text messaging program (eg, "Can you tell me about how you have managed your heart condition over the past 2 months?" and "Has the text messaging program impacted your life over the past 2 months? If so, how?"). Questions to evaluate the text messages will ask about the clarity, tone, and frequency of the messages; the duration of the program; what topics were the least or most helpful; and what proportion of messages they read. Interviews will be recorded and transcribed verbatim and

analyzed through a general inductive approach [47]. Through an iterative process, categories and themes will be created by detailed reading and line-by-line coding. Interviews will continue until theme saturation occurs [48]. NVivo (QSR International) software will be used for qualitative analysis. The findings from the interviews will be valuable in providing the context for the quantitative findings and for assessing the acceptability of the intervention.

## Results

Ethics and institutional approval have been obtained from the Providence Health Care Research Ethics Board and Simon Fraser University's Office of Research Ethics. Study staff have been hired and trained. Recruitment started in June 2015 and was completed by December 2016, with data collection being completed by January 2017.

## Discussion

### Summary

This study aims to evaluate whether a text messaging program can help support patients with ACS after their discharge from hospital. A randomized controlled pilot trial with semistructured interviews will be used to determine preliminary efficacy, feasibility, and acceptability. Although previous studies have looked at text messaging in CVD patients, no known studies have evaluated the use of text messages among patients with ACS during the hospital-to-community transition period, which is a high-risk time for readmission [6].

### Study Considerations

The Txt2Prevent study is an exploratory pilot study to assess preliminary efficacy, acceptability, and feasibility of a text messaging program to improve self-care and management in ACS patients after discharge, which leads to several study considerations. First, due to the nature of the intervention, the participants are not blinded. Additionally, it is difficult to create a suitable attention control, so the intervention group is being compared to usual care. Second, we are unable to objectively determine adherence or even if participants read the messages; however, we will ask participants about their experiences in semistructured interviews. Third, several of the outcomes are self-reported, which may introduce bias; however, the study will use common and validated measures.

### Conclusion

The Txt2Prevent study is a novel project to determine if text messaging can support ACS patients in the critical period immediately after discharge. We intend to use the results of the study to inform a larger clinical trial. If effective, the Txt2Prevent program has the potential to be translated into practice and be scaled up and implemented in clinical settings. Implementing the program on a larger scale is likely to be feasible because the program requires limited human resources and text messages are low cost. The study will contribute to our understanding of mHealth in health services research and will inform future studies on the use of text messaging to support ACS patients as they transition from hospital to home.

### Conflicts of Interest

None declared.

### Multimedia Appendix 1

CIHR Peer Review.

[PDF File (Adobe PDF File), 345KB - resprot_v6i5e91_app1.pdf ]

### Multimedia Appendix 2

CONSORT EHEALTH Check List.

[PDF File (Adobe PDF File), 576KB - resprot_v6i5e91_app2.pdf ]

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## Abbreviations

**ACS:** acute coronary syndrome
**AMI:** acute myocardial infarction
**CIHR:** Canadian Institutes of Health Research
**CONSORT:** Consolidated Standards of Reporting Trials
**CVD:** cardiovascular disease
**heiQ:** Health Education Impact Questionnaire
**MMAS:** Morisky Medication Adherence Scale
**MSFHR:** Michael Smith Foundation for Health Research
**QALY:** quality-adjusted life year

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<u>Protocol</u>

# PREventive Care Infrastructure based On Ubiquitous Sensing (PRECIOUS): A Study Protocol

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## *Abstract*

**Background:**   mHealth has experienced a huge growth during the last decade. It has been presented as a new and promising pathway to increase self-management of health and chronic conditions in several populations. One of the most prolific areas of mHealth has been healthy lifestyles promotion. However, few mobile apps have succeeded in engaging people and ensuring sustained use.

**Objective:**   This paper describes the pilot test protocol of the PReventive Care Infrastructure based on Ubiquitous Sensing (PRECIOUS) project, aimed at validating the PRECIOUS system with end users. This system includes, within a motivational framework, the Bodyguard2 sensor (accelerometer with heart rate monitoring) and the PRECIOUS app.

**Methods:**   This is a pilot experimental study targeting morbidly obese prediabetic patients who will be randomized to three conditions: (1) Group 1 - Control group (Treatment as usual with the endocrinologist and the nurse + Bodyguard2), (2) Group 2 - PRECIOUS system (Bodyguard2 + PRECIOUS app), and (3) Group 3 - PRECIOUS system (Bodyguard2 + PRECIOUS app + Motivational Interviewing). The duration of the study will be 3 months with scheduled follow-up appointments within the scope of the project at Weeks 3, 5, 8, and 12. During the study, several measures related to healthy lifestyles, weight management, and health-related quality of life will be collected to explore the effectiveness of PRECIOUS to foster behavior change, as well as user acceptance, usability, and satisfaction with the solution.

**Results:**  Because of the encouraging results shown in similar scientific work analyzing health apps acceptance in clinical settings, we expect patients to widely accept and express satisfaction with PRECIOUS. We also expect to find acceptable usability of the preventive health solution. The recruitment of the pilot study has concluded with the inclusion of 31 morbidly obese prediabetic patients. Results are expected to be available in mid-2017.

**Conclusions:**  Adopting and maintaining healthy habits may be challenging in people with chronic conditions who usually need regular support to ensure mid/long-term adherence to recommendations and behavior change. Thus, mHealth could become a powerful and efficient tool since it allows continuous communication with users and immediate feedback. The PRECIOUS system is an innovative preventive health care solution aimed at enhancing inner motivation from users to change their lifestyles and adopt healthier habits. PRECIOUS includes ubiquitous sensors and a scientifically grounded app to address three main components of health: physical activity, diet, and stress levels.

**Trial Registration:**  Clinicaltrials.gov NCT02818790; https://clinicaltrials.gov/ct2/show/NCT02818790 (Archived by WebCite at http://www.webcitation.org/6qfzdfMoU)

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## Introduction

Information and communication technologies (ICT) applied to health and health care systems have been shown to increase their efficiency, improve quality of life, and unlock innovation in health markets. eHealth has emerged as a rapidly increasing area of promoting health, as well as bringing together end users and health care professionals to foster information exchange and effective communication. It is therefore the key technology for 21st century health care, as analyzed and projected within the European Commission eHealth Action Plan 2012-2020 [1]. The mHealth subdomain promises to bridge the gap between health settings and real-world scenarios [2]. Currently, mobile phones are widely used across developed countries. Their portability, ease of use, and ubiquity make them excellent tools to enhance the self-management of health and specifically chronic conditions.

The World Health Organization has estimated that in 2020 chronic or noncommunicable conditions accounted for 87% of deaths in high-income countries. Only 7% of deaths were attributed to communicable conditions and nutritional deficiencies and 6% to injuries [3]. The proportion of deaths worldwide caused by noncommunicable diseases is projected to rise from 59% in 2002 to 69% in 2030 [4]. Chronic diseases have traditionally included cardiovascular disease, diabetes, and asthma or chronic obstructive pulmonary disease. As treatments and survival rates have improved, chronic conditions now also include many varieties of cancer, human immunodeficiency virus and acquired immune deficiency syndrome, mental disorders (eg, depression, schizophrenia, and dementia), and disabilities such as visual impairment and joint disease. Many of these conditions are linked to an ageing society but also to lifestyle choices such as smoking, sexual behaviors, diet, and exercise, as well as to genetic predispositions. What these diseases have in common is their need for a long-term and complex response, coordinated by different health professionals with access to the necessary drugs and equipment, and extending into social care.

For these reasons, mHealth is a key element to improving the management of chronic conditions because it includes a huge range of possibilities such as psycho-education, ecological momentary assessments, constant monitoring, reliable biofeedback, immediate tailored feedback, and brief interventions [5-8]. However, ensuring adherence and sustained motivation among users is still a complicated and unresolved problem as users have been frequently shown to lose interest in mHealth solutions resulting in decreased compliance of recommendations in the long run [9].

Health games or specialized motivating apps for mobile phones offer a possible solution to address the motivational factors involved in this problem. Thus, these apps try to bring empowerment, joy, engagement, and to offer a social connection to an otherwise rather dull self-management task [10-12]. As a result, the market for health-related games and apps has exploded in recent years, yielding over 100,000 apps in this area [1,2]. However, the information quality of the content of the apps is merely adequate [9]. In addition to functionality and esthetics, app developers should invest in providing content and quality behavioral tracking features, combined with a solid framework including motivational aspects. It is then recommended that they employ psychological techniques known to be effective in changing relevant behavior patterns and to improve the user experience and foster behavior change. Despite growing development and utilization of apps in research, additional experimental evaluation is required to understand whether the presence of particular content, behavior change techniques, motivational feedback, and so on, is associated with behavior change [9].

The PREventive Care Infrastructure based On Ubiquitous Sensing (PRECIOUS) project is a 7th Framework Programme for Research and Technological Development (FP7) project funded by the European Union and part of the eHealth and Ageing Initiative. Given increasing global obesity rates and physical inactivity, the project aims at preventing diseases such as type 2 diabetes and cardiovascular diseases by promoting healthier lifestyles. The project partners have designed and created a fully personalized system able to adapt to the user's goals and preferences, combined with sensors (Bodyguard2, which is an accelerometer with 24h heart rate monitoring). Food intake, physical activity, stress levels, and sleep patterns are assessed in order to create a complete model of the user's status called Virtual Individual Model, and subsequently certain measures and possibilities are suggested. A mobile phone based client app then finally delivers these interventions by running them within a privacy-ensuring sandbox, hence also facilitating developer's efforts to intelligently integrate health data. A core concept in the PRECIOUS system is to operate under a common motivational umbrella guided by principles of motivational interviewing (MI) [13] in order to ensure long-term behavior change.

## Methods

### Objectives

The main goal of this pilot study is to assess users' overall satisfaction, usability, and acceptability of the PRECIOUS system and to explore if MI is a feasible solution to foster adherence to PRECIOUS in a sample of end users. Moreover, we explore whether it triggers behavior change and builds up motivation to maintain sustained change towards healthy lifestyles.

### Hypothesis

Since this is a pilot study aimed at testing the feasibility of using the technology to achieve behavior change, no specific hypotheses have been put forward. Based on previous research

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on the efficacy of lifestyle apps and MI studies to foster behavior change [9,13-15], it can be expected that intervention groups (Groups 2 & 3) will show a tendency of change towards a healthier lifestyle compared to control group. These changes can be measured with the weight management questionnaires, the substance use/abuse questionnaires, and with several items related to the assessment of one of the main variables of the study (effectiveness).

No preliminary hypotheses have been established about possible differences between intervention Groups 2 and 3. Ideally, both groups will follow PRECIOUS recommendations with no significant differences between them. Thus, the potential benefits of the PRECIOUS app are expected to be achieved without the need for additional support (MI counseling). The PRECIOUS app's continuous monitoring and feedback, as well as psycho-educational content and messages, are expected to effectively foster healthier lifestyles.

## Sample, Recruitment, and Study Design

A convenience sample (non-probabilistic) of patients has been recruited from a specialist outpatient consultation (anonymized for peer review). From an initial list of 55 potential participants, 24 (43.6%) were not included in the study because they were not interested or able to follow the full 3-month protocol. A total of 31 patients (71%, 22 women and 29%, 9 men) meeting the following inclusion criteria has been recruited: (1) patients under the care of medical specialists who adhere to national guidelines for morbid obesity and prediabetic condition following the American Diabetes Association criteria of fasting plasma glucose level from 5.6mmol/L (100 mg/dL) to 6.9mmol/L (125 mg/dL), (2) 18 years old, (3) body mass index ≥30, (4) understand and complete questionnaires in Spanish language, (5) use multimedia platforms such as personal digital assistants, tablets, laptops, mobile phones, or personal computers on a regular basis, and (6) have Android devices with an Internet connection. The rationale for choosing participants with Android devices is mainly technical because at this stage of the project, only an Android version of the app is available. Patients with the following criteria have been excluded from the study: (1) any mental (eg, cognitive impairment, severe psychopathology not stabilized) or physical condition that could interfere with the successful application of the research protocol, and (2) technological illiteracy or any other condition precluding the use of a mobile phone. Table 1 shows the demographic characteristics of the sample. Potential participants have been invited to take part in the study via telephone contact and have been randomly assigned into three groups:

- Group 1: Control group (treatment as usual + Bodyguard2)
- Group 2: PRECIOUS system (PRECIOUS app + Bodyguard2)
- Group 3: PRECIOUS system (PRECIOUS app + Bodyguard2 + MI)

**Table 1.** Demographic and health characteristics of the sample.

| Characteristic | Group, mean (SD) | | | |
|---|---|---|---|---|
| | 1 (n=11) | 2 (n=10) | 3 (n=10) | Total (n=31) |
| Age, years | 37.45 (11.7) | 41.9 (6.2) | 38.9 (8.2) | 39.35 (9) |
| Weight, kg | 129.18 (17.5) | 112.5 (11.7) | 116.86 (21.3) | 119.83 (18.2) |
| Height, cm | 161.45 (9.3) | 165.7 (5.5) | 166.9 (9) | 164.58 (8.3) |
| Body mass index, kg/m$^2$ | 49.56 (5.6) | 40.9 (2.8) | 41.68 (4.4) | 44.23 (5.9) |
| Maximum attained weight, kg | 131.36 (19) | 117.7 (11.5) | 125.2 (20) | 124.97 (17.7) |
| Number of diets last year | 3.18 (4.2) | 2 (3.2) | 2.8 (3.1) | 2.68 (3.5) |

## Measures

Two types of measures will be registered: (1) A set of primary measures to evaluate users' opinions and experiences with the PRECIOUS system, and (2) a set of secondary measures to explore the differences between groups across the sessions.

### *Primary Outcome Measures*

To explore users' acceptance of PRECIOUS system, the following aspects will be assessed:

Usability: 11-item questionnaire (10 items with 5-point Likert scale and 1 item with 10-point Likert scale) to assess users' interaction with app and system interface.

Satisfaction: 14-item questionnaire (10-point Likert scale) to assess satisfaction with the different modules of the app (physical activity, diet diary), reports, feedback messages, and other interface elements.

Acceptance: 4-item questionnaire (10-point Likert scale) to measure the disposition to use and recommend the system to other patients.

Effectiveness: 15-item questionnaire (10-point Likert scale) to assess engagement, change, and adherence to healthy habits.

In Group 1 (control, treatment as usual), all these aspects will be assessed but with an adaptation of the same questionnaires based on their specific follow-up and the use of the Bodyguard2.

These measures were developed ad hoc for this study, but the usability items are based on the System Usability Scale [16] and acceptance and satisfaction items are based on the Questionnaire for User Interaction Satisfaction 7.0 [17].

### *Secondary Outcome Measures*

Additional outcome measures will be included to explore the differences between groups across the sessions. Demographics and clinical data such as date of birth, gender, actual and

maximum attained weight, height, number of diets in previous year, and questions related to self-esteem will be registered.

Health-related quality of life will be assessed with the Spanish version of the Short Form (SF)-12v2 Health Survey [18,19], a shorter version of the SF-36v2 Health Survey that consisted of 12 questions (3 and 5-point Likert scale) to measure functional health and well-being from the patient's point of view. The SF-12v2 covers the same 8 health domains as the SF-36v2: physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health.

Weight management will be assessed with Spanish versions of S-Weight and P-Weight questionnaires [20,21]. P-Weight is a 34-item questionnaire (5-point Likert scale) developed to assess the process of change in weight management. S-Weight consists of 5 mutually exclusive items that allow allocation of participants to one of the five stages of change of the Transtheoretical Model [22] for weight management: precontemplation (not ready), contemplation (getting ready), preparation (ready), action, and maintenance.

The symptoms of depression, anxiety, and stress will be measured with the Spanish version of the Depression, Anxiety, and Stress Scale (DASS) [23]. DASS is a 21-item questionnaire (4-point Likert scale) developed to assess the severity of the core symptoms of depression, anxiety, and stress, and it is not designed as a diagnostic tool. For each scale, it offers a severity rating: normal, mild, moderate, severe, and extremely severe.

Alcohol consumption will be measured with the Spanish version of Alcohol Use Disorders Identification [24,25], a 10-item questionnaire (4-point Likert scale) developed by the World Health Organization as a simple method of screening for excessive drinking and to assist in brief assessment.

Tobacco consumption will be measured with the Spanish version of Fagerstrom Test for Nicotine Dependence [26,27]. It contains 6 items (some with a yes/no response and some with a 4-point Likert scale) that evaluate the quantity of cigarette consumption, the compulsion to use, and dependence.

Sleep quality will be assessed with the Spanish version of the Pittsburgh Sleep Quality Index [28,29], which measures sleep quality and disturbances over a 1-month time interval with 19 items. It assesses the following components: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction.

Physical activity will be assessed with the PRECIOUS app in the intervention groups (Groups 2 and 3). Physical activity will be measured with accelerometer data from the patient's mobile phone. The accelerometer counts the steps walked and provides the patient a graphic result with total accumulated steps and time spent. If the patient cannot wear the mobile phone, the PRECIOUS app allows them to manually introduce the activity performed and it calculates the equivalence in steps.

Nutritional habits will be assessed with the PRECIOUS app in the intervention groups (Groups 2 and 3) with a diary that allows the patient to register the different meals each day.

The PRECIOUS app architecture and the interface of the physical activity and nutritional habits modules includes the four processes of MI (engaging, focusing, evoking, and planning) and MI micro-abilities (open questions, affirmations, reflections, summaries, and offering information to the users with their permission). Figure 1 shows screenshots of the PRECIOUS app. For the control group (Group 1), physical activity and nutritional habits will be assessed with self-reports using a weekly diary on paper. A total of 6 weeks will be registered: 3 weeks at the start of the study and 3 weeks at the end of the study.

To measure cardiovascular activity, the Bodyguard2 (Firstbeat) device will be used. This device works as a Holter measurement and allows recording of 24-hour periods. The Bodyguard2 is a lightweight and unobtrusive device, attached to the chest with two adhesive electrodes, and is reliable for recording heart rate variability (R-R interval) and movement data. A total of 6 days/nights will be registered in the groups: 3 days/nights at the start of the study after the first session (week 1) and 3 days/nights before the last session (week 12). Data collected with Bodyguard2 device will be analyzed with an adaptation of the Lifestyle Assessment Analysis Server Software (Firstbeat) performed by the PRECIOUS consortium partners (Aalto). This software provides a detailed report of the measured period: stress levels, recovery reactions, physical activity, exercise, sleep quality, and expended kilocalories. At the follow-up assessments (Sessions 3 and 5), patients will receive a report accompanied by oral explanations of the results provided by the researcher in charge of the follow-up.

**Figure 1.** Screenshots of PRECIOUS app: a) home screen, b) physical activity app, c) dietary app.
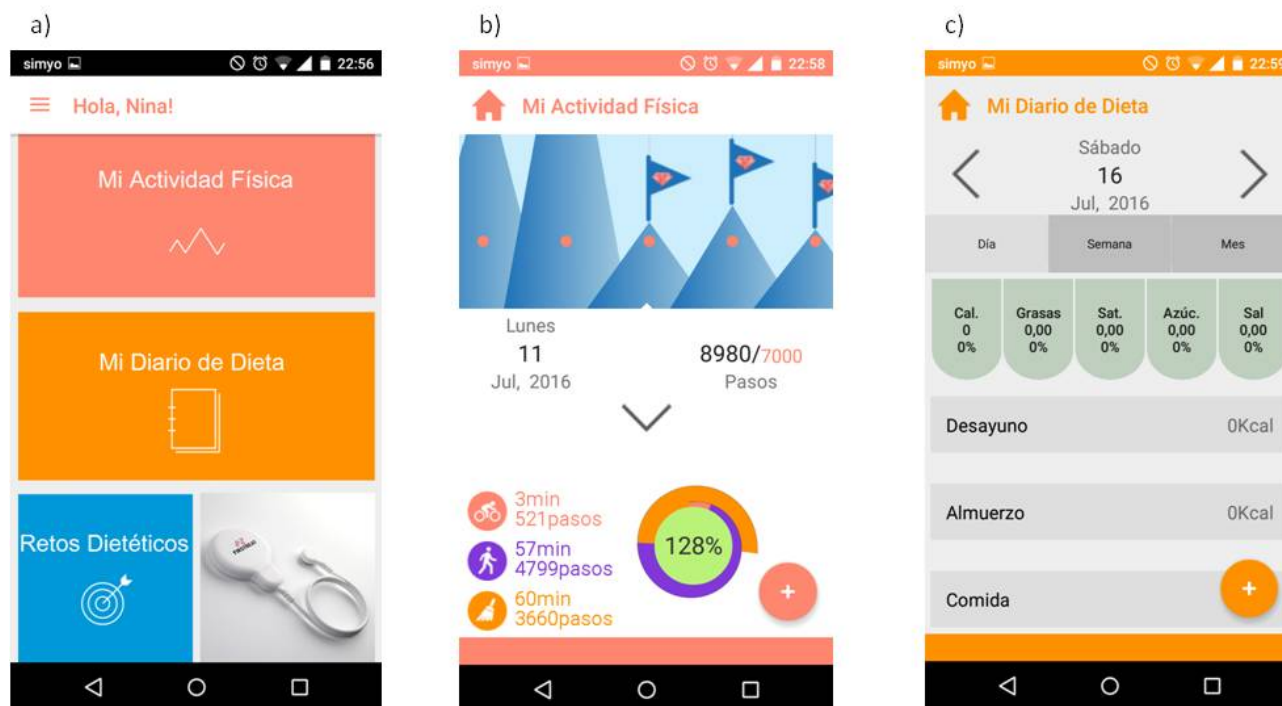


## Procedure

The study will have a duration of 3 months with the following scheduled follow-up appointments: Session 1 (Week 1) as a baseline, Session 2 (Week 3), Session 3 (Week 5), Session 4 (Week 8), and Session 5 (Week 12). Figure 2 shows a detailed timeline of the procedure and measures assessed in each session. In Session 1, patients will receive a detailed explanation of the study, will be provided with written and oral information, and will give informed consent. They will then answer all of secondary measures in a semistructured interview and then receive the Bodyguard2 device. Patients from the intervention groups (Groups 2 and 3) will be invited to download the PRECIOUS app on their mobile phone and create a user account. Patients from the control group (Group 1) will receive a 3-week paper diary to register physical activity and nutritional habits. They will also follow their treatment as usual for morbid obesity. Specifically, treatment as usual consists of regular follow-ups with the endocrinologist and standard routine tests (blood samples, glucose) and anthropometric measurements carried out by a nurse. Session 1 lasts 1 hour approximately. Sessions 2 and 4 will be telephone follow-ups, lasting a maximum of 10 minutes. Only doubts and questions regarding PRECIOUS will be addressed (specific measures not collected) in telephone follow-ups. In all three groups, the use of the Bodyguard2 device during the 3 days/nights after Session 1 will be verified. In these telephone follow-ups, the researchers and users agree on the day of the next session in the hospital. Session 3 will be focused on discussing the results obtained with Bodyguard2 (only in Groups 2 and 3), to understand users' preliminary opinions about the PRECIOUS app. In Group 1, the weekly self-reports of physical activity and nutritional habits will be discussed. Session 3 lasts 1 hour approximately. Session 5 will be the last of the study. Primary and secondary measures will be answered, and the results obtained with Bodyguard2 will be discussed. This last session lasts 1 hour and 30 minutes approximately. All the Group 3 follow-ups will be performed following MI principles. In Groups 1 and 2, MI principles will not be applied. MI has the main goal of getting participants to resolve their ambivalence about changing behavior while not evoking resistance. For such purposes, a directive, person-centered counseling style is employed. This approach is intended to elicit behavior change by helping patients explore and resolve ambivalences and understand the discrepancy between participants' current behaviors in terms of lifestyles and desired goals [13]. The researcher in charge of these groups has specific training to lead MI sessions.

**Figure 2.** Flowchart of sessions during the pilot test and the measures assessed in each one.
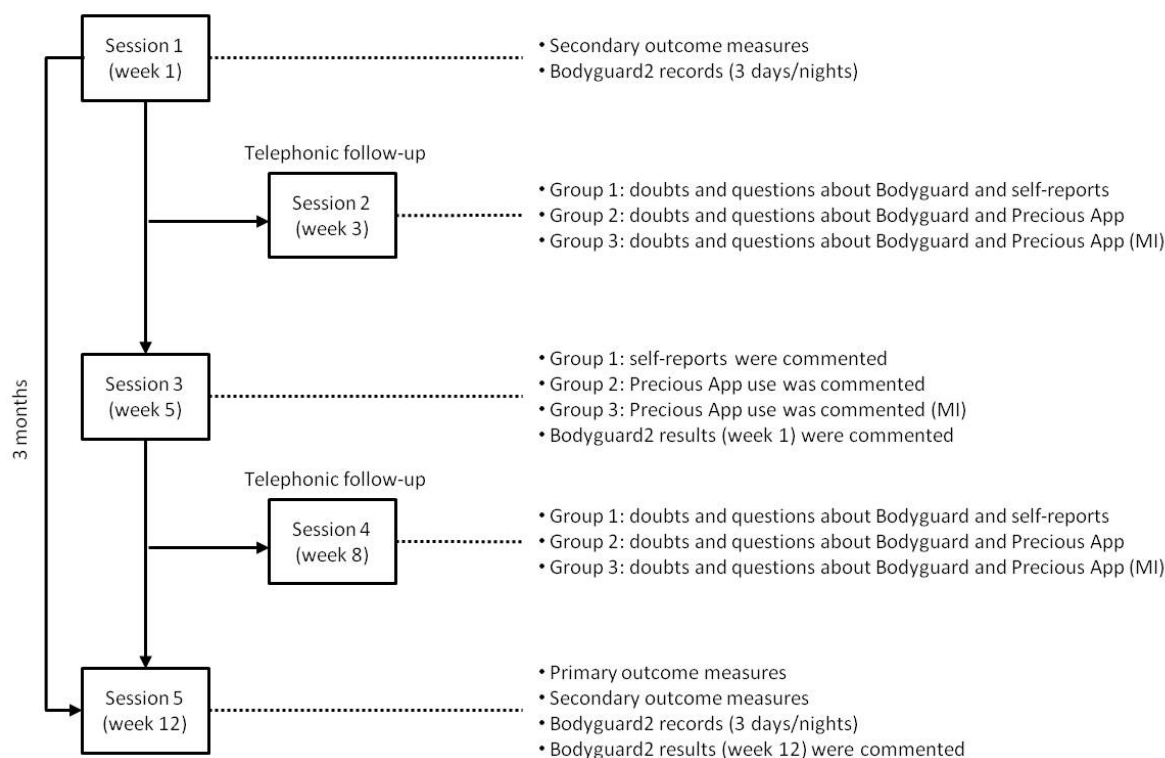


## Statistical Plan

The statistical analysis will consist of intergroup (Groups 2 and 3) descriptive and mean comparison analyses concerning primary outcome measures (usability, user satisfaction, acceptance, and system effectiveness) and overall assessment of the motivational aspects of PRECIOUS. In our pilot test, the method to assess minimal clinically important difference will be employed (distribution-based method, ie, $\pm 1$ mean standard deviation) to study differences between groups related to the main primary outcomes [30].

Secondary analyses will describe and explore changes between groups (inter and intra) in the following secondary outcome measures: (1) health-related quality of life using SF12v2), (2) weight management using S-Weight & P-Weight, (3) severity of the core symptoms of depression, anxiety, and stress using DASS, (4) alcohol consumption using Alcohol Use Disorders Identification test, (5) tobacco use with the Fagerstrom Test for Nicotine Dependence, and (6) sleep quality using the Pittsburgh Quality of Sleep Index. For these purposes, correlational, median comparisons, and nonparametric tests (chi-square tests, Mann-Whitney U) will be performed.

Setting the pilot trial sample size in order to minimize overall size has been based on the Kieser and Wassmer approach. They applied the 80% upper control limit approach to sample size calculation and found that a pilot trial sample size between 20 and 40 would minimize the overall sample size for a main study sample size of 80-250, corresponding to standardized effect sizes of 0.4 and 0.7 (for 90% power based on a standard sample size calculation) [31].

All analyses will be carried out using the Statistical Package for Social Sciences, version 19. A 95% confidence interval will be used for all analyses.

## Ethics

Research procedures in this pilot study complied with European Union and national legislation (ie, the Charter of Fundamental Rights of the EU, Directive 95/46/EC of the European Parliament, and of the Council of October 24, 1995, on the protection of individuals with regard to processing of personal data and the free movement of such data). PRECIOUS partners respect the latest Helsinki Declaration and follow the ethical guidelines provided by their national scientific societies and their local research institutions. This pilot study and all studies included in PRECIOUS have been presented to the hospital research ethics committee for approval and have been accepted (reference PR(AG)212/2014). All participants are adult volunteers, and informed consent has been obtained in all cases. None of the methodologies and technologies used are known to inflict any physiological or psychological damage on participants. The investigations included in the project are not medical examinations. This study has been presented to the University Hospital Vall d'Hebron research ethics committee for approval, and all issues resolved satisfactorily.

The first stages of participant recruitment (already performed) were carried out in the outpatient clinic of the Endocrinology Department of Vall d'Hebron Research Institute and Psychiatry department (ie, the bariatric surgery consultation unit). All individuals interested in taking part were contacted via telephone and introduced to the general nature (eg, purpose, methods) of the study. An informed consent was obtained in a face-to-face interview before starting the study. It included a written description of the study using language and terminology that is

reasonably understandable to the participants (eg, all measurement techniques and procedures). The participants were also told that they may withdraw from the study at any time without consequences of any kind. In addition, the relevant details of data protection and storage were described to them.

Personal data are anonymized and made inaccessible to third parties. All questionnaires (with no participant name) completed by the participants are stored in a dedicated locked room. The digital identification data file containing participant names and contact information is stored in a safe. When analyzing data, researchers used digital data files with no identification data (a participant number will be used for data-linkage purposes). Only the researchers involved in the project have access to these data files. At the end of the 3-year project (or earlier), all questionnaires and identification data files will be destroyed. That is, the remaining digital data files will be such that the participants (data subjects) can no longer be identified.

## Results

This pilot study has concluded with the inclusion of 31 morbidly obese patients. The anticipated completion of data analysis and dissemination of final results is June 2017.

## Discussion

### Principal Considerations

The main goal of this pilot study is to assess users' overall satisfaction, usability, and acceptability of the PRECIOUS system and to explore if MI is a feasible solution to foster adherence to the PRECIOUS system in a sample of end users. Moreover, we explore if PRECIOUS triggers behavior change and builds motivation to maintain sustained change towards healthy lifestyles.

The use of mobile computing and communication technologies in health care and public health is continuously expanding and evolving [32]. A report from the IMS Institute for Healthcare Informatics has shown that more than 165,000 mHealth apps are now available on the market, more than doubling over the past 2 years [1,2]. A high percentage of these apps are focused on healthy lifestyles, providing an attractive offer with different activities and incentives aimed at catching people's attention [8,9,33-35]. Physical activity, healthy diet, and stress management are star products among this huge offering of apps. The World Health Organization discusses the benefits of using ICT in health care settings in terms of better access to information, improved communication between colleagues and patients with health providers, facilitating continuing professional development, and providing learning tools for health care professionals, patients, and the community as a whole. This huge market holds promising benefits, especially for users. A recent report from the European Union assessed the socioeconomic impact of mHealth solutions and found that they offer the potential of a cost saving of €76 billion, with the technology helping 54 million patients avoid the risk of developing a lifestyle disorder [32]. However, 75% of apps are abandoned just 3 months after being downloaded. A possible explanation for such low rates of adherence might be the initial

design of the apps. A vast number of apps already exist for different health conditions, but the majority offer similar functions and fail to include, from the very initial phases of service design, a comprehensive motivational framework and sufficient psychological parameters to ensure engagement and mid- to long-term adherence to the service. PRECIOUS is intended to overcome such limitations and aims to combine a multidisciplinary scientific corpus of knowledge, nurtured from ICT, engineering, psychology, and mental health sciences. Available evidence-based MI interventions showing positive results will also serve as a reference. Thus, the PRECIOUS system integration, verification, and validation are guided by the following primary objectives: (1) to ensure that the PRECIOUS system is free from defects and acceptable for use, and (2) to verify that the PRECIOUS system is able to fulfill the requirements.

mHealth apps with motivational elements provide psychological incentives for users to participate by appealing to their sense of achievement and enjoyment. A reminder alone may not be a compelling enough reason to, for instance, go for a run, keep a healthy diet, or take one's medication over time. Yet, when given rewards for complying, users have been shown to participate at a higher rate. The best approach to ensure sustained motivation is to build a solid motivational framework and also be able to discern the differences of potential users and to treat them differently [36]. PRECIOUS takes into account all these factors and adapts to users by generating a virtual individual model by asking them for their outcome goals from the very beginning and by remembering in a personalized manner progress, achievements, and meaning of actions. In this sense, users will establish their outcome goals from the start and these will be linked to health behaviors (eg, physical activity, healthy diet, stress). PRECIOUS will meet their needs by offering them different apps to guide them to success. Thus, the comprehensive motivational framework of PRECIOUS puts the user in the center of the action and promotes adherence, empowerment, and health self-management by creating a positive journey for users. All of this is expected to promote and contribute to maintenance of long-term motivation for behavior change.

In brief, interventions that merge up-to-date cognitive-behavioral science and MI with interactive technology may be an efficient and innovative way to address some of these issues because they can be disseminated to new settings, populations, and areas that might not otherwise have the capacity for in-person evidence-based care. MI delivered by new technologies (eg, mobile apps) can address these issues because the content is programmable, automated, and personalized, which may be particularly important when disseminating MI in diverse populations and in different languages. This approach is also less expensive than one-on-one treatment, offers easy access, and the anonymity overcomes the stigma sometimes associated with formal treatment [37].

### Limitations

Our study protocol has some drawbacks that should be taken into account. First, representativeness and thus, generalization of preliminary findings are likely to be an issue, specifically, due to the nature of the sample (ie, a nonprobabilistic

convenience sample) and because we will limit the pilot test to users with Android operating systems. It may be possible that users with iOS devices have a different profile and motivations towards healthy lifestyles and behavior change. To understand this limitation, the PRECIOUS project consortium plans to perform future trials with users of iOS. Second, the PRECIOUS app will experience some updates within the scope of the trial. Considering that app schedule updates are not fully customizable, it is possible that patients will not have exactly the same experience since availability of some features could vary. Additionally, assessment sessions and the data collection process are planned to be long because more than 150 items are expected to be collected and commented on. This might reduce the validity and accuracy of the answers. Thus, future studies should focus on the most relevant aspects to reduce bias in the data collection process and reporting. Finally, technological literacy and familiarity with eHealth solutions should also be considered a potential limitation. The literature on this topic lacks empirical research on the social practice of ICT and

possible social/health exclusions if these solutions were implemented on a large scale. Research should enable us to extend our understanding of the barriers to adoption and integration of ICT in the health context and with specific sample populations. However, in this protocol study we devoted the initial assessment session to explain the eHealth solution. This was reinforced by follow-ups (telephone and face-to-face).

## Conclusions

The PRECIOUS project will provide new innovations in preventive health care that include (1) a new automated service that analyzes user health to identify present and future risk factors, (2) a novel motivational system that boosts the required user actions to reduce unhealthy habits and promote healthy ones, and (3) an innovative gamified user interface, including key motivation elements from the gaming industry to trigger and maintain behavioral change. Research on the health-specific effects of this solution on users must be carried out, as well as the economic impact on the health care system that such a preventive system could have.

## Authors' Contributions

PLP and CCT were responsible for the study design and app theoretical framework development. PLP was responsible for coordination with the relevant hospital departments (Endocrinology and Psychiatry Departments) to recruit the pilot sample of participants. AC and GPP provided a list of potential participants and supported sample recruitment. CCT and JMS will be responsible for all tasks involved in the development of the PRECIOUS pilot test (eg, recruitment, assessments, monitoring, follow-up appointments, data entry). CCT and JMS will analyze data and wrote the first draft of the manuscript. CCT, JMS, and PLP have participated in later versions of this manuscript, and all made important contributions to its final version. All authors have read and have approved this final manuscript.

## Conflicts of Interest

None declared.

## Multimedia Appendix 1

Evaluation report fro PRECIOUS project.

[PDF File (Adobe PDF File), 131KB - resprot_v6i5e105_app1.pdf ]

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## Abbreviations

**FP7:** 7th Framework Programme for Research and Technological Development
**ICT:** information and communication technologies
**MI:** motivational Interviewing
**PRECIOUS:** PREventive Care Infrastructure based On Ubiquitous Sensing

Protocol

# Optimizing Protein Intake and Nitrogen Balance (OPINiB) in Adult Critically Ill Patients: A Study Protocol for a Randomized Controlled Trial

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## Abstract

**Background:** Adequate nutrition of critically ill patients plays a key role in the modulation of metabolic response to stress.

**Objective:** This paper presents the development of a protocol for a randomized controlled trial (RCT) aimed at comparing clinical outcomes of patients in the intensive care unit (ICU) administered with standard and protein-fortified diet. Together with the RCT study protocol, the results of the observational analysis conducted to assess the feasibility of the RCT are presented.

**Methods:** An RCT on adult patients admitted to ICU and undergoing mechanical ventilation in the absence of renal or hepatic failure will be conducted. Patients enrolled will be randomized with an allocation rate of 1:1 at standard diet versus protein-fortified diet. The estimated sample size is 19 per arm, for a total of 38 patients to be randomized.

**Results:** Enrollment began in January 2017. In the feasibility study, 14 patients were enrolled. Protein administration increased significantly ($P<.001$) over time but was significantly lower compared to that recommended ($P<.001$). Blood urea nitrogen significantly increased ($P<.03$) over the period of observation. Such increased catabolism resulted in negative cumulative nitrogen balance (NB) in all patients, and some patients presented with a more negative NB compared to the others.

**Conclusions:** Results of the feasibility study clearly confirmed that protein provision in ICU patients is below that recommended and that this results in impaired NB. The emerging of an interindividual variability in NB will be further analyzed in the RCT.

**Trial Registration:** ClinicalTrials.gov NCT02990065; https://clinicaltrials.gov/ct2/show/NCT02990065 (Archived by WebCite at http://www.webcitation.org/6prsqZdRM).

## Introduction

In recent years, several studies have focused on the molecular and biological effects of nutrients in maintaining homeostasis in patients admitted in intensive care unit (ICU), and ad hoc recommendations have been developed for the assessment and provision of nutritional support in adult critically ill patients [1,2]. In such patients, specific metabolic mechanisms are activated to face stresses related to critical conditions (eg, trauma and sepsis). These metabolic responses consist of changes in substrate utilization and substance synthesis rates, as well as catabolism and hypermetabolism, resulting in increased energy

expenditure, hyperglycemia, loss of body mass, and eventually psychological and behavioral problems [3]. Given such framework, monitoring the metabolic response is crucial in the management of ICU patients. However, this represents a major clinical challenge since it is generally assessed indirectly using nonspecific clinical and biochemical markers such as secondary infections, muscle atrophy and weakness, respiratory insufficiency, delayed wound healing, and incidence of secondary complications indicating prolonged catabolism [4]. Adequate nutrition plays a key role in the modulation of metabolic response to stress, contributing to the prevention of oxidative cellular injury and positively modulating immune responses.

All patients admitted in ICU require a full nutritional assessment for determining both energy and protein requirements to prevent malnutrition. According to international guidelines [2], the best approach is to reach the energy goal by indirect calorimetry (IC) when available. In the absence of IC, a predictive formula or simple weight-based equation (25-30 kcal/kg/day) may be used to determine energy requirements [2]. Although no consensus has been reached about the most accurate formula to be used in ICU, the Harris-Benedict equation (HBE) is the most often employed to estimate the resting energy expenditure (REE) in ICU patients [5]. However, these equations suffer from several limitations, including poor accuracy. Their poor accuracy is related to the fact that the variables affecting energy expenditure in critically ill patients (eg, weight, medications, treatments, and body temperature) are sensitive to changes over time. For mechanically ventilated patients in ICU, the main factors influencing REE have been found to be weight, height, body temperature, and minute ventilation [6].

In the critical setting, protein is the macronutrient most often lacking in such patients, and its supplementation is likely to result in beneficial effects [7]. Disorders of protein metabolism are documented as physiologic responses to stressful events and are reflected by important nitrogen loss and muscle wasting, which are proportional to the severity of illness [8]. Current evidence supports the early administration of protein supplementation because a stressful event alters homeostatic balance, resulting in an increased protein catabolism [9]. Administering exogenous protein or amino acid is crucial to reduce the breakdown of endogenous proteins by providing an alternative source of amino acids for gluconeogenesis and protein synthesis. Protein-energy deficit is associated with an increased rate of infection, poor wound healing, reduced respiratory muscle mass, and delayed weaning from mechanical ventilation, resulting in increased length of stay in ICU and increased care costs [10]. A high protein intake, estimated using a weight-based equation (1.2-2 g/kg/day), is recommended during the ICU stay regardless of the simultaneous caloric intake [9,11].

This paper presents the development of a protocol for a randomized controlled trial (RCT) aimed at assessing changes of nitrogen balance (NB) in ICU patients administered with standard parenteral/enteral diet and protein-fortified parenteral/enteral diet. Together with the study protocol, results of the pilot study conducted to assess the feasibility of such a trial are also presented.

## Methods

### Randomized Controlled Trial

#### Study Design and Randomization

This study has been designed as a parallel arm RCT enrolling patients admitted at the Department of Anaesthesia and Intensive Care – Azienda Sanitaria Universitaria Integrata di Udine (Italy). Medical and surgical adult patients admitted to ICU undergoing mechanical ventilation at the time of admission or in the first 12 hours will be enrolled. See Textbox 1 for selection criteria.

**Textbox 1.** Selection criteria.

Inclusion criteria:

- Aged 18 years and older

- Receiving parenteral nutrition or enteral nutrition

- Having an indwelling catheter

- Undergoing mechanical ventilation

Exclusion criteria:

- Current or 6-month past history of gastrointestinal bleeding

- body mass index <18.5 kg/m$^2$ or ≥ 30 kg/m$^2$

- Terminal illness

- Pregnancy

- Acute renal failure defined using Kidney Disease Improving Global Outcomes (KDIGO) Clinical Practice Guidelines [12]: patients with a KDIGO stage 2 (serum creatinine 2-2.9 times baseline or urine output <0.5 mL/kg/h for 12 hours) and 3 (increase in serum creatinine ≥4 mg/dL, anuria for more than 12 hours, or starting of renal replacement therapy)

- Hepatic failure

Patients enrolled will be randomized to standard nutritional care (standard diet) to meet daily patient caloric requirement (control group) or appropriate amount of protein feeding (protein-fortified diet) to meet daily patient protein requirement (intervention group). Random allocation will be performed using a computer-generated algorithm (with an allocation rate of 1:1). Subjects enrolled will remain in the study until they are no longer mechanically ventilated. Participants will be blinded to treatment allocation. The flowchart of the study protocol is shown in Figure 1.

**Figure 1.** Flowchart of the study protocol.
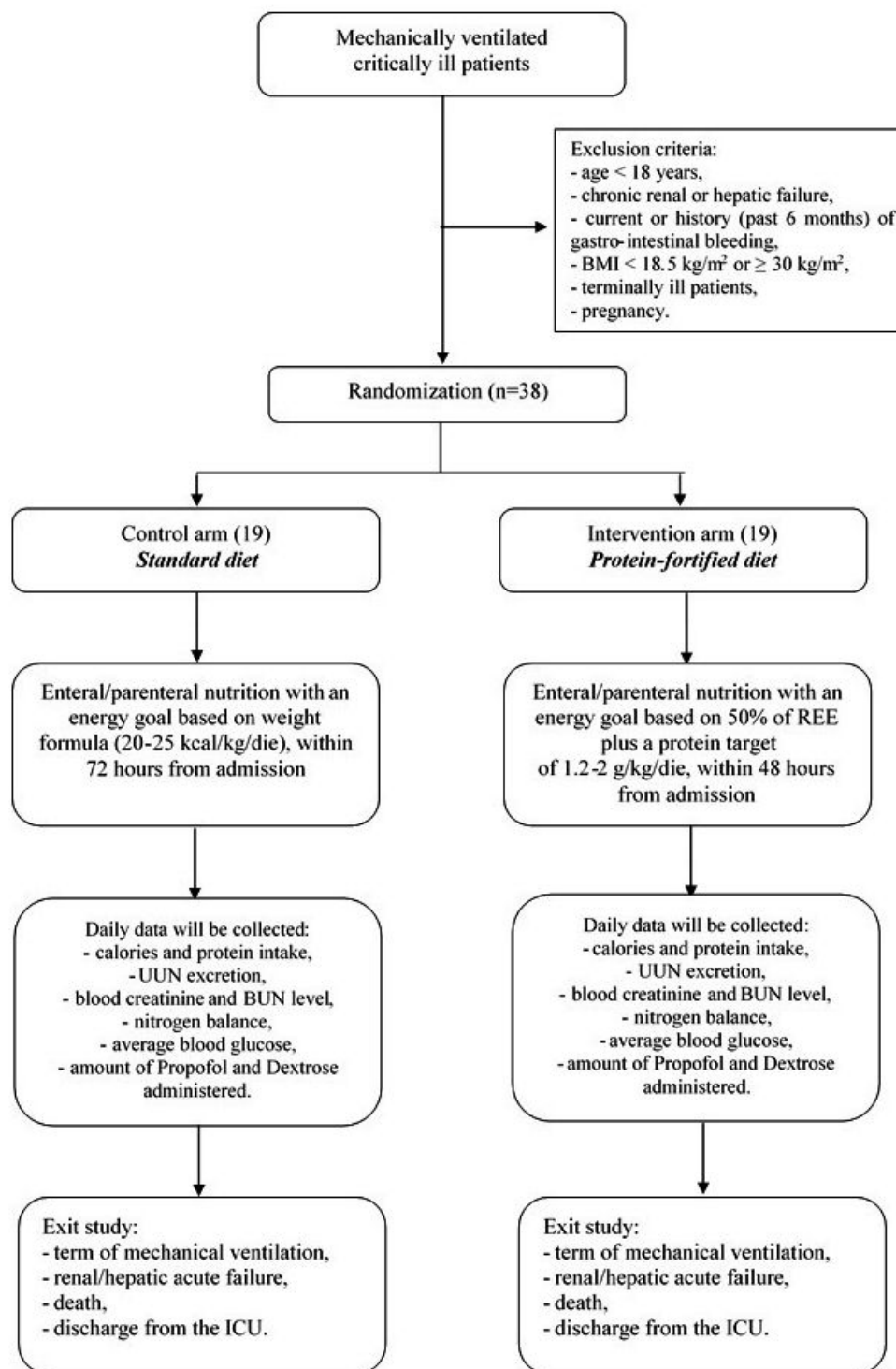


## Treatment Arms

The standard diet consists of an energy goal based on weight formula (20-25 kcal/kg/day). According to the ICU nutritional protocol, enteral nutrition (EN) will be started at an initial rate of 10 mL/h and increased by 20mL/h every 12 hours in the absence of significant gastric residuals (<250 mL), with the aim of reaching the energy goal within 72 hours of admission. The

EN formulae used are standard (1-1.5 kcal/mL, 40 g/L protein). If EN is not tolerated or not indicated, supplemental parenteral nutrition (PN) will be used to make up the energy shortfall. The PN formula used is standard (1000 kcal/L, 37 g/L protein).

The protein-fortified diet consists of an energy goal based on REE and a protein target based on the most recent literature recommendations (1.2-2 g/kg/day) [2]. Daily caloric requirement and subsequent protein content for patients enrolled in the intervention group will be calculated using formulae reported in Multimedia Appendix 1 [10,13,14]. For each patient, it will be calculated based on the REE and the daily protein requirement (1.2-2 g/kg/day of body weight registered at time of admission) and the corresponding caloric intake (1 g=4 kcal). Daily total caloric intake will be represented by 50% protein (1 g=4 kcal) and another 50% nonprotein (ie, fat and carbohydrates).

For the intervention group, EN will be started at an initial rate of 10 mL/h and increased by 20 mL/h every 8 hours in the absence of significant gastric residuals (<250 mL) with the aim of reaching the energy goal within 48 hours of admission. The EN formulae used are high in protein (1-1.5 kcal/mL, 74 g/L protein). If EN is not tolerated or not indicated, supplemental PN is used to make up the energy shortfall. The PN formula used will be arranged by the hospital pharmacy to meet the energy targets set for the intervention group.

For patients enrolled in the control group and the intervention group, gastric residuals will be checked 4 times per day and electrolytes will be closely monitored and replaced. Adequacy of nutritional support will be determined daily by measuring NB.

### Data Collection

Age (years), gender, weight (kg), height (cm), body mass index (BMI) (kg/m$^2$), main diagnosis, clinical history, and illness severity assessed using the Acute Physiology and Chronic Health Evaluation (APACHE) II score [15] will be collected at time of admission in ICU (baseline assessment). The Simplified Acute Physiology Score (SAPS) II for mortality prediction in ICU [16] will also be calculated.

The following parameters will be recorded at midnight of each day: caloric intake, protein intake, measurement of 24-hour urine urea nitrogen (UUN) excretion, blood creatinine, NB, blood urea nitrogen (BUN) level, average blood glucose, amount of propofol administered (mL/day), amount of dextrose administered (mL/day).

A standard formula will be used for NB calculation [17,18]: total protein intake (g)/6.25 –(UUN + 4 g), where 6.25 = 6.25 g of protein per gram of nitrogen, UUN = grams of nitrogen excreted in the urine over 24-hour period of time, and 4 = 4 g of nitrogen lost each day as insensible losses via the skin and gastrointestinal tract. Additionally, for each patient, the duration of mechanical ventilation and any infection or skin alteration discovered during the study period will be reported.

### Sample Size

Considering NB as primary outcome, a sample size estimation has been performed considering a *t* test difference in means between the 2 groups (standard and protein-fortified diet). For a specified alpha of .025 and a power of 0.90, which aimed at detecting a difference of at least –6 g of NB between the 2 groups (assuming an equal standard deviation in the 2 groups of 5 g), the estimated sample size is 19 per arm for a total of 38 patients to be randomized. The sample size has been estimated using the sample size package in R software (The R Foundation) [19].

Data will be entered and managed using REDCap (Research Electronic Data Capture), a Web-based application for managing databases hosted at the Department of Cardiac Thoracic and Vascular Sciences, University of Padova (Italy).

### Statistical Analysis Plan

The primary endpoint will be analyzed for the intention-to-treat (ITT) population. After having reached the sample size foreseen, a *t* test with an alpha level equal to .025 will be performed to assess the statistical differences in NB between protein-fortified diet and standard diet arms. As secondary endpoint, the hospital mortality rate will be considered. On the ITT population, the secondary endpoint will be evaluated by testing the difference between the 2 groups in a logistic model framework (alpha=.025).

The study was approved by the regional ethics committee of Friuli Venezia Giulia, Italy (CEUR-2016-Sper-066-ASUIUD). Each patient or legally authorized representative must provide written informed consent for the study procedures.

## Feasibility Study

### Study Design

An observational analysis was conducted to assess the feasibility of the trial. This observational study enrolled patients admitted to the ICU *of* the Department of Anaesthesia and Intensive Care – Azienda Sanitaria Universitaria Integrata di Udine (Italy). The study was undertaken in a group of mixed medical, surgical, and trauma patients undergoing mechanical ventilation. Exclusion criteria were age (less than 18 years), chronic renal (identified using KDIGO recommendations) or hepatic failure, current or 6-month past history of gastrointestinal bleeding, body mass index <18.5 kg/m$^2$ or ≥30 kg/m$^2$, terminal illness, and pregnancy. This study aimed at investigating the level of energy intake (kcal and protein) and nitrogen excretion in an ICU population receiving standard diet.

### Treatment

Our nutritional approach was led by current guidelines that recommend providing 25-30 kcal/kg/day. Both EN and PN were used to achieve energy goals. EN formula was the Nutrison standard (1000 kcal and 40 g of protein per 1000 mL); an all-in-one solution containing 1000 kcal and 47 g of protein per 1000 mL was used for PN.

### Data Collection

Using REDCap, the following patient information were collected: admission diagnosis, comorbidities, age, sex, BMI, APACHE II score, SAPS II score (at baseline), type and amount of nutrition received (both caloric and protein intake), amount of propofol and dextrose (mL/day) administered, and blood

chemistry (urea nitrogen level, creatinine, glucose) (at midnight of each day). A daily 24-hour urine collection was conducted in all patients and NB was calculated. For each patient, any infection or skin alteration occurring during the study period was reported. Daily data were collected until the end of mechanical ventilation or until renal/hepatic acute failure, death, or discharge from the ICU.

### Data Analysis

Continuous variables were reported as median (I quartile and III quartile), and discrete parameters were reported as absolute value (percentage). The distribution of the quantitative variables was summarized using simple barplots for trend. To assess if the series has an increasing or decreasing trend, a nonparametric Spearman test was performed between the observations and time. To calculate trends, means of patient measures of interest were considered. A *t* test was carried out to test the significance of mean difference from the amount of protein actually administered and that recommended by international guidelines. All analyses were performed using R software (The R Foundation) [19].

## Results

### Randomized Controlled Trial

Enrollment in the study began in January 2017. Data collection is expected to be conducted until April 2017. Data analysis will start once the data collection is completed and the database is locked.

### Feasibility Study

Sample characteristics are summarized in Table 1. A total of 14 patients were enrolled, with a median age of 48 years. Median weight was 83 kg, and median BMI was 25.5 kg/m$^2$. For about

a half of the patients (6/14, 43%) the main diagnosis reported at time of admission was trauma (especially multiple trauma). Of the 14 patients evaluated, 8 (57%) completed the observation until the end of mechanical ventilation.

Figure 2 shows the contribution of EN, PN, extra proteins (represented by albumin), and propofol and dextrose infusions to the mean energy (kcal) intake over the feasibility study period. During the first 3 days of observation, propofol contributed to about half of the daily caloric intake. Additionally, calories introduced by PN increased over the days, while calories provided by EN remained stable. Overall, caloric intake increased over time. Along with caloric intake, protein administration also increased significantly (*P*<.001) over the period of observation (Figure 3).

Despite the increased provision of protein during hospitalization, the BUN significantly increased (*P*=.03) over the period of observation (Figure 4), thus indicating an increased catabolism in patients enrolled (since urea represents the waste product from protein metabolism). Increased catabolism resulted in negative NB, as shown in Figure 5. All patients had a negative cumulative NB in the first 72 hours of observation, and some patients presented with a markedly more negative NB compared to the others.

Finally, Figure 6 reports the comparison between patients' actual protein intake and that recommended by international guidelines (considering a value of 1.8 g/kg/day in the range between 1.2 and 2 g/kg/day). Clearly, the amount of protein actually administered is significantly lower compared to that recommended (*P*<.0001) (for patient 7, PN/EN was not administered in the first 24 hours due to medical procedures, resulting in fasting). The median difference between actual and recommend protein intake was found to be –360 g/kg (range –638 to 52).

**Figure 2.** Composition of the calories administered.

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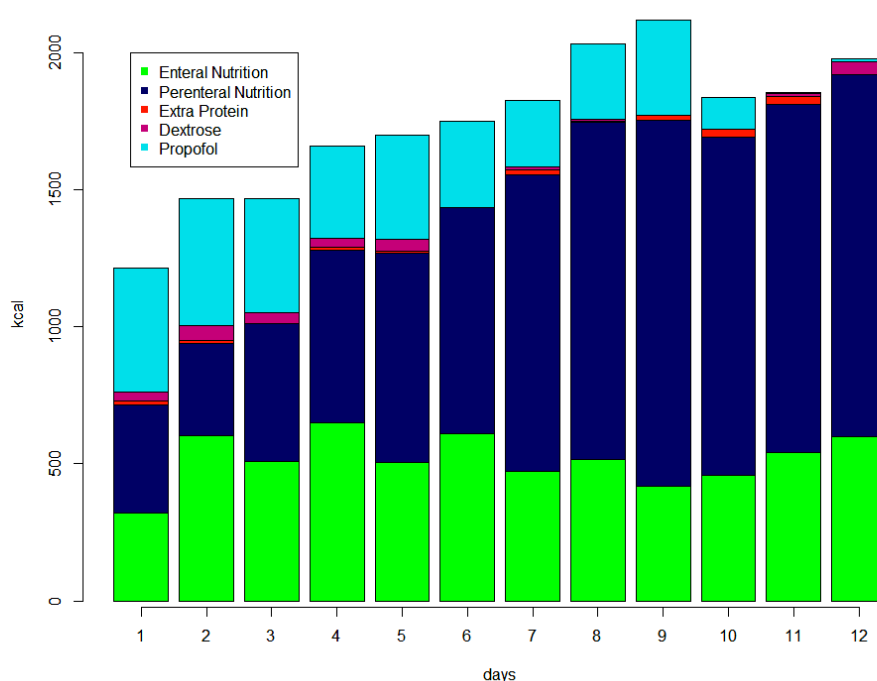
**Table 1.** Characteristics of the patients enrolled in the feasibility study.

| Characteristics | | | Number |
|---|---|---|---|
| Age (years), median (I and III quartile) | | | 48 (43-55) |
| **Sex, n (%)** | | | |
| | Male | | 8 (57) |
| | Female | | 6 (46) |
| Weight (kg), median (I and III quartile) | | | 83 (66-94) |
| BMI[a](kg/m$^2$), median (I and III quartile) | | | 25.5 (24.2-27) |
| APACHE[b]II score, median (I and III quartile) | | | 10.5 (9-16) |
| SAPS[c]II score, median (I and III quartile) | | | 29 (24-36) |
| Observation period (days), median (I and III quartile) | | | 8 (6-12) |
| **Admission diagnosis, n (%)** | | | |
| | Organ failure | | 4 (29) |
| | | Respiratory failure | 3 (75) |
| | | Sepsis and infection | 1 (25) |
| | Trauma | | 6 (43) |
| | | Multiple trauma | 5 (83) |
| | | Spinal trauma | 1 (17) |
| | Cerebrovascular disease | | 4 (29) |
| | | Cerebral hemorrhage | 2 (50) |
| | | Coma | 2 (50) |
| **Comorbidities, n (%)** | | | |
| | Cerebrovascular accident | | 3 (21) |
| | Chronic obstructive pulmonary disease | | 1 (7) |
| | Diabetes | | 2 (14) |
| | Hypertension | | 3 (21) |
| | Smoking | | 2 (14) |
| | Anxiety/depression | | 2 (14) |
| | Neoplasia | | 1 (7) |
| **Exit study, n (%)** | | | |
| | Transfer to another hospital | | 2 (14) |
| | Term of mechanical/spontaneous breathing | | 8 (57) |
| | Acute renal or hepatic failure | | 3 (21) |
| | Death | | 1 (7) |

[a]BMI: body mass index.

**Figure 3.** Protein intake trend.
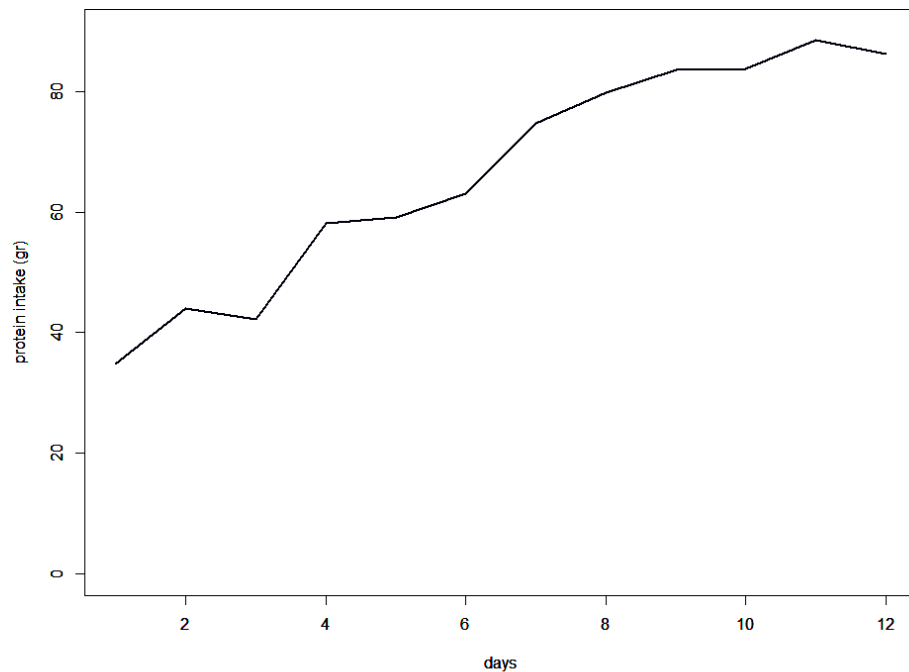


**Figure 4.** Blood urea nitrogen trend.
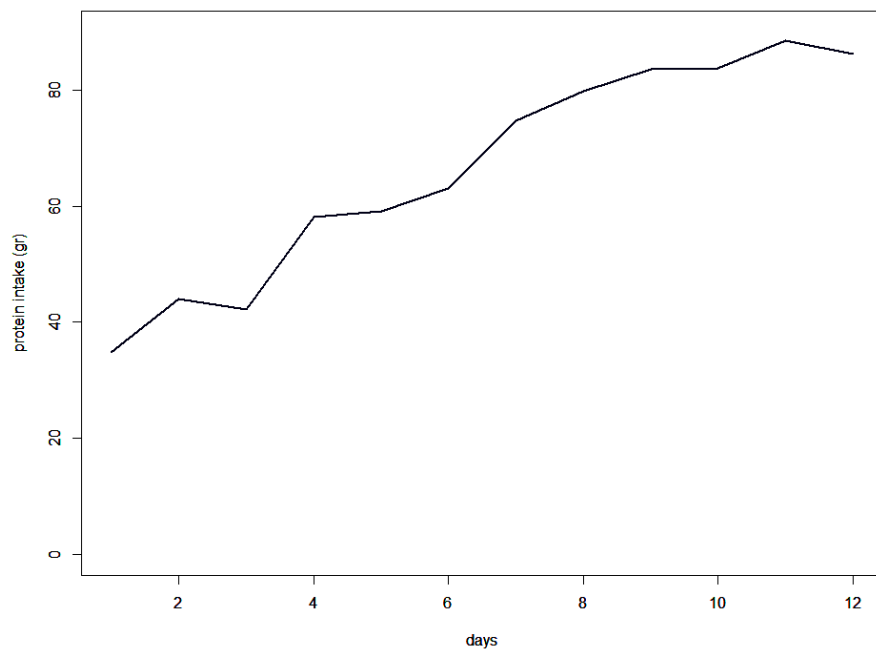
**Figure 5.** Cumulative nitrogen balance during the first 72 hours.
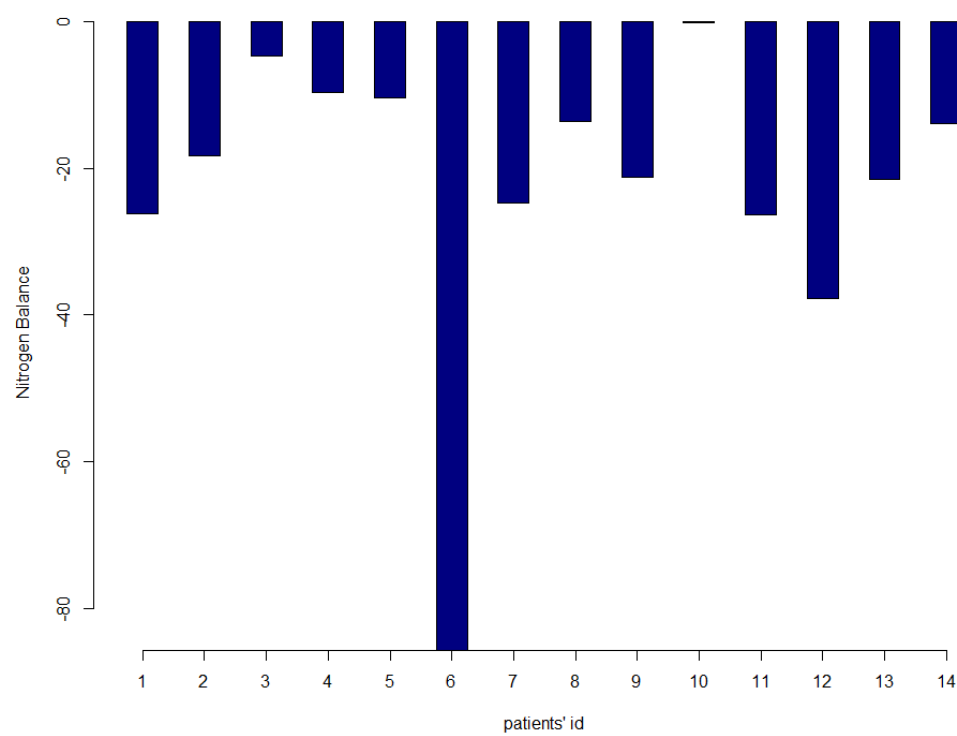


**Figure 6.** Protein intake administered versus ideal protein target in the first 24 hours.
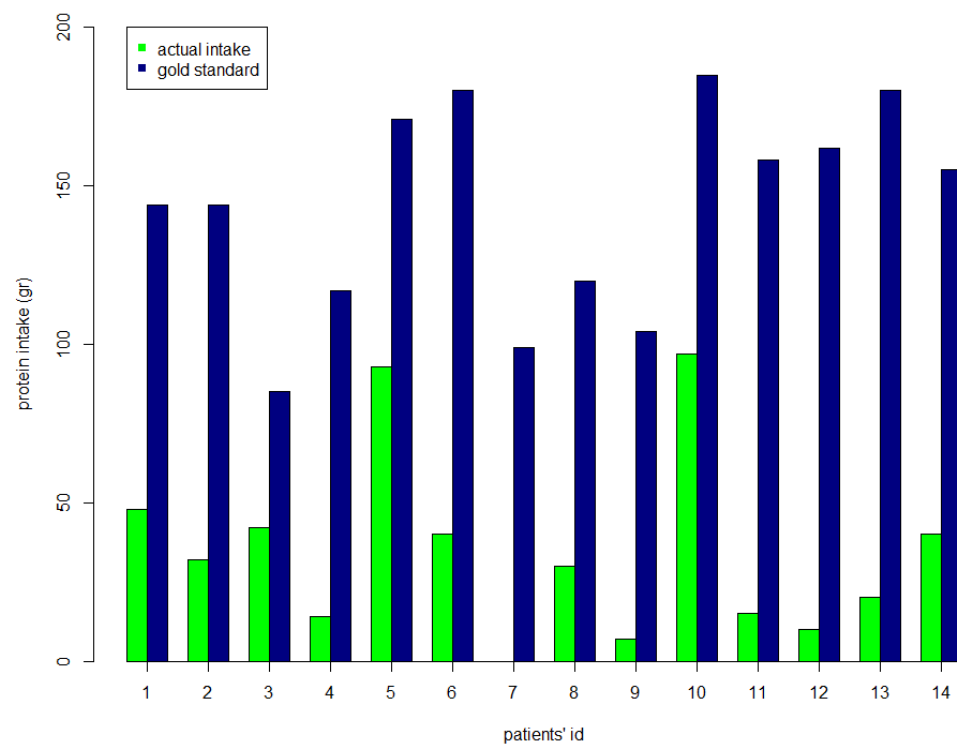
## Discussion

### Principal Findings

In recent years, several studies have focused on the importance of an adequate caloric intake in critically ill subjects. However, specific evidence about protein intake (adequate amount to be administered, adverse outcomes associated with inadequate protein intake) is sparse, even though several studies have demonstrated that in critically ill patients protein breakdown is greatly increased [3,11,20]. Adequate provision of protein represents a relevant issue in patients admitted in ICU, because pathological conditions such as surgical procedures and infection diseases result in increased protein requirements [11,21]. A high protein intake is recommended during the early phase of the ICU stay due to increased catabolism [9]. Allingstrup et al [22] observed a lower mortality in patients receiving a mean of 1.46 (SD 0.29) g/kg/day than those receiving 0.79 (SD 0.29) or 1.06 (SD 0.29) g/kg/day. This suggested that an optimal protein provision may result in better clinical outcomes compared to an optimal caloric provision alone in critically ill patients [21].

Considering this framework, the main issue in the nutritional management of ICU patients is represented not only by the identification of the most adequate daily caloric intake but also by the identification of the optimal contribution of each nutrient to the daily caloric intake, focusing particularly on protein content. The aim of our study protocol is to provide evidence about the effectiveness of a protein-fortified diet in patients admitted to ICU.

To assess the feasibility of this study protocol, a pilot study was conducted. Consistent with previous research [3,11], our feasibility study confirmed that critically ill patients had a severe protein catabolism that resulted in a strong negative NB. Literature has suggested that this situation may result in prolonged ventilator dependence and increased risk of brain dysfunction, neuromuscular weakness, metabolic changes, muscle wasting, malnutrition, skin breakdown, and symptoms distress like pain, anxiety, and depression [23].

Although the NB was negative in all patients, we observed that cumulative NB in the first 72 hours was different among subjects observed. This is probably due to an interindividual variability in the lean body mass that results in a different amount of protein metabolism waste. Beyond its action on protein metabolism, dietary protein intake affects body composition [18]. This interindividual variability might be considered in the estimation of protein intake. However, while a high protein intake is able to preserve lean mass, especially during the early or most catabolic phases of illness, the specific goal of protein requirement to minimize the loss of lean mass is not yet clear [21,24]. Additionally, together with the marked negative NB, actual protein intake was found to be dramatically lower than that recommended by international guidelines for patients undergoing mechanical ventilation.

Weight-based equations (1.2-2 g/kg/day) may be used to monitor adequacy of protein provision [2,25], but in adult critically ill patients admitted to ICU, it is difficult to achieve this target. This is because standard nutritional formulations are rich in lipid and carbohydrate calories, but the protein content is inadequate. Furthermore, our findings showed that the contribution of EN to caloric intake remained stable over the period of observation. This may be attributable to feeding intolerance and high gastric residual volumes or to interruptions for medical procedures (eg, bronchoscopy, computed tomography, as with patient 7). If EN is insufficient, supplemental PN should be considered [9]. However, even if PN administration progressively increased during the period of observation, the composition of both PN or EN did not allow the achievement of protein optimal requirements.

### Conclusions

Even though several studies have shown that the provision of an appropriate protein intake may reduce net muscle catabolism, to our knowledge this is the first study protocol aimed at comparing clinical outcomes of standard and protein-fortified diet in an ICU population. Results of the feasibility study clearly confirmed that protein provision in ICU patients is below that recommended in international guidelines and that this results in impaired NB. Moreover, it provided evidence that protein catabolism is different among patients, probably due to differences in body composition (eg, lean body mass). Such interindividual variability will be further analyzed in the trial to understand if and how it may be considered in the titration of protein intake.

### Conflicts of Interest

None declared.

### Multimedia Appendix 1

Energy and protein intake calculation for intervention group only.

[PDF File (Adobe PDF File), 17KB - resprot_v6i5e78_app1.pdf ]

### Multimedia Appendix 2

Peer review and approval from Etichs Committee.

[PDF File (Adobe PDF File), 1MB - resprot_v6i5e78_app2.pdf ]

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## Abbreviations

**APACHE:** Acute Physiology and Chronic Health Evaluation
**BMI:** body mass index
**BUN:** blood urea nitrogen
**EN:** enteral nutrition
**HBE:** Harris-Benedict equation
**IC:** indirect calorimetry
**ICU:** intensive care unit
**ITT:** intention-to-treat
**KDIGO:** Kidney Disease Improving Global Outcomes
**NB:** nitrogen balance
**PN:** parenteral nutrition
**RCT:** randomized controlled trial
**REDCap:** Research Electronic Data Capture
**REE:** resting energy expenditure
**SAPS:** Simplified Acute Physiology Score
**UUN:** urine urea nitrogen

Protocol

# Diagnosis, Prevalence, Awareness, Treatment, Prevention, and Control of Hypertension in Cameroon: Protocol for a Systematic Review and Meta-Analysis of Clinic-Based and Community-Based Studies

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## Abstract

**Background:** Hypertension holds a unique place in population health and health care because it is the leading cause of cardiovascular disease and the most common noncommunicable condition seen in primary care worldwide. Without effective prevention and control, raised blood pressure significantly increases the risk of stroke, myocardial infarction, chronic kidney disease, heart failure, dementia, renal failure, and blindness. There is an urgent need for stakeholders—including individuals and families—across the health system, researchers, and decision makers to work collaboratively for improving prevention, screening and detection, diagnosis and evaluation, awareness, treatment and medication adherence, management, and control for people with or at high risk for hypertension. Meeting this need will help reduce the burden of hypertension-related disease, prevent complications, and reduce the need for hospitalization, costly interventions, and premature deaths.

**Objective:** This review aims to synthesize evidence on the epidemiological landscape and control of hypertension in Cameroon, and to identify elements that could potentially inform interventions to combat hypertension in this setting and elsewhere in sub-Saharan Africa.

**Methods:** The full search process will involve several steps, including selecting relevant databases, keywords, and Medical Subject Headings (MeSH); searching for relevant studies from the selected databases; searching OpenGrey and the Grey Literature Report for gray literature; hand searching in Google Scholar; and soliciting missed publications (if any) from relevant authors. We will select qualitative, quantitative, or mixed-methods studies with data on the epidemiology and control of hypertension in Cameroon. We will include published literature in French or English from electronic databases up to December 31, 2016, and involving adults aged 18 years or older. Both facility and population-based studies on hypertension will be included. Two reviewers of the team will independently search, screen, extract data, and assess the quality of selected studies using suitable tools. Selected studies will be analyzed by narrative synthesis, meta-analysis, or both, depending on the nature of the data retrieved in line with the review objectives.

**Results:** This review is part of an ongoing research program on disease prevention and control in the context of the dual burden of communicable and noncommunicable diseases in Africa. The first results are expected in 2017.

**Conclusions:** This review will provide a comprehensive assessment of the burden of hypertension and control measures that have been designed and implemented in Cameroon. Findings will form the knowledge base relevant to stakeholders across the health system and researchers who are involved in hypertension prevention and control in the community and clinic settings in Cameroon, as a yardstick for similar African countries.

**Trial Registration:** PROSPERO registration number: CRD42017054950; http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42017054950 (Archived by WebCite at http://www.webcitation.org/6qYSjt9Jc)

## Introduction

### Rationale

The term "blood pressure" (BP) was coined over 300 years ago by the British Reverend Stephen Hales, who first measured it [1]; yet our understanding of the pathogenesis, consequences, and treatments of hypertension (or raised BP, or elevated BP, or high BP) had remained greatly limited and inadequate until only the past four decades or so [2]. Moreover, despite improvements in the prevention of hypertension and control of BP in patients with hypertension, the condition remains a "silent killer" of major public health significance globally [3-6],

because these improvements have not always been tangibly extended from the individual patient to the entire population [7,8].

As one of the most important preventable contributors to the global burden of disease and death [9], high BP remains a major risk factor for cardiovascular and renal morbidity and mortality [10-12], and systolic blood pressure (SBP) is associated with the highest burden among cardiovascular risk factors above and beyond either smoking or obesity [13]. Hypertension leads to myocardial infarction, stroke, renal failure, and death if not detected early and treated appropriately [14-18]. There is also a close relationship between BP levels and the risk of cardiovascular events, strokes, and kidney disease: the risk of these outcomes is lowest at a BP of around 115/75 mm Hg, whereas above 115/75 mm Hg, for each increase of 20 mm Hg in SBP or 10 mm Hg in diastolic blood pressure (DBP), the risk of major cardiovascular and stroke events doubles [19]. In 2010, hypertension was responsible for 9.4 million deaths and 7% of the global disease burden as measured in disability-adjusted life-years [20]. Between 1990 and 2015, the global estimated annual death rate per 100,000 associated with high SBP increased from 97.9 (95% uncertainty interval [UI] 87.5-108.1) to 106.3 (95% UI 94.6-118.1), and the loss of disability-adjusted life-years associated with high SBP increased from 5.2 million (95% UI 4.6-5.7 million) to 7.8 million (95% UI 7.0-8.7 million) [21]. During the same period, hypertension was responsible for the largest numbers of deaths worldwide caused by ischemic heart disease (4.9 million, 95% UI 4.0-5.7 million; 54.5%), hemorrhagic stroke (2.0 million, 95% UI 1.6-2.3 million; 58.3%), and ischemic stroke (1.5 million, 95% UI 1.2-1.8 million; 50.0%) [21].

There is an urgent need for stakeholders—including patients and families—across the health system, researchers, and decision makers to work collaboratively to improve prevention, screening and detection, diagnosis and evaluation, awareness, treatment and medication adherence, management, and control for people with or at high risk for hypertension, thereby preventing complications and reducing the need for hospitalization, costly interventions such as cardiac bypass surgery and dialysis, and premature deaths. In rapidly changing socioeconomic, demographic, epidemiological, nutritional, cultural, and physical environments typical of many resource-constrained countries in sub-Saharan Africa (SSA) such as Cameroon, the evidence on the epidemiology and control of noncommunicable diseases (NCDs) in general and hypertension in particular is scattered and poorly documented [4,8,22-25]. High BP contributes to 75% of all strokes and heart attacks [26]; in Cameroon, stroke (4.6%) and ischemic heart disease (3.8%) are the top killers among all NCDs and the fifth and sixth cause of death, respectively, preceded by human immunodeficiency virus (HIV)/AIDS (13.4%), lower respiratory infections (12.2%), diarrheal diseases (6.0%) and malaria (5.0%) [27]. In such environments, the distribution of hypertension-related disease and its population impact are expected to be geographically heterogeneous with variations in ecological setting, population aging, rate of urbanization, and unhealthy lifestyles [11,12,28-32].

We plan to identify and systematically synthesize available data on hypertension in Cameroon in order to generate new knowledge and produce up-to-date information designed to (1) provide a countrywide portrait on estimates and influential factors of prevention, screening and detection, diagnosis and evaluation, awareness, treatment and medication adherence, management, and BP therapeutic (pharmacological and nonpharmacological) interventions for people with or at high risk for hypertension; (2) assess variation in hypertension prevention and control at both the population and health care organization levels across regions and ecologies within Cameroon; and (3) identify data needs, research gaps, user and patient needs, and needs of primary care clinicians for BP treatment for people with hypertension wherever they are located, to support national hypertension prevention and control efforts that can improve patient outcomes.

Thus, this review seeks to appraise evidence in order to provide valuable information that will contribute to facilitating the design, implementation, or furthering of strategies for the epidemiology and control of hypertension in various settings and across at-risk population subgroups in Cameroon, given the changing scope of public health within constantly altering global, national, and local health ecologies.

## Objectives

We will undertake a systematic review of the epidemiology and control of hypertension in Cameroon using a broad set of eligibility criteria and a thorough search strategy. We aim to (1) review overall and within-country diagnostic practices, prevalence, awareness, treatment, prevention, and control of hypertension; and (2) examine the pattern and disparities of this condition across different socioeconomic and demographic groups, and areal and agroecological milieus. Clinical practice guidelines in resource-limited settings should be designed, developed, and improved within the context of areal and sociocultural realities of the health care system and its stakeholders, including the individual patient, so as to embody and support the interrelationships among enduring behavioral and structural changes in societies that are critical contributors to hypertension risk and clinical decision making. Rather than dictating a one-size-fits-all approach to hypertension prevention and patient care, nationally appropriate clinical practice guidelines are most suitable to enhance culturally appropriate prevention strategies and measures targeted at the general population, as well as clinician and patient decision making, by clearly describing and appraising the evidence and the likely benefits and harms behind recommendations for hypertension prevention in adulthood and control of BP in people with hypertension.

Because health occurs within constantly changing socioeconomic and health care environments in much of SSA, this review will address two high-stake questions with broad population health and health care impacts in resource-limited settings such as Cameroon: (1) What is the epidemiological landscape of hypertension among adults aged 18 years or older in Cameroon? (2) What control strategies have been designed and implemented in clinic or community settings to reduce the

burden of hypertension in a socioculturally and environmentally diverse setting such as Cameroon?

## Methods

### Protocol and Registration

Many guidelines in health and health care are based on systematic review of the evidence. Before undertaking this systematic review, we searched the Database of Abstracts of Reviews of Effects, the Cochrane Database of Systematic Reviews, the National Institute for Health and Care Excellence website, the National Institute for Health Research Health Technology Assessment program website, the Campbell Collaboration website, the Evidence for Policy and Practice Information and Co-ordinating-Centre (a database of systematic and nonsystematic reviews of public health interventions, or database of promoting health effectiveness reviews), the National Guideline Clearinghouse, the previous year (2015) of Medline, and other appropriate bibliographic databases that could be helpful in identifying recently published reviews. We found no existing or ongoing reviews.

The planned review is being spearheaded by members of our International and Interdisciplinary Research Team on the Dual Burden of Communicable and Noncommunicable Diseases in Africa forming the review team. They have expertise in systematic reviews and meta-analysis, hypertension, primary care (including geriatrics, cardiology, nephrology, nursing, and pharmacology), research (including clinical trials), evidence-based medicine, preventive medicine, epidemiology, informatics and biostatistics, development and implementation of clinical guidelines in systems of care, and other important fields relevant to hypertension prevention and control in high-income countries (HICs), as well as low- and middle-income countries (LMICs).

This protocol conforms to the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols guidelines [33]. Our systematic review rationale and methods were specified in advance and documented in the PROSPERO register on January 16, 2017 (CRD42017054950).

### Eligibility Criteria

We will select studies according to the two general categories of eligibility criteria (ie, study characteristics and report characteristics) outlined below for the planned review. This review will seek information on the epidemiological landscape of hypertension in terms of geographical coverage (ie, rural, urban, or both), agroecological zones and region of residence of study participants, and costs (at the individual, family, community, and national levels) on the one hand, and the control of hypertension on the other hand.

### Population

We will include studies examining the general adult Cameroonian population, or healthy adult Cameroonians, or those with hypertension and related comorbidities aged 18 years or older, who consented to participate in studies that will be reviewed. To be selected, a quantitative study must include a group of 10 or more participants, since at least 10 data points

per predictor parameter are required in a regression model. We will exclude unpublished articles, commentaries, editorials, newspaper articles, theses, conference abstracts, and conference proceedings. We will also exclude studies without a description of how patients with hypertension were identified.

### Interventions

Of interest in this review are interventions addressing hypertension prevention, control, or both, in a broad perspective, using pharmacological or nonpharmacological approaches. We will also include nonspecific or multifaceted behavioral, educational, policy, or other types of interventions given what exists in the literature, subject to the level of information available from clinic-based and community-based studies.

Regarding the first review question, the included studies will cover exposure to the risk factors and determinants of hypertension. We will identify the incidence and prevalence of hypertension and its morbidity, mortality, and burden in adults exposed to these risk factors in Cameroon. Concerning the second review question, the included studies will address the strategies, intervention, and programs that have been designed, implemented, and evaluated for the prevention and control of hypertension in various settings and among various adult population subgroups in Cameroon.

### Comparators

Given the broad perspective for interventions of interest, several comparisons will be relevant to include. Some may be more likely to come from hospital-based studies and others from population-based studies. We will draw on recommendations of the World Hypertension League [34,35] and the *Global Action Plan on Prevention and Control of NCDs 2013-2020* [8] to distinguish adult hypertensive versus normotensive populations. We will define people with normotensive BP as the adult population who have a measured SBP less than 140 mm Hg and DBP less than 90 mm Hg in the absence of treatment with medication for high BP. We will define people with optimal BP as the adult population having measured SBP less than 120 mm Hg and measured DBP less than 80 mm Hg in the absence of treatment with medication for high BP.

With regard to the first review question, the comparison among adults within subgroups will be multilevel (type of place of residence [rural, urban, or both] nested within 5 agroecological zones nested within the 10 regions of Cameroon). For the second review question, the control adults will be those not receiving the treatment or the intervention, or not participating in the program.

### Outcomes

The ability to reliably evaluate the impact of interventions and changes in hypertension prevention and control is critical if the burden of hypertension-related disease is to be reduced [35]. End points important for decision making of primary interest in this review are BP testing, diagnosis of hypertension, awareness of hypertension, treatment of hypertension, BP medication adherence, and BP control for hypertension. End points important for decision making that are secondary outcomes in this review are morbidity attributed to hypertension,

mortality attributed to hypertension, and screening for modifiable risk factors in adults with hypertension (or with prehypertension). As some outcomes may be reported as a composite measure, we will extract all composite and individual outcomes as reported in the studies. Due to possible variation in definitions over time of hypertension and hypertension-related diseases and conditions, we will extract definitions of outcomes as reported in individual studies. We will extract outcomes in all data forms (eg, dichotomous, continuous) as reported in the included studies.

For the hypertension outcomes, inclusion criteria comprise hypertension indicators reported or deducible from subgroup estimates, at a population level in population-based surveys or in primary health care; hypertension assessed as BP 140/90 mm Hg or higher, or hypertension assessed as BP 160/95 mm Hg or higher, or other assessment criteria; use of antihypertensive drugs; or self-reported physician-diagnosed cases. We will use both self-reported data from population-based surveys and physician-reported data, because the accuracy of self-reported diagnosis of hypertension compared with chart reviews and physician-reported history has been demonstrated in various clinic and community settings [34,36-39]. In fact, the inclusion of self-reported diagnosis, including individuals who have controlled their BP using lifestyle changes as stand-alone therapy, increased the estimated prevalence of hypertension by 5% to 10% in the United States [40-42]. For meta-analysis, we will restrict analyses to studies for which hypertension was assessed as BP 140/90 mm Hg or higher, or use of antihypertensive drugs, or self-reported physician-diagnosed cases.

### Study Design

We will include all clinic, hospital-, community-, and population-based studies, regardless of design. We will include studies conducted using quantitative, qualitative, or mixed research approaches. For quantitative studies, we will only include studies reporting the presence versus absence of at least one of the outcome variables in the total number of participants with or without a given exposure variable (2 × 2 table); such data will be sufficient to calculate odds ratios [43]. To maximize sensitivity, we will place no limitations on whether there was blinding for clinical information in a trial, whether there was a measure of intrarater or interrater reliability, or whether the level of experience or background (cardiologist, endocrinologist, neurologist, etc) of the raters is specified, although we will extract this information if available and it will contribute toward assessment of risk of bias.

### Time Frame

We will select all journal articles and reports for inclusion if they were published up to December 31, 2016.

### Setting

This review will focus on Cameroon. Situated in the crook of the Gulf of Guinea and with a surface area of 475,442 km$^2$, the Republic of Cameroon is bounded to the northwest by Nigeria, to the north by Chad, to the east by the Central African Republic, and to the south by Congo, Equatorial Guinea, and Gabon [44,45]. It is commonly referred to as "Africa in miniature"

because of its multitude of ecosystems and associated biodiversity, agroecological richness, cultures and traditions, and ethnolinguistic diversity, which together capture much of tropical Africa [44-49]. The country also harbors very ancient human populations with very intimate relationships with nature and where animals play important roles for the populations' livelihood [48,49]. Globally, the incidence and pattern both of cardiovascular disease and cancer vary with the ecology of different regions [50-52]. Given the fragmented nature of most tropical ecosystems, the landscape epidemiological investigation of hypertension in Cameroon representing a variety of agroecosystem types with its 5 agroecological zones will offer a microcosmic portrait of hypertension in diverse ecosystems in tropical Africa; hence, what will be seen in miniature in Cameroon may be seen enlarged upon an SSA ecological scale. The 5 agroecological zones are highland and grassfield (West and Northwest regions), humid forest with monomodal rainfall (Littoral and Southwest regions), humid forest with bimodal rainfall (Centre, East, and South regions), high guinea savannah (Adamawa region), and Sudano-Sahelian (North and Far North regions) [53].

English and French are the 2 official languages spoken across its 10 regions (English is spoken by about 20% and French by about 80% of the population), with more than 250 ethnic groups speaking approximately 200 different dialects [44,45]. Cameroon's major ethnic groups in terms of proportion are 38% Western Highlanders/Grassfielders (Bamileke, Bamoun); 12% Coastal Tropical Forest Peoples (Bassa, Douala, etc); 18% Southern Tropical Forest Peoples (Ewondo, Beti [Bulu and Fang subgroups], Maka, and Pygmies/Bakas); 14% Fulani (Islamic Northerners); and 18% Kirdi (non-Islamic Northerners).

The health system and health status vary widely by region and ecology, and several health care systems coexist. Cameroon's public health sector is pyramidal in structure, with a centralized system of administration that runs from the central (ministry), through the intermediary (regional delegations), to the peripheral (health districts) levels. A total of 3 different levels of health care delivery services are evident: the tertiary, the secondary, and the primary services. Since 1992, the Minister of Public Health has promoted a national health policy of decentralization designed to maximize available resources at the district level; the nonprofit, private sector has an important place in Cameroon's health system, offering a wide network of services throughout the country; the private, for-profit sector operates in the large cities, while traditional medicine is omnipresent. Traditional medicine—health practices, approaches, knowledge, and beliefs incorporating plant-, animal-, and mineral-based medicines, spiritual therapies, manual techniques, and exercises, applied singularly or in combination to treat, diagnose, and prevent illnesses or maintain well-being—is very popular in Cameroon [54]. This has prompted the government, in line with the provisions of the World Health Organization (WHO) strategies on traditional medicines [55], to take steps toward regulating the practice and use of traditional medicine in Cameroon. Notable steps taken as early as during the 1980s include the creation of the Traditional Medicine Service within the Unit of Community Medicine in the Yaoundé Central Hospital and the setting up of the Office of Traditional Medicine

in the Ministry of Public Health [24]. Cameroon's health care system is pluralistic in nature, characterized by multiple sources of financing and health care providers. The main financing sources are the government, public enterprises, foreign aid donors, private enterprises, households, religious missions, and nongovernmental organizations. Government health facilities, public enterprise health clinics, health facilities of religious missions and nongovernmental organizations, private clinics, pharmacies and drug retailers, and traditional doctors constitute the main providers [25]. Infectious diseases such as malaria, HIV/AIDS, and lower respiratory infections are still the primary causes of morbidity and mortality; however, in recent years, evidence has emerged that NCDs such as stroke, ischemic heart disease, diabetes, and cancers are also contributing causes [27].

### *Language*

We will include all journal articles and reports in the English and French languages.

### Information Sources

We will develop literature search strategies using MeSH and text words related to the epidemiology and control of hypertension. We will search for relevant studies published in English or French from the following databases: PubMed, Medline, Embase, CINAHL, Web of Science, POPLINE, Scopus, and Banque de données en santé publique. We will use the appropriate Boolean operators to combine the following search terms: "hypertension," "hypertensive," "high blood pressure," "raised blood pressure," "screening," "diagnosis," "measurement," "incidence," "prevalence," "awareness," "morbidity," "mortality," "treatment," "prevention," "control," and "Cameroon." The titles and abstracts of the resulting studies will be screened for further review. We will also manually search for relevant gray literature from sources such as publications by the WHO, the African Development Bank, the World Bank, the Cameroon National Institute of Statistics, and the Cameroon Ministry of Public Health. We will include studies on hypertension (1) in human male and female adults aged 18 years or older (2) published up to December 31, 2016 that (3) are either clinic or community-based, (4) used qualitative, quantitative, or mixed research methods and (5) were published in English or French.

In regard to gray literature, we will search the proceedings of the European Society of Hypertension, the South African Hypertension Society, the American Society of Hypertension, the World Hypertension Congress, and the Annual General Meeting of the American Society of Hypertension. We will also search the World Heart Federation, International Society of Hypertension, World Hypertension League, American Heart Association, Cameroon Cardiac Society, Pan-African Society of Cardiology, *Integrated Blood Pressure Control* journal, the Hypertension, Diabetes and Dyslipidemia Conference, and Canadian Hypertension Congress-General through PapersFirst (WorldCat), ProceedingsFirst (WorldCat), and Web of Science. The websites of pertinent organizations will also be examined for articles and the names of researchers.

We will undertake several additional approaches to increase our retrieval of relevant articles and to ensure literature saturation. We will search our personal files to make sure that we have captured all relevant material. We will circulate a bibliography of the included articles to the systematic review team, as well as to hypertension experts identified by the team. To ensure that we have not missed studies, we will hand search hypertension-relevant journals such as *Hypertension*, *International Journal of Hypertension*, *Journal of the American Society of Hypertension*, *American Journal of Hypertension*, *Hypertension Research*, *Journal of Human Hypertension*, *The Journal of Clinical Hypertension*, *Current Hypertension Reports*, *American Heart Journal*, *International Journal of Cardiology*, *European Heart Journal*, and *Cardiovascular Journal of Africa*. These journals are considered to have the highest impact for the clinical subject of interest. Subject experts on hypertension in or on Cameroon will also be contacted to enquire about any studies felt to be applicable but not retrieved by our search strategy. Articles meeting the inclusion criteria will be searched in the Web of Science and Elsevier ScienceDirect for articles citing these articles. We also review references from included articles.

### Search Strategy

An expert librarian at the paramedical library of the University of Montreal provided assistance for the selection of relevant databases, keywords, and MeSH terms, and the construction of an effective combination of search terms involving breaking down the 2 review questions into concepts. We will seek qualitative, quantitative, and mixed-methods studies. The search for studies will be comprehensive as determined by the 2 review questions and thorough searching by using a variety of search methods, including electronic and manual searches, and by searching multiple and conceivably intersecting resources so as to minimize publication and language biases. We will also search more widely to identify research results circulated as reports or discussion papers, as well identifying gray literature; an expert librarian at the paramedical library of the University of Montreal will also provide access to collections of gray literature. We will acquire the full reports for all unpublished literature before considering whether to include their results in our systematic review. These various strategies for searching studies for the planned review will reduce the impact of publication bias.

We will use the bibliographic software EndNote X8 (Clarivate Analytics) to record and manage references, which will help in documenting the process, streamlining document management, and making the production of reference lists for reports and journal articles easier.

Table 1 lists the search conceptualization and draft search strategy as will be performed in the Ovid Medline database for the 2 review questions (search strategy). We will record and explain any changes or amendments we make. We will record all searches, including Internet searches, hand searching, and contact with experts.

**Table 1.** Ovid Medline search strategy (1946 to December 31, 2016).

| Search no. | Query |
|---|---|
| 1 | exp Epidemiology/ OR exp Epidemiologic Methods/ OR exp Epidemiologic Studies/ |
| 2 | Incidence/ |
| 3 | Prevalence/ |
| 4 | Awareness/ |
| 5 | risk factors/ |
| 6 | Protective Factors/ |
| 7 | "Social Determinants of Health"/ |
| 8 | exp Risk/ |
| 9 | exp Morbidity/ |
| 10 | exp Mortality/ |
| 11 | Comorbidity/ |
| 12 | 1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 |
| 13 | (epidemiolog* OR incidence OR prevalence OR awareness OR "risk factor*" OR burden OR risk* OR determinant* OR morbidit* OR mortality OR comorbidit*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] |
| 14 | 12 OR 13 |
| 15 | exp Hypertension/ |
| 16 | (Hypertens* OR "raised blood pressure" OR "high blood pressure" OR "systolic blood pressure" OR "diastolic blood pressure").mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] |
| 17 | 15 or 16 |
| 18 | Cameroon/ NOT Nigeria.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] |
| 19 | Cameroun.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] |
| 20 | ("Western ADJ highland*"OR Grassfield* OR Bamileke OR Bamoum OR Bamoun OR "Coastal ADJ tropical ADJ forest" OR Bassa OR Douala OR "Southern ADJ tropical ADJ forest" OR Ewondo OR Beti OR Bulu OR Fang OR Maka OR Pygm* OR Baka OR Fulani OR Fulbe OR Peul OR Peuhl OR "Islamic ADJ Northerners" OR "Non-Islamic ADJ Northerners" OR "Centre ADJ region" OR "East ADJ region" OR "South ADJ region" OR "Littoral ADJ region" OR "South ADJ West ADJ region" OR "West ADJ region" OR "North ADJ West ADJ region" OR "Adamawa ADJ region" OR "North ADJ region" OR "Far-North ADJ region" OR "Centre ADJ province" OR "East ADJ province" OR "South ADJ province" OR "Littoral ADJ province" OR "South ADJ west ADJ province" OR "West ADJ province" OR "North ADJ West ADJ province" OR "Adamawa ADJ province" OR "North ADJ province" OR "Far-North ADJ province").mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] |
| 21 | 18 OR 19 OR 20 |
| 22 (Q1[a]) | 12 AND 17 AND 21 |
| 23 | Mass Screening/ |
| 24 | exp Diagnosis/ |
| 25 | exp Therapeutics/ |
| 26 | exp Tertiary Prevention/ OR exp Secondary Prevention/ OR exp Primary Prevention/ |
| 27 | exp Disease Management/ |
| 28 | Early Medical Intervention/ |
| 29 | exp Policy/ |
| 30 | 23 OR 24 OR 25 OR 26 OR 27 OR 28 OR 29 |
| 31 | (Control OR screening OR diagnosis OR measurement OR treatment OR prevention OR management OR intervention OR program OR policy OR action OR Trial).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] |

| Search no. | Query |
|---|---|
| 32 (Q2[b]) | 22 AND 31 |

[a]Q1: review question 1.

[b]Q2: review question 2.

## Updating Literature Searches

We will update the search toward the end of the review, if we carried out the initial searches some time before undertaking the final analysis (eg, 6 months). Updating literature searches will involve rerunning the searches to ensure that no recent articles are missed, after being validated to ensure that the search strategy retrieves a high proportion of eligible studies found through any means and information sources for the planned review. To do this successfully, we will record the date the original search was conducted and the years covered by the search. When doing update searches if necessary, we will use the update date field rather than the actual date, thereby ensuring that we will identify any additions to the database after we conducted the original search. For databases that do not include an update date field, we will run the whole search again and then use reference management software EndNote X8 to remove those records that we have already identified and assessed.

## Study Records

### Selection Process

The selection process will be wholly computerized and the search results will be provided in electronic format, so that they can be imported into the reference management software, EndNote X8, being used by the review team. To determine eligibility of identified studies, parallel independent assessments will be conducted to minimize the risk of errors by two review authors, who will independently screen titles and abstracts during the study selection process, based on the inclusion and exclusion criteria. Neither of the review authors will be blinded to the journal titles or to the study authors or institutions. We will obtain full texts for all titles that appear to meet the predefined eligibility criteria or where there is any uncertainty. We will seek additional information from study authors where necessary to resolve questions about eligibility. Disagreements between the 2 reviewers will be resolved using consensus and arbitration as appropriate by a third member of the review team, or by contacting authors of original studies to resolve any uncertainties; interrater agreement will not be calculated. This should create a sensitive search strategy to capture relevant studies for this review. We will document the study selection process, including detailing reasons for excluding studies. These preventive steps will help minimize bias and errors in the study selection process.

### Piloting the Study Selection Process

To minimize bias, we will pilot the selection process by applying the inclusion criteria to a sample of articles to check that they can be reliably interpreted and that they classify the studies appropriately. We will use the pilot phase to refine and clarify the inclusion criteria and ensure that the criteria can be applied consistently by more than one person. Piloting will also give an indication of the likely time needed for the full selection process.

### Reporting Study Selection

To document the study selection process, we will produce a flow chart showing the number of studies or articles remaining at each stage. This flow chart will adhere to recommendations for reporting and presentation of a flow chart when reporting systematic reviews with or without a meta-analysis [33]. The subject headings of studies meeting the inclusion criteria will be examined to ensure that all relevant terms have been captured. If needed, additional searches will be undertaken. A list of studies excluded from the review will also be reported with the reasons for exclusion and will be included in the report of the review as an appendix. This list will be restricted to "near misses" (ie, those studies that only narrowly failed to meet inclusion criteria and that readers might have expected to see included) rather than all the research evidence identified.

### Data Collection Process

We will keep a record of all searches and search decisions to ensure reproducibility. Search results will be exported to the citation management software EndNote X8. Duplicates will be removed and retained separately. The resulting references will be exported separately to the 2 reviewers for independent review using Excel version 2010 (Microsoft Corporation). As with screening, data extraction will be carried out in duplicate by 2 independent reviewers to reduce bias and reduce errors in data extraction [56]. Using this standardized data collection format, 2 review authors will extract data independently and in duplicate from each eligible study. To ensure consistency between the 2 reviewers, we will conduct calibration exercises before starting the review. Data abstracted will include study design, period of data collection, year of publication, study setting, geographic coverage, demographic information, intervention details, and all reported hypertension-related outcomes. Disagreements between the 2 reviewers will be resolved by a third member of the review team or by contacting authors of original studies to resolve any uncertainties.

Data extraction will also involve collection and scrutiny of detailed raw databases in collaboration with authors of the original study, some of whom are members of the review team (see Conflicts of Interest, below). We will confirm the accuracy of the extracted information to be included in the systematic review and meta-analysis with original researchers, by sending them a copy of the draft review when available with all working files used for data synthesis, assessment of risk of bias, and meta-analysis.

Since data in primary studies may not always be presented in a format that is useful to systematic reviewers, we will contact authors for missing information about exposure and outcome variables and ask authors for this information. We plan to

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contact authors of included studies by email and will endeavor to make up to a maximum of 3 email attempts to obtain missing information.

### Dealing With Duplicates

We will look for duplicate publications of research results to ensure they are not treated as separate studies in the planned review. Multiple articles of a study may be published for reasons such as translation of results to different audiences or reporting of different outcomes, but this may be often concealed (ie, not cross-referenced to one another), and neither authorship nor sample size is a reliable criterion for identifying duplication [57]. Multiple reports from the same study may include identical samples with different outcomes reported or increasing samples with the same outcomes reported. Multiple reporting can lead to biased results, as studies with significant results are more likely to be published or presented more frequently, leading to an overestimation of treatment effects when findings are combined [58]. When we identify multiple reports of a study, we will treat them as a single study, and we will make reference to all the publications. We will also compare multiple publications for any discrepancies, which we will highlight, and contact the study authors for clarification.

### Data Management

To ensure the efficient management of retrieved records, 1 review author will screen the references and record decisions about which documents to obtain and how to code these decisions. We will have a record of decisions made for each article. Decisions about rejecting or obtaining documents will not be made blind to others' decisions, and documents received will be stored in our PRONUSTIC Research Laboratory at the University of Montreal. In addition, 1 review author will be responsible for identifying and removing duplicate references, ordering interlibrary loans, recording the receipt of documents, and following up on nonarrivals. The bibliographic software EndNote X8 will be used to record and manage references, in documenting the process, streamlining document management, and making the production of reference lists for reports and journal articles easier. We will create a "library" (database) of references, so that the whole review team can share information. One review author will be responsible for the library of references. These data management steps will contribute to minimize bias and errors in the data extraction process.

We will search each of the databases using the selected keywords, together with a set of MeSH terms. The retrieved search results will be exported to the reference management software EndNote X8, where duplicates will be excluded. The first step in the selection process will then be completed by 2 independent reviewers, reading through the titles and abstracts of the articles retained. Articles not meeting the eligibility criteria will be excluded. The remaining articles with available full text will be further reviewed by the 2 reviewers based on the defined exclusion criteria, with each reviewer independently reading each of them. Disagreements will be resolved by consulting a third reviewer and during reconciliation meetings. Full-text versions of selected studies will then be examined and coded by 2 reviewers working independently. They will seek to identify relevant information in line with the review questions

and the aim of the review. Once all pertinent literature has been collected and assessed by the 2 reviewers, the main findings of the retained articles will be extracted and integrated into a synthesis table (data extraction form) to ease the manipulation of findings and to organize them for evidence synthesis. Coding will enable reviewers to obtain information on the design, period of data collection, year of publication, study setting, and geographic coverage (ie, rural, urban, or both). Data to be extracted from each article will include author name (s), date of data collection, date of publication, study design, age range of participants, type of place of residence of participants, and ecological zone and region of residence of participants within the country. Coded data will then be extracted using a data extraction sheet, which will be designed based on the objectives of the review. That datasheet will be shared among review team members and will facilitate collaboration among reviewers.

### Data Items

This review will assess the epidemiological landscape of hypertension in terms of geographic coverage (ie, rural, urban, or both), ecological zones and regions of residence of study participants aged 18 years or older, and costs (at the individual, family, community, and national levels) on the one hand, and the control of hypertension on the other hand, both from clinic-based and community-based studies.

From each study, we will extract outcome variables for hypertension and hypertension-related diseases, conditions, and events; hypertensive patient characteristics (eg, average age, sex, age at diagnosis); study design; sample size; and type and source of financial support. Multimedia Appendix 1 presents further definitional details on primary and secondary outcomes to be included in the review. Variables for which data we will seek data are as follows. (1) The frequency and distribution of hypertension and its population impact as measured by its incidence, prevalence, morbidity, or mortality due to hypertension. (2) The occurrence and causes of health effects of hypertension in population subgroups in Cameroon. (3) The awareness of hypertension in the Cameroonian population. (4) The impact of individual-level risks and protective factors (background risk factors such as age, sex, level of education, and genetic composition; behavioral risk factors such as tobacco use, unhealthy diet, and physical inactivity; and intermediate risk factors such as elevated blood lipids, hypertension comorbidities, and overweight and obesity), family-level factors (eg, age of the head of household, family income, family size, family composition, and family socioeconomic status), and community-level factors (social and economic conditions such as poverty level, employment level, socioeconomic status, and social and health infrastructures; environmental factors such as climate or air pollution; and cultural factors such as practices, norms, and values; and urbanization, which influences housing, and access to products and services) in the Cameroon context on morbid conditions. (5) The strategies that have been designed and implemented for the prevention and control of hypertension in various settings and among various population subgroups in Cameroon.

When necessary, we will approximate means and measures of dispersion from figures in the reports. Whenever possible, we

will use results from an intention-to-treat analysis. If we cannot calculate effect sizes, we will contact the study's authors for additional data.

## Outcomes and Prioritization

We will seek the following primary outcomes: diagnosis, evaluation, detection, incidence, prevalence, awareness, treatment, treatment adherence, management, prevention, and control of hypertension.

We will seek the following secondary outcomes: hypertension-related morbidity and mortality, costs of treatment of hypertension, and influential risk factors of hypertension amenable to intervention and prevailing in Cameroon (eg, overweight and obesity) [25].

Specification of the duration of hypertension or a measure of the severity of hypertension by physical examination, retinal funduscopy, chest roentgenogram, electrocardiogram, blood urea nitrogen measurement, and urinalysis using a range of clinical assessments, exercise tests, biochemical markers, and echocardiographic and hemodynamic assessments (eg, presence of end-organ damage, including the kidneys, eyes, and heart) will not be required for inclusion, although this information will be extracted if available and will contribute toward assessment of risk of bias.

## Risk of Bias of Individual Studies

Our review will critically appraise relevant studies conducted using either quantitative, qualitative, or mixed research approaches. To ease the assessment of possible risk of bias (or "quality") for each study and the evaluation of the overall strength of evidence of the planned review, we will use a tool designed and validated for this purpose by Downs and Black [59]. The Downs and Black checklist consists of 27 items that cover the following risk-of-bias domains: reporting, external validity, internal validity (bias and confounding), and power. The psychometric properties of the Downs and Black checklist have been validated previously [59]. For each domain in the tool, we will describe the procedures undertaken for each study. In the event of insufficient detail reported in the study to judge the risk of bias, we will contact the study investigators for more or missing information. We will judge the possible risk of bias on each of the 6 domains based on the extracted information.

Two review authors with extensive risk-of-bias assessment experience will independently perform these assessments. The 2 review authors will not be blinded to studies, agreement between them will not be evaluated, and disagreements between them will be resolved first by discussion and then by consulting a third author for arbitration. We will compute graphic representations of potential bias within and across studies using Excel version 2010. We will first consider each item in the risk-of-bias assessment independently, and then we will collate and assign an overall score. Scores range from 0 to 28, with higher scores indicating a better methodological quality of the study. The following cut offs have been suggested to categorize studies by quality: excellent (26-28), good (20-25), fair (15-19), or poor (≤14), based on how likely further research is to change the confidence in the estimate of the effect [60]. Risk-of-bias assessments will be incorporated into data synthesis through

subgroup analyses and their potential influence on findings of the planned review.

## Data

Our planned systematic review aims to synthesize the results of all relevant studies on hypertension in Cameroon. Synthesis will involve the collation, combination, and summary of the findings of individual studies included in the systematic review. Synthesis will be done quantitatively using meta-analysis or, if formal pooling of results is inappropriate, through a narrative approach. As well as drawing results together, synthesis will consider the strength of evidence, explore whether any observed effects are consistent across studies, and investigate possible reasons for any inconsistencies. This will enable reliable conclusions to be drawn from the assembled body of evidence.

We will summarize and present our findings in text and tables to describe the characteristics of included studies, as well as their findings, in line with the objectives of the review and the 2 review questions. We will present results in order by (1) review question, (2) within each review question, in order of primary and then secondary outcomes, and (3) within each outcome, in order of "concept" in the title of the manuscript. To be comprehensive, we will include studies with any level of risk of bias in our analyses, and we will present information in tables by risk-of-bias level.

### Quantitative Synthesis

We will use quantitative synthesis involving meta-analyses using a random-effects model and a metaregression model if the included studies are sufficiently homogeneous in terms of design and comparator. In Multimedia Appendix 1, we describe, with reference to the PICO (population, intervention or indicator, comparison, outcome) criteria, primary and secondary outcomes by study setting (clinic vs community or population-based studies) that we will consider for such statistical synthesis. These outcomes will rely on measured SBP and DBP, self-reported diagnosis of hypertension by a health professional, and self-reported current use of antihypertensive medication.

For analyses of dichotomous-event data (eg, hypertension-related morbidity and mortality; hypertension with other comorbidities present), we will use risk ratio with 95% CI. Continuous outcomes will be analyzed using weighted mean differences (with 95% CI) or standardized mean differences (95% CI) if different measurement scales are used. Skewed data and nonquantitative data will be presented descriptively.

### Unit of Analysis

The unit of analysis will be the individual study.

### Dealing With Missing Data

When data are missing, we will attempt to contact the original authors of the study to obtain the relevant missing data. Important numerical data will be carefully evaluated. If we cannot obtain missing data, we will use an imputation method. We will use sensitivity analysis to assess the impact on the overall treatment effects of inclusion of trials that do not report an intention-to-treat analysis, have high rates of participant attrition, or have other missing data.

## Assessment of Heterogeneity

We will test clinic and community heterogeneity by considering the variability in participant factors across studies (eg, age, sex, type of place of residence, ecological zone of residence, hypertension with or without comorbidity) and study factors (eg, study location, study design, year of data collection, type of BP measurement device used). Statistical heterogeneity will be tested using the chi-square test (significance level: 0.1) and $I^2$ statistic (0% to 40%: might not be important; 30% to 60%: may represent moderate heterogeneity; 50% to 90%: may represent substantial heterogeneity; 75% to 100%: considerable heterogeneity) [61]. If heterogeneity among the studies is high ($I^2 \geq 50\%$ or $P < .1$), we will analyze the study design and characteristics in the included studies. We will try to explain the source of heterogeneity by subgroup analysis or sensitivity analysis. The pooled odds ratio (or rate ratio) will be calculated and between-study heterogeneity will be determined by visual inspection of the forest plots and with consideration of the $I^2$ statistic. The Egger test and visual inspection of funnel plots will assess small study effects [62].

## Statistical Data Synthesis

Meta-analysis will be carried out on the published results of relevant empirical studies on hypertension in Cameroon to address the 2 review questions. Pooled analyses will be undertaken for relevant studies of the adult population aged 18 years or older, for each review question and for each outcome of interest in turn. Each outcome will be combined and calculated using the statistical software STATA 13.1 (StataCorp LP). If we observe statistical heterogeneity (ie, $I^2 \geq 50\%$ or $P < .1$), we will choose the random-effects model because this model assumes that the aggregated results should be valid beyond the sample used by each study and are based on both participant characteristics and study design [62]. If heterogeneity is considerable (ie, $I^2 \geq 75\%$), we will not perform a meta-analysis; instead, we will do a narrative, qualitative summary.

## Qualitative or Narrative Synthesis

Due to diversity in study populations, interventions, and outcomes, quantitative synthesis may not be appropriate. If this happens, we will provide a systematic narrative synthesis including information presented as text and in tables to summarize and explain the characteristics and findings of the included studies. The narrative synthesis will explore the relationship and findings both within and between the included studies, in line with the guidance from the Centre for Reviews and Dissemination [63].

The strategy for data narrative synthesis will be as follows. We will present the general characteristics of the reviewed studies in tables. Content analysis will be carried out by each of the 2 independent reviewers of each study to identify therein evidence on the epidemiology and control of hypertension in various settings and among various population subgroups in Cameroon.

## Analysis of Subgroups or Subsets and Metabiases

For each review question, we plan to carry out pooled analyses for examining the extent to which measured indicators of the epidemiology and control of hypertension vary by type of place of residence (ie, rural, urban, or both) and agroecological zone or region in Cameroon, if data are appropriate for such analyses. Separate meta-analyses will be done for studies conducted in people with hypertension only versus hypertension with other conditions or diseases.

We will incorporate the risk-of-bias assessments into data synthesis through pooled analyses undertaken for exploring how a potential source of bias may influence our review findings, by presenting estimates of prevalence, awareness, and risk factors of hypertension by quality category (ie, excellent, good, fair, or poor).

We will explore the robustness of meta-analyses by using pooled analyses undertaken for investigating possible causes of between-study heterogeneity and variability based on (1) the characteristics of participants (eg, age, sex, type of place of residence, agroecological zone or region of residence), and (2) the characteristics of studies (eg, sample size, study location, study design, year or period of data collection).

Sensitivity analysis will be performed to explore the source of heterogeneity by doing subgroup or metaregression analyses according to risk of bias by comparing the high-risk versus the low-risk studies. Pooled sensitivity analyses will be performed with a hypertension definition and measurement procedure (duration of rest prior to measurement, measurement arm, position of patient during measurement, BP measuring device, cuff size, number of measurements taken, and interval between measurements).

## Dissemination

To ensure that the essential messages from the planned review reach the appropriate audiences, we will disseminate the review findings (1) in Cameroon, especially to relevant ministries, institutions, and organizations involved in hypertension and comorbidities; (2) through national and international conferences; and (3) through publication in peer-reviewed journals.

## Ethical Approval of the Protocol

Since this will be a systematic review of published literature, we required no ethical approval for developing this protocol. However, we will ensure that all studies included in our review provided evidence of ethical approval and informed consent from all patients or respondents where required.

Data from studies included in the review will have been obtained with participant consent and ethical approval. If this is not stated in the article, we will contact the authors for confirmation.

Our funding bodies or the institutions of affiliation did not require that they formally approve the protocol, and they took no part in its design or development.

## Protocol Amendments During the Review

To ensure that our review is useful to end users, we will readily amend the protocol during the review if required, should consideration of the primary research raise questions that we did not anticipate at the protocol stage. If such consideration results from a clearer understanding of the review question(s), we will carry out documented and justified amendments to the

protocol. In that case, in the report of the review findings, we will distinguish between the initial review question(s) and any subsequent amendments. Protocol amendments (if any) will be documented in a protocol addendum and in the final report of the review.

## Results

This review is part of an ongoing research program on disease prevention and control in the context of the dual burden of communicable diseases and NCDs in Africa. The first results are expected in 2017.

## Discussion

Studies of hypertension detection, prevalence, awareness, treatment, management, and control over the last 70 years or so show globally increasing hypertension disparities across geographic and ecological settings in a wide range of populations and health care systems of HICs and LMICs [12,51,64-67], as well as strikingly divergent portraits across countries. The highest BP levels have shifted from HICs to low-income countries in South Asia and SSA, while BP levels have been consistently high in Central and Eastern Europe [12,51,67]. The global prevalence of raised BP in adults aged 18 years or older was 22% in 2014, with Africa being the most affected region with a 30% prevalence [3]. By and large, published international and WHO guidelines are unsuitable for application in many ethnically diverse populations of countries in SSA because their economic, ecological, sociocultural, and health care environments, poor infrastructure hindering health-promoting lifestyles, and unaffordability for the patients impede the adoption of recommended nonpharmacological and pharmacological treatment [23,30,32,68-70]. Moreover, good-quality data on hypertension in different ethnic populations in much of SSA are notoriously missing in the treatment guidelines, which are largely based on white populations, whereas cardiovascular disease varies with ethnic origin [71]; of the more than 180 studies that met the standards of the Eighth Joint National Committee, fewer than 30 were from nonwhite, non-African American groups [9]. National hypertension evidence in SSA is urgently needed for translating new knowledge and providing up-to-date information and recommendations for hypertension prevention and control to health care providers at different levels of the health care system pyramid, including primary health care and community programs at the base of the pyramid for the primary prevention of hypertension especially.

The world population is projected to reach 9.7 billion by 2050 and, with the highest rate of population growth, Africa is expected to account for more than half of the world's population growth between 2015 and 2050 [72]. Hypertension in SSA is viewed as "a massive and increasing health disaster" [73]. It is estimated that the number of adults with raised BP increased from 594 million in 1975 to 1.13 billion in 2015, with the increase largely in LMICs; moreover, the global increase in the number of adults with raised BP is a net effect of increase due to population growth and aging on the one hand, and of decrease due to declining age-specific prevalence of hypertension on the

other [11,12]. Such divergent trends are indicative of underlying large and widening disparities in hypertension prevention and control across countries [51,65-67]. They are also expressions of fundamental within-country differences between rural and urban communities in hypertension awareness, diagnosis, treatment, and management [19,23,51], and effective use and appropriateness of medications for controlling hypertension for the SSA populations. Current guidelines are generally extrapolations of findings among people of African descent living in Western countries [23,32], despite differences in prevailing influential country-specific factors affecting hypertension risk, including ecological factors [74-82], community endowments [83,84], and social disparities [85], above and beyond social and economic inequalities [86]. Indeed, advances in a wide range of biomedical, biological, behavioral, and social sciences have been expanding our understanding of how early and continuing environmental influences (the ecology) and genetic predispositions (the biologic program) independently or synergistically affect human behaviors, functions, and lifelong health [79,83,87-89]. It is estimated that incidence rates of hypertension range between 3% and 18%, depending on the age, sex, ethnicity, and body size of the population studied [90]. According to recent estimates, the geographical variation in the distribution of hypertension is intensifying in several regions of the world, notably in LMICs, which now simultaneously have to grapple with the double burden of communicable diseases and NCDs despite limited health care resources [91-93].

These divergent trends and widening disparities call for urgent interdisciplinary and intersectoral collaborative endeavors between national and international stakeholders and researchers to combat the rising hypertension burden in LMICs. This could be done using country-specific knowledge bases and circumstances to develop or improve national hypertension guidelines for the control and prevention of hypertension, in order to reverse these trends and reduce the hypertension-related preventable and avoidable burden of morbidity, disability, and mortality in LMICs.

What is urgently needed is a better and locally situated understanding of the risk and protective factors associated with within-country disparities in hypertension prevention and control in the context of these divergent trends across countries. While we are learning more about levels and trends across countries from models providing estimates using existing and often defective but comparable data [11,12], there is an alarming lack of local data. Such data are more informative for designing and monitoring the effectiveness of the implementation of nationally appropriate policies, standards, and guidelines for medical practice in primary care typically found in the health care environments of LMICs in general and those of SSA in particular.

The evidence assembled from the planned review will fill some of the gaps in knowledge in these areas for Cameroon. With limited human and financial resources and increasing rates of NCDs, paramount among which is hypertension, African countries such as Cameroon must prioritize more cost-effective preventive approaches tailored to local circumstances and that can reach not only hypertensive patients coming to health facilities, but also the overwhelming majority of the population,

who rarely attend health care facilities and yet are at risk of hypertension-related diseases, conditions, and events. Well-informed and trained stakeholders through the health system pyramid urgently need such evidence for fulfilling their important role in disease prevention (primary, secondary) and control, as they provide a primary point of contact for individuals who are healthy, at risk, or have diagnosed chronic illnesses such as hypertension. These stakeholders are also trusted sources of health information. Indeed, the World Health Assembly endorsed the WHO Global Action Plan for the Prevention and Control of Noncommunicable Diseases 2013-2020 in May 2013, according to which governments from member states were urged to (1) set national NCD targets for 2025 based on national circumstances, and (2) develop multisectoral national NCD plans to reduce exposure to risk factors and enable health systems to respond in order to reach these national targets in 2025 [8]. For raised BP, the target is a 25% relative reduction in the prevalence of raised BP or to contain the prevalence of raised BP, according to national circumstances; the indicators are the age-standardized prevalence of raised BP among persons aged 18 years or older (defined as SBP ≥140 mm Hg, DBP ≥90 mm Hg, or both) and mean SBP. The Global Plan provides a roadmap for country-led action for the prevention and control of NCDs; any effective action by a national government will depend on the extent of understanding of its country-specific circumstances, for which there are huge data needs, and gaps in knowledge and evidence, for African countries [23,30,32,67-70,91]. There is an urgent need to systematically map evidence on hypertension and comorbidities from clinic-based and community-based data reflecting within-country circumstances, so that the implementation of strategies and actions to curb the epidemic of hypertension is evidence based at the local or hospital level, where the costs, impacts, and benefits of health technologies and strategies can be directly assessed. Such assessment will have an impact on a hospital's budget, clinical practices, and patient outcomes. It is also needed to better inform health care costs, which have become a primary concern of public policy in HICs, and increasingly in LMICs, due to the growing size of the aging population. The prevention and control of NCDs hinges on hypertension, which is the most common noncommunicable condition seen in primary care in HICs and LMICs alike [9,11,64,66,94].

The epidemiology and control of hypertension within the national circumstances of LMICs, which are increasingly bearing the greatest burden of NCDs in general and hypertension in particular, have only started to be fully described and appreciated in the continuing epidemiological landscape of the dual burden of communicable diseases and NCDs in SSA [88]. Much research still remains to be done into how the risk factors for hypertension are distributed in subpopulations across the ecological and areal contexts of these countries, especially across the sociocultural and environmental diversity of a country such as Cameroon, where patients with hypertension-related diseases, conditions, and events are a large portion of adults with cardiovascular diseases [27].

This review will shed light on the epidemiological landscape of hypertension in Cameroon, as well as the control strategies that have been designed and successfully implemented to mitigate the burden of hypertension. It will depict the quality and quantity of hypertension-related research output in Cameroon. This information will be relevant for mapping out mitigation strategies. We also hope that this review will highlight important aspects of hypertension in Cameroon that require further research and evidence. Cameroon is commonly denoted as "Africa in miniature," and what will be documented in miniature in Cameroon may be enlarged to an SSA ecological scale for hypertension prevention and control.

## Authors' Contributions

BKD is the guarantor of the review. BKD conceived of this study, conceptualized the review, and prepared the protocol manuscript. All other authors reviewed and contributed to this manuscript. The corresponding author had final responsibility for the decision to submit the manuscript for publication.

## Conflicts of Interest

The review members were selected in Cameroon and internationally, based on expertise in hypertension, primary care, geriatrics, cardiology, neurology, endocrinology, nephrology, gynecology and obstetrics, nursing, pharmacology, clinical trials, pharmacogenomics, genetics, computational medicine, program evaluation, ethnomedicine/medical anthropology, public health and epidemiology, health care systems, informatics, the development and implementation of clinical guidelines in systems of care, malaria, HIV/AIDS, translational research, health promotion, psychology and psychopharmacology, lifestyles, nutrition, smoking, alcohol, study design, economics of health and health care, governance in the health sector, the design, implementation, and evaluation of health interventions, sociohistorical aspects of health and pluralism in health, knowledge transfer, implementation science, inequity and inequality in health, and biostatistics. The review members also include the Technical Advisor of the Ministry of Public Health of Cameroon (Samuel Kingue), the former president of the International Diabetes Federation (Jean-Claude

Mbanya), and the Chair of the Pan-African Society of Cardiology (PASCAR) Task Force on Hypertension (Anastase Dzudie). All review members will disclose any potential conflicts of interest, including their publications that may be evaluated in this review and any relationships with industry. Those with conflicts will be allowed to participate in discussions and appraisal of evidence from published work as long as they declare their relationships, but they will recuse themselves from voting on evidence statements and recommendations relevant to their relationships or conflicts. Review members who have relationships with industry or potential conflicts to disclose will do so at the outset of the process of systematic review.

## Multimedia Appendix 1

Outcomes of hypertension, definitions, and core indicators for clinic-based or community-based studies.

[PDF File (Adobe PDF File), 38KB - resprot_v6i5e102_app1.pdf ]

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## Abbreviations

**BP:** blood pressure
**DBP:** diastolic blood pressure
**HICs:** high-income countries
**HIV:** human immunodeficiency virus
**LMICs:** low- and middle-income countries
**MeSH:** Medical Subject Headings
**NCD:** noncommunicable disease
**SBP:** systolic blood pressure
**SSA:** sub-Saharan Africa
**UI:** uncertainty interval
**WHO:** World Health Organization

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Protocol

# An mHealth Framework to Improve Birth Outcomes in Benue State, Nigeria: A Study Protocol

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## Abstract

**Background:** The unprecedented coverage of mobile technology across the globe has led to an increase in the use of mobile health apps and related strategies to make health information available at the point of care. These strategies have the potential to improve birth outcomes, but are limited by the availability of Internet services, especially in resource-limited settings such as Nigeria.

**Objective:** Our primary objective is to determine the feasibility of developing an integrated mobile health platform that is able to collect data from community-based programs, embed collected data into a smart card, and read the smart card using a mobile phone-based app without the need for Internet access. Our secondary objectives are to determine (1) the acceptability of the smart card among pregnant women and (2) the usability of the smart card by pregnant women and health facilities in rural Nigeria.

**Methods:** We will leverage existing technology to develop a platform that integrates a database, smart card technology, and a mobile phone-based app to read the smart cards. We will recruit 300 pregnant women with one of the three conditions—HIV, hepatitis B virus infection, and sickle cell trait or disease—and four health facilities in their community. We will use Glasgow's Reach, Effectiveness, Adoption, Implementation, and Maintenance framework as a guide to assess the implementation, acceptability, and usability of the mHealth platform.

**Results:** We have recruited four health facilities and 300 pregnant women with at least one of the eligible conditions. Over the course of 3 months, we will complete the development of the mobile health platform and each participant will be offered a smart card; staff in each health facility will receive training on the use of the mobile health platform.

**Conclusions:** Findings from this study could offer a new approach to making health data from pregnant women available at the point of delivery without the need for an Internet connection. This would allow clinicians to implement evidence-based interventions in real time to improve health outcomes.

**Trial Registration:** ClinicalTrials.gov NCT03027258; https://clinicaltrials.gov/ct2/show/NCT03027258 (Archived by WebCite at http://www.webcitation.org/6owR2D0kE)

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# Introduction

## Background

An estimated 10% of the 2.8 million newborns who died worldwide in 2013 within 28 days of birth were born in Nigeria [1]. Most of these deaths were from diseases and conditions that are often associated with the quality of care around the time of childbirth and are readily preventable or treatable with effective interventions [2-4]. The most recent figure for under-5 child mortality in Nigeria is 124 per 1000 live births [5]. Among preventable diseases that contribute to these deaths and related morbidities are HIV and hepatitis B virus (HBV) infection and sickle cell disease (SCD), with their occurrence facilitated by health system challenges such as delays in accessing quality care. The outcome is that, despite the availability of evidence-based interventions for prevention, HIV and HBV infections and SCD remain endemic in sub-Saharan African countries [1,2,6].

Nigeria alone accounted for an estimated 26% of the global burden of new HIV infections among children [7,8]. Nigeria is one of the 22 priority countries identified by the World Health Organization that collectively account for nearly 90% of all new HIV infections among children annually [7,9]; it is one of only four countries with an HIV testing rate less than 20% among pregnant women [7]. Early identification of HIV-infected pregnant women remains a critical component of prevention of mother-to-child transmission (PMTCT) of HIV.

HBV infections remain endemic in Nigeria with liver cancer now the most common cause of cancer deaths [10,11]. The risk of perinatal transmission is higher when a pregnant woman is coinfected with HIV and HBV [11-16]. Administration of hepatitis B vaccine shortly after birth and hepatitis B immunoglobulin when available has been shown to greatly reduce the risk of perinatal transmission of HBV [15]. However, missed opportunities for prevention continue to occur in resource-limited settings; this is due to poor quality of care for at-risk pregnant women and their newborns related to lack of point-of-care diagnosis and early intervention at the time of delivery [17].

Nigeria has the highest burden of SCD in the world with an estimated 150,000 children born annually with the disease [6,18]. Despite the availability of inexpensive interventions, such as pneumococcal vaccination and penicillin prophylaxis, an estimated 50%-80% of these children with SCD suffer early death before their fifth birthday due to infections [19]. Identification of infants with SCD through newborn screening and early implementation of these simple interventions have been shown to decrease mortality.

Nigeria has developed a policy framework for introduction of critical information and communication technology (ICT) infrastructure by 2020 to support the efforts toward universal health coverage [20]. The Nigeria Federal Ministry of Health (FMOH), which provides leadership for the government's health agency, seeks to establish and scale up innovative point-of-care tools, including mHealth solutions to improve patient care and shared use of health information. Such integrated approaches will support service delivery to HIV-infected patients and provision of primary care through agencies of government, including the National Agency for the Control of AIDS and the National Primary Health Care Development Agency. Previous efforts of the FMOH, supported by the United Nations Foundation and other partners, led to the development and ongoing implementation of a strategic project (project No. ICT4SOML) to support the scale-up of maternal and child health services in the country in order to save one million lives of women and children [21].

To effectively improve health outcomes and to avoid significant social and economic losses, a health system has to be suited to use health technology to inform early interventions [4]. However, Nigeria's health system faces great challenges in tackling perinatal transmission of HIV and HBV and in reducing deaths among children with SCD. Major barriers to effective intervention include lack of adequate health facilities, limited access to health care providers, long distance to health facilities, transportation, and high out-of-pocket costs for patients. Other barriers, such as low perception of personal risk, poor access to testing sites, cost, confidentiality, and HIV-related stigma, have been identified to impair HIV testing and PMTCT completion in Nigeria [22].

Our initial focus on HIV, HBV, and SCD is based on several factors: (1) they are prevalent in the communities where the Healthy Beginning Initiative (HBI) was implemented; HIV prevalence among pregnant women was 2.7%, prevalence of hepatitis B surface antigen was 5%, and sickle cell trait was 23%; (2) they were identified by pregnant women, their male partners, and community leaders as conditions important to their health; (3) community screening for these conditions were well accepted during HBI implementation; (4) the integration of both communicable and noncommunicable health problems showcase the dual problem facing sub-Saharan Africa; and (5) evidence-based guidelines exist for the management of infants with SCD and infants at risk of HIV and HBV.

## Potential Opportunities to Improve Health Outcome Using Mobile Technologies

To maximize effectiveness of lifesaving interventions for maternal, newborn, and child health, available evidence suggests that such strategies should be delivered under the principle of continuum of care for mother and child, from pregnancy through birth, the newborn period, infancy, and childhood [4,23]. Yet, in resource-constrained settings like Nigeria, there are often delays in implementing lifesaving interventions due to difficulties in accessing care and problems with the quality of care provided [22]. Information gaps on maternal and child health interventions, as well as structural barriers and behavioral limitations on the demand side, hinder access to lifesaving interventions [24]. As a result, implementation of simple,

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cost-effective, culturally adapted, and sustainable interventions are needed to save more children's lives [4].

## Integration of Mobile Health Technologies and Medical Decision Making

The use of mHealth with integrated data and medical decision algorithms has the potential to spread implementation of evidence-based interventions. As a marked departure from current practice, we propose integrated community-based screening and availability of data at the point of delivery using mHealth to enhance care. Nigeria is Africa's largest mobile market with over 114 million mobile phone users and a high penetration of Internet services through mobile networks [25]. The use of mHealth is a feasible and cost-effective intervention for improving maternal and perinatal outcomes in Nigeria. It can be used to increase access to health information and reduce turnaround times for receipt of laboratory test results.

## Preliminary Studies

The HBI is a community-driven, congregation-based intervention that provides health education and on-site integrated laboratory testing—HIV plus hepatitis B and sickle cell genotype—during church-organized baby showers. In 2014, we demonstrated that the HBI was feasible, acceptable, and effective in increasing uptake of HIV, hepatitis B, and sickle cell genotype testing among pregnant women and identification of infected/affected women in southeast Nigeria (National Institutes of Health [NIH] grant No. R01HD075050) [22,26]. We subsequently demonstrated that when maternal results are made available at the point of delivery, clinicians were more likely to initiate antiretroviral prophylaxis for the HIV-exposed infant and give the first dose of hepatitis B vaccine to an infant born to a mother with hepatitis B surface antigen within 24 hours. Clinicians were also more likely to screen infants for SCD, who were born to mothers with sickle cell trait, to allow for early institution of penicillin prophylaxis and appropriate immunization. Until recently, the use of information technology to make prenatal data available at the point of delivery has been limited to high-income countries due to poor infrastructure in developing countries. Fortunately, the unprecedented spread of mobile technology has made it possible to develop mHealth platforms that can be used to provide similar services to hard-to-reach communities in resource-limited settings [23,27]. This has led to improved quality of care and decreased rate of unnecessary testing, and has allowed for early institution of evidence-based interventions that improve birth outcome [28-31].

## Our Proposal and Objectives

We propose to develop an integrated mobile health platform that is able to collect data in the community, integrate collected data into a smart card, and read the smart card using a mobile phone-based app without the need for Internet access.

Our primary objective is to determine the feasibility of developing this integrated mobile health platform. Our secondary objectives are to (1) determine the acceptability of the smart card among pregnant women and (2) determine the usability of the smart cards by the pregnant women and health facilities.

# Methods

## Ethical Consideration

This study was approved by the Institutional Review Board of the University of Nevada, Las Vegas, and the Nigerian National Health Research Ethics Committee. This study was registered with ClinicalTrails.gov (ClinicalTrials.gov identifier NCT0302725).

## Theoretical Framework

Glasgow's Reach, Effectiveness, Adoption, Implementation, and Maintenance (RE-AIM) framework is used as a guide to assess the implementation of the mHealth platform. The RE-AIM framework offers a comprehensive approach to considering five dimensions important for evaluating the potential public health impact of an intervention [32]. The model includes the following: (1) *Reach*, the percent and representativeness of individuals willing to participate; (2) *Effectiveness*, the impact of the intervention on targeted outcomes and quality of life; (3) *Adoption*, the percent and representativeness of settings and intervention staff that agree to deliver a program; (4) *Implementation*, the consistency and skill with which various program elements are delivered by various staff; and (5) *Maintenance*, the extent to which individual participants maintain behavior change long term and, at the setting level, the degree to which the program is sustained over time within the organizations delivering it [32]. *Reach* and *Effectiveness* will assess feasibility and acceptability, while *Adoption*, *Implementation*, and *Maintenance* will assess usability and sustainability of the mHealth platform.

## Study Settings and Participants

Our proposed study is anchored on the intervention for Sustained Testing and Retention (iSTAR) Among HIV-infected Patients, an ongoing NIH-funded study in Benue state, north-central Nigeria (NIH grant No. R01HD087994-01). The iSTAR is based on the HBI, our previous work that demonstrated that pregnant women and their male partners can be effectively screened in the community for HIV, SCD, and HBV (NIH grant No. R01HD075050) [22,26]. In 2012, Benue state was projected to have a population of 4,768,877, with 49.6% females and a fertility rate of 4.9% [33]. According to the 2013 Nigeria Demographic and Health Survey, about 70% of the female population had attained less than a secondary education with a literacy rate of 52.8%. Most (74.8%) were farmers residing in rural areas [34]. Preliminary data from our ongoing study demonstrates that in Benue state, prevalence rates of HIV, HBV, and SCD among pregnant women is 7.8%, 11.13%, and 19.1%, respectively.

## Participant Recruitment—Healthy Beginning Initiative

A detailed description of the baby shower program has been published previously [22]. The HBI was designed and initially tested in southeastern Nigeria as a sustainable, culturally adapted, community-driven program delivered by community health advisors to identify pregnant women, implement health interventions, and support linkage to health services for women and their families. Briefly, it has three main platforms: (1) prayer sessions during church services are used to identify pregnant

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women, allowing for multiple opportunities to offer health interventions; (2) church-organized baby showers are used to implement interventions that include health education and on-site integrated laboratory screening, including HIV testing; and (3) baby receptions held 6-8 weeks after birth following infant baptism to enhance postdelivery follow-up and increase early infant diagnosis [22,23]. The United States President's Emergency Plan for AIDS Relief (PEPFAR)-supported implementing partner in Benue state, Caritas Nigeria, has scaled up this approach in the priority areas where the proposed study will be conducted.

## Study Procedure

### Overview

We will leverage existing technology to develop a mobile health platform that integrates a database, smart card technology, and a mobile phone-based app to make results available at the point of care without the need for Internet connection. Subsequently, we will recruit 300 women who attend church-organized baby shower programs in the four priority local government areas and who consent to participate in the study.

### Inclusion and Exclusion Criteria

Participants are eligible if they have a positive test result for (1) HIV, (2) hepatitis B surface antigen, and/or (3) sickle cell trait or disease, as defined by heterozygosity (AS) or homozygosity (SS), respectively, for the S variant of hemoglobin β-subunit; and (4) are residing in the local government areas where the four health facilities are situated. Those who decline to have their test results uploaded on the secure Web-based database will be excluded.

Data from the ongoing HBI will be reviewed by study staff to determine eligible participants. Trained research assistants will approach each participant independently to inform them about the study. HBI participants who consent to enroll in the study will have data collected from their community screening session stored in a secure, Web-based database. The stored data will be encrypted into a Quick Response (QR) code embedded on a *smart card* with a unique identification number printed on the outside of the card. There will be no names or any other identifiers. The smart card will be offered to each participant. The research assistants will administer a questionnaire to each participant to collect information on acceptability of the smart card. Each participant will be asked to present the smart card at prenatal visits and delivery at the selected health care facility. At the health care facility, we will identify dedicated delivery room staff that will be trained to scan the smart card and read its contents using the mobile phone app without the need for Internet connection. Mobile phones will be provided to each facility to use for the duration of the study. When a participant presents at delivery without the card, information can still be obtained from the secure, Web-based database and confirmed using the participant's name, date of birth, and mobile phone number.

## Study Outcomes and Analysis

### Acceptability

We will assess the proportion of pregnant women who are willing to allow health care workers to retrieve information from their card.

### Reach and Effectiveness

Reach will be calculated as the number of enrolled pregnant women relative to the number of eligible pregnant women in the study catchment area. The effectiveness will be determined by assessing the impact of the mHealth platform on key outcomes, such as screening for HIV, HBV, and sickle cell genotype and health care utilizations for follow-up visits. This will be measured by calculating the percentage of pregnant women that use the smart cards at the point of delivery, thus reducing the need for repeat testing and reducing missed opportunities for reduction of perinatal transmission of HIV and HBV and deaths among children with SCD. The reach and effectiveness of the mHealth platform will be captured through patient records and recruitment assessments.

### Assessing Usability by Participants

We will conduct semistructured key informant interviews and focus group discussions with participants to assess perceived social support, obstacles, or barriers with using the cards at the point of delivery. The Perceptions, Enablers, and Nurturers (PEN-3) cultural model [35-37] centralizes culture in the design, implementation, and evaluation of any health intervention. This model will be used as a guide to assess how well informed participants feel with using the tools provided (ie, the smart card), whether its values are clarified, and whether they feel supported in using it as a resource in delivering their personal health information. In particular, we will examine (1) perceptions that may contribute to or hinder use of the smart cards; (2) the enablers or community/health factors, such as the role of health care workers in influencing participants' use of the cards; and (3) the nurturers, or the role of family, social, or community networks in reinforcing the use of the smart cards. These perceptions, enablers, and nurturers will then be examined to identify whether they are positive (ie, factors that will lead participants to engage with the mHealth platform in general), existential (ie, practices that are unique and have no harmful health consequences), and/or negative (ie, factors that lead participants not to engage with the mHealth platform). The interviews and focus group discussions will be digitally recorded and transcribed verbatim. All data will be analyzed using NVivo version 11 (QSR International) and Krueger's framework analysis approach, which provides a clear series of steps for qualitative data analysis, including familiarization, identifying a thematic framework, indexing and charting (ie, managing the data, data reduction), mapping, and interpretation [38].

### Assessing Usability by Health Care Workers

We will assess the proportion and representativeness of health care settings and health care workers who are willing to use the mobile health platform in the study catchment area. To achieve this, we will calculate adoption rates using the proportion of interested health care settings relative to the total number eligible for participation. For implementation, we will capture the degree

to which the mHealth platform is used as intended (ie, delivery fidelity) and by trained health care workers (ie, enactment fidelity). For maintenance, we will examine the extent to which the mHealth platform is sustained as part of routine practice in the health care settings (ie, institutionalization) at least 6 months postintervention, leadership support for sustainability or in the health care settings, as well as sustainability climate (ie, providers' perceptions of the extent to which policies and practices in the health care settings support sustainment of the mobile health platform).

Following introduction and invitation to participate in this study, an expert panel of health care workers (n=8) [39] will assess the usability of the mHealth platform using a diverse *think-aloud heuristic* protocol. Think-aloud and heuristic evaluations are the most commonly used usability evaluation methods [39]. With *think aloud*, potential users are asked to complete a set of tasks with the artifact tested (ie, mHealth platform) and verbalize their thoughts as they work on the task [39,40]. It has been found to have high face validity since the data collected reflects actual use of an artifact and not the participant's judgment about its usability [40]. With heuristic evaluation, the experts inspect a system (ie, mHealth) and evaluate its interface against a list of recognized usability principles known as heuristics [41,42]. These heuristics, which refer to common properties of usable systems, are based on Nielsen's set of 10 usability principles: (1) use simple and natural dialogue, (2) speak the user's language, (3) minimize memory load, (4) be consistent, (5) provide feedback, (6) provide clearly marked exits, (7) provide shortcuts, (8) provide good error messages, (9) prevent errors, and (10) provide help and documentation [39,43]. For this study, each expert will individually evaluate the mHealth platform in two steps: navigation and analysis. In the navigation step, the expert will become familiar with the structure and scope of the mHealth platform. In the analysis step, the expert will focus on the design of the platform to determine whether it complies with Nielsen's 10 general usability principles for interaction design. Following the evaluation, a consensus meeting will be held with the experts to identify usability problems and quantify the severity of the problems based on Nielsen's severity rating scale, which takes into account the frequency (ie, Is the problem common or rare?), impact (ie, Is it difficult or easy for end users to address?), and persistence (ie, Is it a one-time problem or does it trouble end users repeatedly?) of the problem [44]. The problems and notes from the evaluations will be analyzed using standard descriptions that will compare the number of problems among experts and their severity.

## *Conducting the Concept-Mapping Sessions*

We will use concept mapping to gather crucial information from stakeholders regarding sustainability of the overall mHealth platform in the study area. Concept mapping is a structured, participatory, mixed-methods approach to data collection that engages stakeholders in the research and theory generation process [45,46]. It integrates qualitative data with quantitative multivariate statistical analyses to describe ideas on a topic of interest and represent these ideas visually through a series of related two-dimensional maps [47]. It will be used in this study to assess the factors that may facilitate or limit the continued use of the mHealth platform in the study area over time. The

recommended minimum number of participants for concept mapping is 40 [47]. We seek to recruit approximately 60 participants in order to enable subgroup analyses and to allow for modest attrition rates at each step of the concept-mapping exercise. Baseline demographics will be collected from all participants.

The concept-mapping sessions will be conducted in the following stages:

1. Preparation Stage: In this stage, stakeholders are identified and the focus question that will guide discussions on the sustainability of the mHealth medical decision model is developed.

2. Generation Stage: In this stage, key stakeholders (ie, midwives, nurses, obstetricians, primary care physicians, study staff, etc) will participate in focus group discussions to generate as many statements as possible in response to a focus question on sustainment of the mHealth platform.

3. Structuring Stage: In this stage, the stakeholders will be asked to sort the statements they generated into similar piles that make sense to them and provide names for the piles created. The stakeholders will then rate each statement based on perceived importance (ie, How important is this factor?) and likelihood (ie, How likely is it that the factor will be sustained over time?).

4. Representation Stage: In this stage, the concept-mapping analyses will be conducted using the Concept System Global Max software program (Concept Systems Inc). Data will be used to conduct multidimensional scaling (MDS) analysis with a two-dimensional solution. The MDS analysis is based on the measurement model that assumes that the relative similarity of objects can be represented in terms of the relative distance between pairs of points [46,47]. From these analyses, coordinate estimates and a two-dimensional *point map* of distances between the statements will be generated for each set of sorted data. The two-dimensional point map is chosen for its ease and interpretability [46]. To indicate the goodness of fit, a *stress value* of the point map will be developed to determine how well the MDS solution maps the original data. While it is not possible to conduct power analysis given the nature of the data, with concept mapping, a lower stress value indicates a better fit and reflects a stronger relationship between the optimal and actual configurations [46,47]. Furthermore, hierarchical cluster analysis will be conducted using the two-dimensional x-y coordinate data obtained from the MDS analysis as input and applying Ward's algorithm as the basis for defining clusters. This approach forces the cluster analyses to partition the MDS configuration into nonoverlapping clusters in two-dimensional space [47]. This technique will also group the outcome statements on each map such that statements placed in the same cluster will be contiguous areas of the map [45]. The resulting output will be a *cluster map*, which will reveal how the statements generated, as represented by points, are grouped.

5. Interpretation Stage: In this stage, result interpretation is typically a real-time, participatory process where stakeholders interact with the total-group ideas generated. This stage involves gathering stakeholder participants to explain and discuss the results of the concept maps, pattern matching, and go-zones.

This includes examining the point map to understand which statements are most related to each other, examining the cluster maps to determine which clusters of statements were rated most important to the focus statement, examining the pattern matching to determine key areas to target based on high ratings, and examining the go-zones to determine the area of most importance for each stakeholder group.

6. Utilization Stage: In this stage, the research team will work with the stakeholders to determine the best ways to use the maps and reports produced as part of the concept-mapping procedures. Possible use of the output from concept mapping includes creating a sustainability plan, which will serve as the basis for tracking the continued use of the mHealth platform in the study catchment area.

## Results

Regarding health facility recruitment, we reviewed data from 26 primary health facilities supported by PEPFAR funds in the seven priority local government areas (LGAs) in Benue state, Nigeria. We identified six comprehensive care and treatment (CCT) sites in five priority LGAs with the highest HIV incidence in pregnant women during this period. CCT sites are primary health care centers that offer HIV testing services, antiretroviral therapy for both adults and children, and PMTCT services. We excluded two health facilities in one LGA due to poor road accessibility to the sites. We selected the remaining four health facilities for the study: (1) Father Matthias Clinic, Naka (Gwer West LGA); (2) Nongu u Kristu ke Sudan hen Tiv Comprehensive Health Center, Garagbohol (Buruku LGA); (3) Nongu u Kristu ke Sudan hen Tiv Health Center, Uchi (Tarka LGA); and (4) Mimidoo Clinic, Gungul (Konshisha LGA).

## Discussion

The critical unanswered questions in low-income countries are how to identify pregnant women at risk of infections and diseases early and how to implement interventions to improve infants' birth outcomes and survival. Whether the availability of maternal medical information, including laboratory data at the point of delivery, will enhance the implementation of proven, evidence-based interventions for prevention has not been well demonstrated in many resource-limited settings. Our proposed study is innovative in its approach to make prenatal results available at the point of care using an integrated, non-Internet-dependent, mobile health platform to guide management of mother-infant pairs in Nigeria. If successful, this approach could become a game changer in early identification of pregnant women with diseases of interest, implementation of intervention to improve birth outcomes, and reductions in loss to follow-up between testing and birth in the country.

Key stakeholders within the ICT and health sector have demonstrated the need to support the scale-up of maternal and child health services in Nigeria through ICT in order to save one million lives of women and children [21]. Accordingly, our proposed study seeks to develop a mobile health platform that is cost-effective, readily scalable, and can be integrated with other solutions to improve efficiency in health care service delivery in the country.

Our study is conducted in the context of three conditions: HIV, HBV, and SCD. Therefore, our findings may not be generalizable to other conditions. Similarly, our choice of a nonprobability sampling technique may limit the generalizability of our findings. Infrastructure gaps, such as unreliable power supply, may hinder effective implementation at our study sites.

### Authors' Contributions

EEE conceived the study. EEE, JI, DS, AO, and DP designed the study. EEE and SG coordinated the study. SG, JO, AO, and DP oversaw recruitment and data collection. SG and EEE drafted the manuscript. All authors revised and approved the final manuscript.

### Conflicts of Interest

None declared.

### Multimedia Appendix 1

NIH R21 Peer-Review Summary Statement.

[PDF File (Adobe PDF File), 173KB - resprot_v6i5e100_app1.pdf ]

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## Abbreviations

**CCT:** comprehensive care and treatment
**FMOH:** Federal Ministry of Health
**HBI:** Healthy Beginning Initiative
**HBV:** hepatitis B virus
**ICT:** information and communication technology
**iSTAR:** intervention for Sustained Testing and Retention
**LGA:** local government area
**MDS:** multidimensional scaling
**NIH:** National Institutes of Health
**PEN-3:** Perceptions, Enablers, and Nurturers
**PEPFAR:** Presidents' Emergency Plan for AIDS Relief
**PMTCT:** prevention of mother-to-child transmission
**QR:** Quick Response
**RE-AIM:** Reach, Effectiveness, Adoption, Implementation, and Maintenance
**SCD:** sickle cell disease

Protocol

# The Parasol Protocol: An Implementation Science Study of HIV Continuum of Care Interventions for Gay Men and Transgender Women in Burma/Myanmar

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## Abstract

**Background:** Efforts to improve HIV diagnosis and antiretroviral therapy (ART) initiation among people living with HIV and reduce onward transmission of HIV rely on innovative interventions along multiple steps of the HIV care continuum. These innovative methods are particularly important for key populations, including men who have sex with men (MSM) and transgender women (TW). The HIV epidemic in Myanmar is concentrated among key populations, and national efforts now focus on reducing stigma and improving engagement of MSM and TW in HIV prevention and care.

**Objective:** This study aims to test the use of several innovations to address losses in the HIV care continuum: (1) use of respondent-driven sampling (RDS) to reach and engage MSM and TW in HIV testing, (2) HIV self-testing (HIVST) to increase HIV testing uptake and aid early diagnosis of infection, (3) community-based CD4 point-of-care (POC) technology to rapidly stage HIV disease for those who are HIV infected, and (4) peer navigation support to increase successful health system navigation for HIV-infected MSM and TW in need of ART or HIV engagement in care.

**Methods:** To assess the effect of HIVST, we will implement a randomized trial in which MSM and TW adults in the greater Yangon metropolitan area who are HIV uninfected will be recruited via RDS (N=366). Participants will complete a baseline socio-behavioral survey and will be randomized to standard, voluntary counseling and testing (VCT) or to HIVST. Biologic specimens will be collected during this baseline visit for confirmatory testing using dried blood spots. Participants will be asked to return to the study office to complete a second study visit in which they will report their HIV test result and answer questions on the acceptability of the assigned testing method. Aim 1 participants with confirmed HIV infection and who are not engaged in care (N=49) will be offered direct enrollment into Aims 2 and 3, which include immediate CD4 POC and the option for peer navigation, respectively. Aims 2 and 3 participants will be prospectively followed for 12 months with data collection including interviewer-administered sociobehavioral survey, CD4 POC, and viral load testing occurring biannually. Participants who accept peer navigation will be compared to those who decline peer navigation. Analyses will estimate the impact of CD4 POC on engagement in care and the impact of peer navigation on ART adherence and viral load.

**Results:** Formative qualitative research was conducted in June and September 2015 and led to further refinement of recruitment methods, HIVST instructions and counseling, and peer navigation methods. Aim 1 recruitment began in November 2015 with subsequent enrollment into Aims 2 and 3 and is currently ongoing.

**Conclusions:** These innovative interventions may resolve gaps in the HIV care continuum among MSM and TW and future implementation may aid in curbing the HIV epidemic among MSM and TW in Myanmar.

## Introduction

Efforts at both international and national levels have been re-energized toward ending the HIV epidemics. The United Nations and national strategies now focus on increased testing for the identification of previously undiagnosed HIV infection for linkage to care and treatment engagement [1]. Since the HIV Prevention Trials Network (HPTN) study 052 highlighted the preventive benefits of early antiretroviral therapy (ART) treatment [2], most countries have adapted their treatment criteria to initiate treatment at CD4 <500 cells/µL, in accordance with 2013 World Health Organization (WHO) guidelines, while some countries have begun adopting the 2015 WHO guidelines of providing treatment for all people living with HIV [3]. The majority of these global efforts focus on the general populations, although for settings where HIV is concentrated among key populations, such as gay men and other men who have sex with men (MSM), transgender women (TW), sex workers, and people who use drugs, it is imperative to ensure that access to treatment and care is available for key populations in order to have true impact on the epidemic trajectories [4,5].

Achieving such goals for MSM and TW is challenging given contexts of stigma, discrimination, and criminalization and require innovative approaches to overcoming these challenges and engaging these populations in HIV testing and care. Considering the HIV care continuum (Figure 1), these innovative approaches can be viewed in terms of several stages for MSM and TW: (1) initial contact with or outreach to MSM and TW, (2) HIV testing and diagnosis, (3) HIV staging according to national criteria, (4) engagement and retention in care, (5) treatment initiation, and (6) viral load suppression.

A long-standing approach to reaching MSM and TW has been the use of mobile and other forms of street or venue-based outreach to engage these populations in HIV testing. These methods assume at-risk members of the population are present in sites accessible to outreach workers and often result in frequent retesting of the same individuals. Respondent-driven sampling (RDS), however, has become popular in the last decade as an alternative sampling method that can effectively penetrate deep into social networks of key populations and recruit a more representative sample [6,7]. RDS is a peer-based recruitment method that has been developed as a nonprobability sampling approach for surveys of hidden and stigmatized populations [8]. It has shown benefit in reaching individuals who may not be present at venues or who frequent health facilities less often [9]. As such, RDS may have a role beyond research in engaging MSM and TW in HIV testing and other HIV prevention and care interventions, particularly in settings of stigmatization and criminalization [10-12].

Self- or home-based HIV testing (HIVST) has also emerged as an important tool to promote HIV screening and, potentially, to increase frequency of HIV testing among key populations for whom more frequent testing is recommended [13]. Salivary-based HIV self-test kits have been approved by the US Food and Drug Administration (FDA) and are commercially available in the United States [14]. They have also been increasingly used in research and programs in developing countries as an alternative to facility-based testing [15]. One of the most beneficial aspects of HIVST is its empowerment of individuals to take control of their own health and HIV prevention or care while allowing users to test at their own convenience and in the privacy of their own home or setting of their choice.

A systematic review and meta-analysis of supervised and unsupervised HIVST in both low- and high-risk populations found that self-testing was highly acceptable, preferred by persons at high risk for HIV, and was more likely than clinic-based testing to result in partner HIV testing [15]. Self-testing has the potential to overcome the barriers experienced by MSM and TW as it relates to HIV testing uptake by placing the locus of control on the individual, increasing confidentiality, and allowing members of stigmatized groups to test in settings of privacy, safety, and dignity [16]. HIV rapid tests have grown more sensitive and less complex, making self-testing a viable alternative to clinic-based testing.

**Figure 1.** HIV care continuum among people living with HIV.
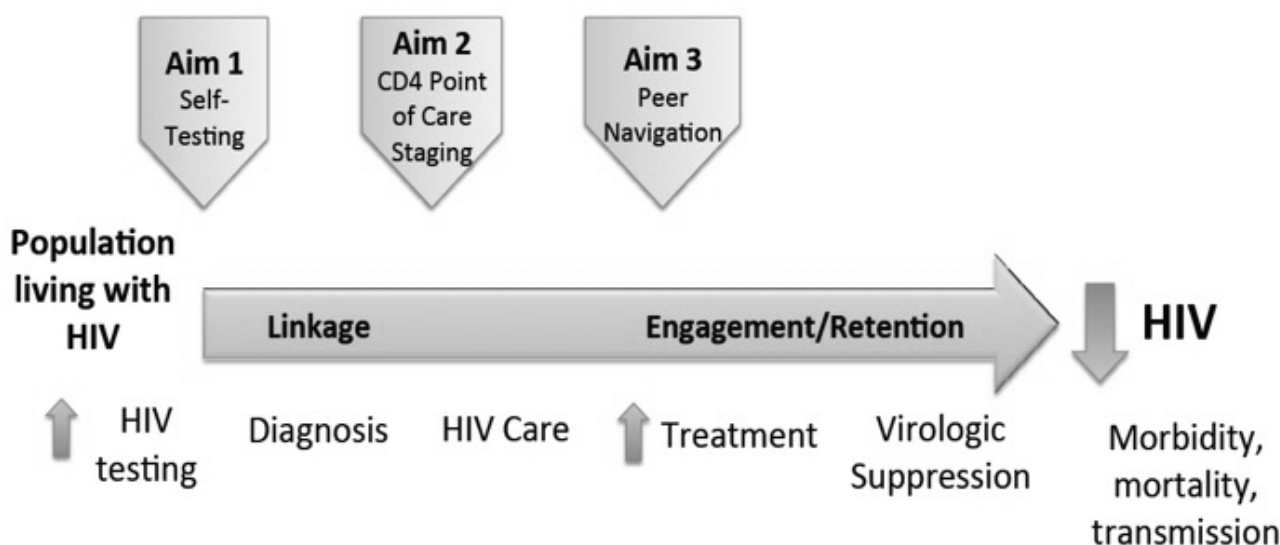


Beyond HIV diagnosis, there is considerable evidence that a major loss of HIV-infected persons in the treatment continuum occurs during disease staging [17]. In most settings, seeking and receiving clinical staging and CD4 testing is required for initiation of ART and generally requires visits to additional facilities where CD4 testing is available. This is often accompanied by long waiting times for results, concerns of unintentional disclosure of sexual or gender identity and disease status to others, and additional steps after staging to link patients to ART [18-20]. These issues around the availability of CD4 testing are common causes of losses at this critical step in the continuum.

Further, there are multiple challenges to successful navigation of the health care system, including but not limited to discrimination and stigma in health care settings. Recently, peer-navigation has been increasingly used among MSM and TW and other key populations to support navigation through a complex system of care, retention in care, and treatment adherence [21-23]. Peer navigators further provide health and HIV information and social support when coping with diagnosis, dual stigmatization of HIV and sexual or gender identity, and disclosure [21-23].

All of these challenges in the HIV care continuum are relevant in Myanmar (formerly known as Burma) and particularly so for MSM and TW populations in the country. Since the early 1990s, the HIV epidemic in the country has seen high rates of morbidity and mortality, very low access to ART, and limited and problematic HIV surveillance and reporting [24,25]. Further, the epidemic has disproportionately affected several key populations in Myanmar, including MSM and TW. While HIV rates appear to have declined among the general population, what limited data are available on key populations suggest that HIV remains concentrated in these groups, disease burdens are high, and access to voluntary counseling and testing services, prevention, and HIV treatment and care remain elusive to many [26,27]. The most recent Joint United Nations Program on HIV/AIDS and Ministry of Health report estimates that some 11.6% of the estimated 230,000 MSM and TW in Myanmar are

living with HIV, with prevalence as high as 26.6% among MSM and TW in Yangon, compared to 0.53% of reproductive aged adults [28,29]. With approximately 53% estimated to be reached by prevention services and 20% reached with HIV testing, the same report highlights the need for programs that can reach MSM and TW who are not openly gay and do not seek services [28].

Barriers to HIV care have been common and chronic issues in Myanmar [26]. CD4 criterion for ART initiation in Myanmar is 350 cells/μL, and until 2014, when ART availability was limited, priority was given to patients with CD4 count below 150 cells/μL [30]. The median actual starting level of CD4 in 2012 in Myanmar was 60 cells/μL [26]. National guidelines also recommend treatment initiation at CD4 <500 cells/μL for coinfected patients and for patients from key affected populations, such as MSM and TW [31]. Recent increases in treatment access as a result of support from United States President's Emergency Plan for AIDS Relief (PEPFAR), the Three Millennium Development Goals Fund (3 MDG, a joint donor fund established in Myanmar before the Global Fund began activities in the country), the Global Fund, and the World Bank have led the National AIDS Program to estimate the availability of at least 50,000 new treatment slots in Myanmar in the next 2 years [28]. MSM and TW in Myanmar, and in many settings, are more likely to have undiagnosed HIV infection, since the stigma and discrimination they face in the community, wider society, and in health care settings can be a barrier to testing, disclosure, and seeking health care overall [32].

The primary aim of the Parasol study is to use the overarching framework of the HIV care continuum [17] to measure and overcome barriers to HIV testing and access to care through a series of 4 primary innovations for MSM and TW in Myanmar. We propose to test the following innovations to address losses in the HIV care continuum: use of RDS to reach and engage MSM and TW in HIV testing, HIV self-testing to increase testing uptake, staging of HIV disease for those who are infected through CD4 point-of-care (POC) technology [33,34], and

training and capacity building of a cadre of peer health navigators for MSM and TW to increase successful health system navigation for HIV-infected MSM and TW in need of ART or HIV engagement in care [22,23,34]. Longer-term engagement in care will be assessed through the current gold standard for HIV treatment: successful HIV viral suppression as measured by quantitative viral load at 12 months posttreatment initiation [35].

The research protocol described here is a collaboration between the Center for Public Health and Human Rights at the Johns Hopkins University School of Public Health, the International HIV/AIDS Alliance Myanmar, the Myanmar Department of Medical Research, and 3 community-based organizations (CBOs): Lotus Project, Phoenix Association, and *Aye Nyien Myitta*. Funding has been provided by amfAR, the Foundation for AIDS Research.

## Methods

### Study Design

This study is conducted in a staged process, beginning with a qualitative, formative phase that is intended to inform further development of recruitment and intervention methodologies, followed by a 3-step continuum interventions study in Yangon, Myanmar. Specific aims and hypotheses are dedicated to each step along the continuum from engagement in HIV testing through RDS and evaluation of HIVST (Aim 1), evaluation of CD4 POC staging (Aim 2), and assessment of peer navigation for treatment initiation and adherence support (Aim 3). This manuscript describes the methodology for the continuum interventions study (qualitative methods have been described elsewhere) [36]. The participant flow diagram displays the study flow, randomization point, and target sample size (Figure 2).

**Figure 2.** Participant flow diagram.
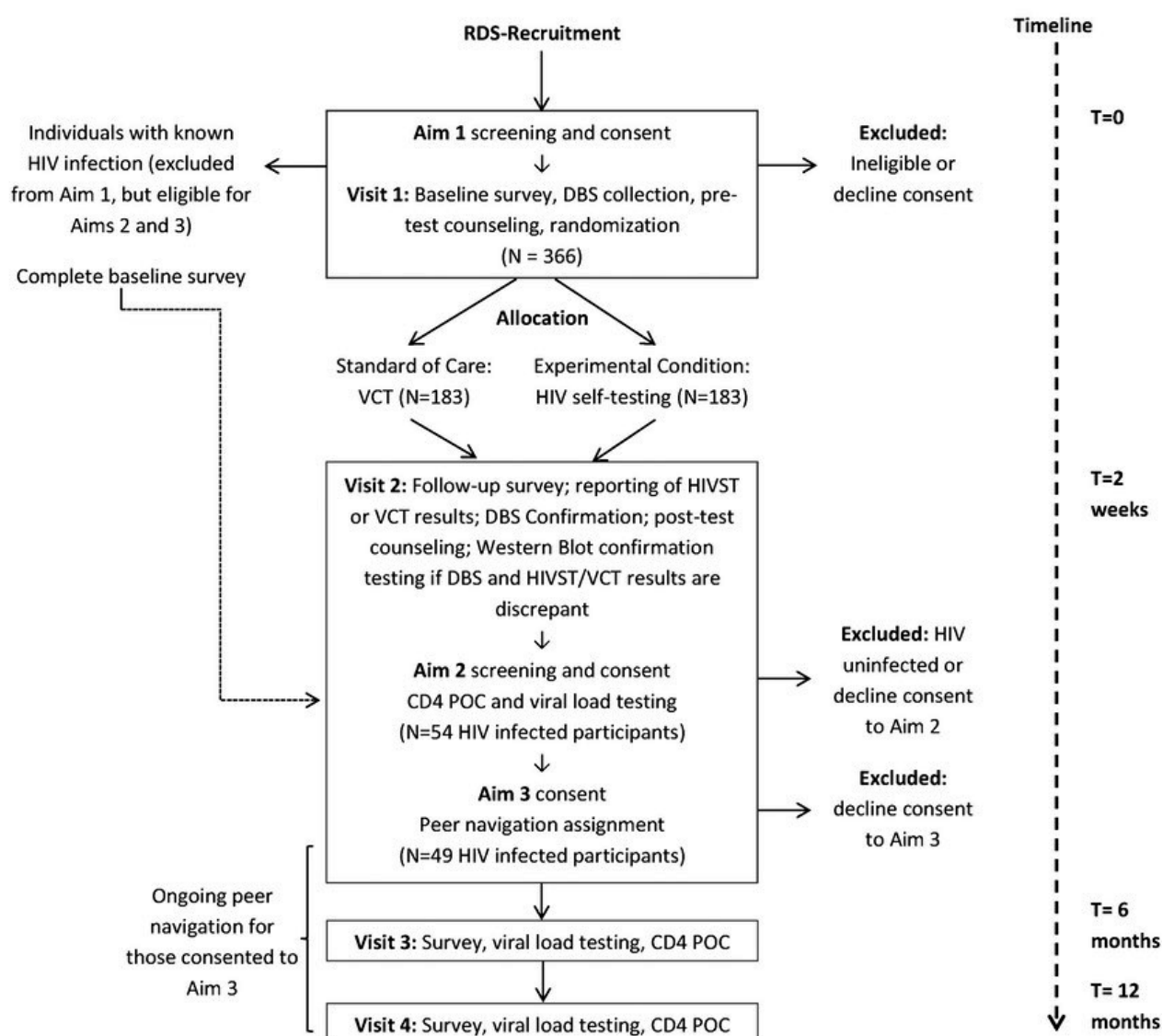
## Study Site

The study is conducted in Yangon, Myanmar. Yangon, formerly the capital of Myanmar, remains an important urban center and is the largest city in Myanmar with a population exceeding 7.3 million persons in 2014 [37]. There is growing recognition and acceptance of the lesbian, gay, bisexual, and transgender (LGBT) populations in Yangon and a substantial emergence of community-based HIV prevention and care services for MSM and TW within the city.

## Aim 1: HIV Self-Testing Versus Clinic-Based Testing

To assess the effect of HIVST, we have designed a randomized trial in which MSM and TW adults in the greater Yangon metropolitan area will be recruited through RDS and offered HIV testing. Participants are randomized to receive standard clinic-based voluntary counseling and testing (VCT) or the HIVST intervention.

### Aim 1 Study Sample

Aim 1 participants are included on the basis of the following inclusion criteria: assigned male sex at birth, aged 18 years or older, reports having had any type of sex with another man in the past 12 months, presents to the study with a valid RDS coupon (except seeds), speaks Myanmar, currently a resident of the greater Yangon area, is mentally sound and capable of providing consent to participate, and has provided informed consent to participate in the study. Participants who have been tested for HIV within the last 6 months or who are known to be living with HIV infection are excluded from participation in Aim 1. However, individuals who disclose a positive HIV status when Aim 1 eligibility is determined are considered for enrollment in Aims 2 and 3, provided they meet all eligibility criteria for those aims. While there are emerging and increasingly open gay communities in Yangon, the traditional categories of sexual orientation and gender identity in Myanmar culture are blurred; locally, the term MSM is often used interchangeably across male and transgender-identified populations and these groups often attend similar community-based events [38]. Thus, this study focused on the inclusion of both MSM and TW populations.

The target sample size needed for the RDS sample is 366 MSM and TW participants. This estimate achieves 2 goals. First, it allows for a comparison of HIVST versus clinic-based HIV testing. Assuming an error of .05 and 80% power to detect a 15% difference in acceptability between the 2 testing methods (60% acceptability of clinic-based testing and 75% acceptability of self-testing), a sample of 330 (or 165 per group) is needed. Upon factoring a 10% nonresponse in both testing methods, an effective sample size of 366 MSM and TW participants is calculated. Second, this allows for subsequent enrollment of MSM and TW participants into Aims 2 and 3. Assuming a conservative 15% prevalence of HIV among the sample [28], this identifies 54 participants who are then eligible for Aims 2 and 3.

### Aim 1 Recruitment

Participants are recruited via RDS, given demonstrated benefits to (1) potentially recruit a more representative sample and (2) reach deep into social networks to recruit participants who are often not reached through outreach, venue-based, or snowball sampling methods for engagement in HIV testing [6,7,9]. In this method, 8 to 10 MSM and TW seeds will be recruited by study investigators. Seeds, who begin recruitment, are individuals who represent a range of characteristics and are well-networked within the MSM and TW population. The study team works with local CBO partners in Yangon to identify MSM and TW seeds. Seeds complete the first visit study activities and are then given a maximum of 3 coupons with which to recruit their peers from within their social or sexual networks. These peers are invited by the seed to present to the study office with their coupon for participation in the study. If eligible and after completing baseline study activities, the recruited participant may, in turn, become a recruiter. Participants who agree to become a recruiter undergo recruitment training and receive a maximum of 3 coupons for distribution. This process continues until the sample size has been reached. This sampling method has been successfully used by the research team for several research studies of HIV among MSM, including in Malawi and Russia [7,39,40]. RDS has also been used by other investigators to research HIV among people who inject drugs, MSM, and TW in Myanmar [41,42].

Recruitment coupons are prenumbered with a unique coupon number prior to distribution (Figure 3). Coupons contain other information including the study telephone number, site operating hours, and coupon expiration date. There is no information on the coupon that could be used to identify the holder as MSM or TW and no personal information is recorded on the coupon. Coupons are collected from recruited candidate participants at the study site at the time of eligibility screening and the returned coupon number is recorded. Coupons allow for the research team to trace the recruitment process and create analytical weights for the sampling process.

**Figure 3.** Respondent-driven sampling coupons (front and back).
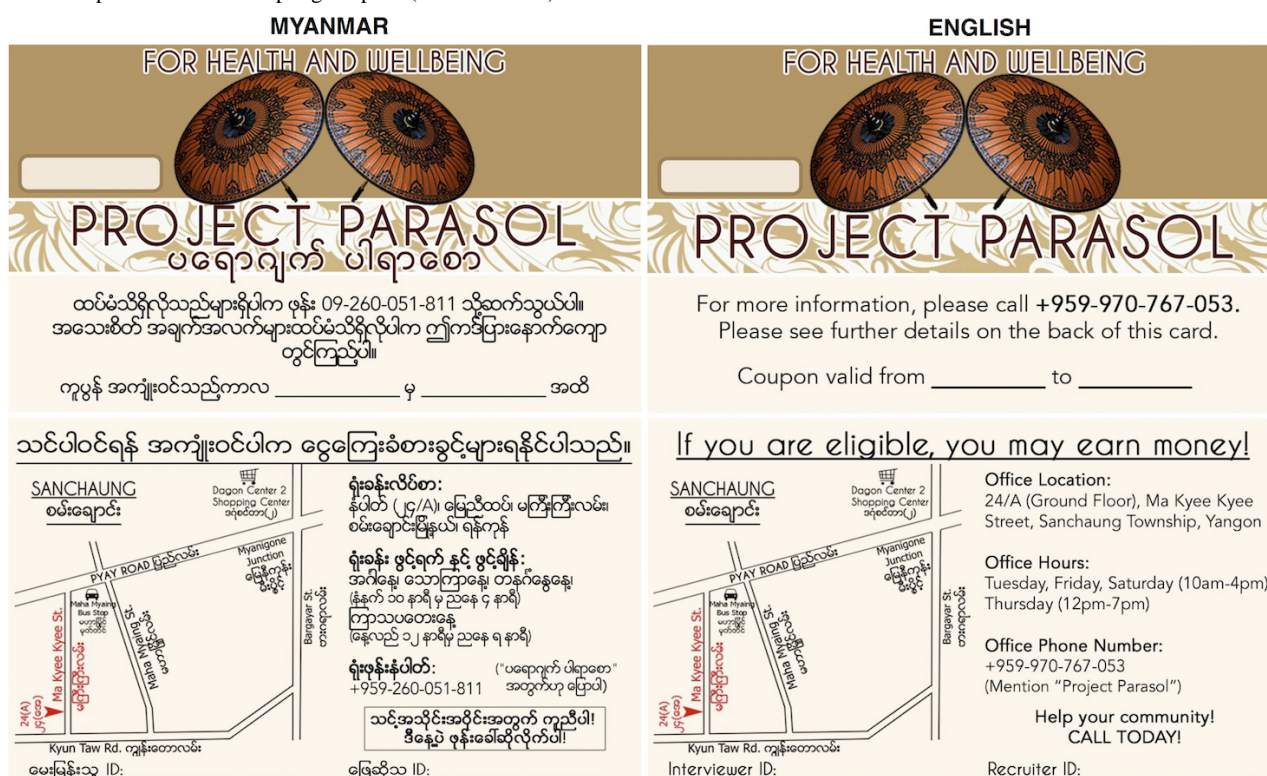


### Aim 1 Data Collection

Eligible participants recruited through the RDS are verbally consented using paper-based consent forms in private rooms within the study office. Upon providing consent, participants complete a structured, 30- to 45-minute interviewer-administered, tablet-based questionnaire, which serves as the baseline assessment. The questionnaire allows for comparison of HIVST versus clinic-based testers and attrition analysis of those who return versus do not return for their follow-up visit. Measures in this questionnaire include demographic and network characteristics, previous testing history and experiences, sexual and substance use risk profiles, access to HIV and sexually transmitted infection prevention and care, measures of perceived and experienced stigma in health care settings, concerns over police or other security harassment, and factors related to cost, distance, convenience of testing venues, and acceptability of assigned testing method. Individual network size measures, commonly collected for the analysis of RDS data, assess the number of MSM and TW in the Yangon area the participant knows and has seen or spoken to in the last 6 months. The questionnaire also includes 2 of 5 parameters recommended by Pant Pai et al [15] for HIVST assessments, specifically acceptability of testing methods and motivations for HIVST among users.

Following the questionnaire, pretest counseling is administered prior to collection of dried capillary blood spot collection (DBS) via a finger prick. DBS is analyzed at a local reference lab in Yangon. The primary purpose of DBS collection is to ensure that the study team receives HIV test results for any participants who do not return to the clinic for their follow-up visit. The DBS will also confirm clinic-based HIV test or preliminary

HIVST results during visit 2, allowing for further validation of the self-testing and clinic-based results.

Following pretest counseling, participants will be electronically randomized to clinic-based VCT or HIVST. Participants assigned to VCT are provided with referral information for partner clinics and instructed to complete clinic-based HIV testing services within 2 weeks. Individuals randomized to HIVST will be provided with the OraQuick in-Home HIV Test (OraSure Technologies) self-testing kit and instructions for use. OraQuick in-Home HIV Test is an FDA-approved oral HIV test that allows the user to self-administer the salivary test in private and displays results within 20 minutes. The OraQuick in-Home HIV Test tests for HIV-1/2 antibody test and has a sensitivity of 91.7% and specificity of 99.9%. The test is recommended for use as a method to screen for HIV infection to be followed with confirmatory testing. Johns Hopkins University (JHU) has partnered with OraSure to provide Myanmar language instructions within the kit. Participants randomized to HIVST are instructed to complete HIVST any time before their scheduled second visit. HIVST participants are provided with a study telephone number that they can call for assistance at any time of day.

All participants are instructed to call the project office immediately if they receive a preliminary positive HIV test result. Study staff schedule these participants to return to the project office for visit 2 as soon as possible. This ensures that all participants are offered posttest counseling, confirmatory testing, and enrollment in Aim 2 (CD4 POC staging) as quickly as possible. DBS analysis is expedited for participants who cannot be reached or who do not disclose their HIV testing results. HIV testing is considered complete when participants

have received results from their assigned method of testing and report awareness of their HIV status.

## Aim 1 Follow-Up

All participants are scheduled for a second visit 2 to 3 weeks after the primary visit. During this visit (visit 2), self-reported VCT and HIVST results are ascertained. Analysis of DBS specimens is conducted between visit 1 and 2 to serve as confirmatory testing of results identified through clinic-based VCT or HIVST. Special effort are made to recontact, counsel, and provide appropriate referrals for participants who do not return for the follow-up visit but who are identified with HIV infection during analysis of DBS. Participants found to be preliminarily HIV-negative are given posttest counseling, which includes an explanation of the test result, advice on risk reduction, and the provision of condoms, lubricant, and referrals. These participants are advised to seek HIV testing again in 3 months and are provided with contact information for local nongovernmental organizations who provide HIV testing and care services to MSM and TW. Participants confirmed HIV infected are given posttest counseling and offered enrollment in Aim 2 to conduct immediate CD4 POC staging. Participants who decline enrollment in Aim 2 are provided with referrals for standard CD4 testing as well as treatment and care services. Participants with discordant DBS and self-reported HIVST or VCT results are asked to provide an additional blood sample for confirmation by Western blot.

All participants are asked to complete a structured, 30-minute interviewer-administered questionnaire during visit 2 that serves to evaluate uptake and acceptability of clinic-based or HIVST methods. Participants also receive secondary reimbursement for recruitment of peers at the second visit, which is a standard practice of RDS and will incentivize this follow-up visit.

## Aim 1 Analytical Approach

Baseline characteristics are analyzed using a program written for Stata (StataCorp LLC), which makes statistical adjustments for RDS sampling to characterize unbiased asymptotic estimates of disease burden and other characteristics by weighting for social network size (RDS-II estimator) [43]. Exploratory analysis is conducted to evaluate recruitment depths and potential biases induced by recruitment [7]. Results include descriptive statistics related to sociodemographic characteristics, knowledge of STI/HIV, and sexual behavior and attitudes of MSM and TW populations. Bivariate and multivariable analyses using multiple logistic regression or log binomial regression, depending on the calculated prevalence [44], are performed to determine the association between HIV infection and key behavioral outcomes and other variables. Additional analysis focuses on the parameters recommended by Pant Pai et al [15] for HIVST assessments, conducting a stratified analysis of acceptability of testing methods, accuracy, concordance with health care worker testing, feasibility and motivations for testing among consumers, and comparability of HIVST to VCT.

The primary hypothesis for this continuum innovation step is that a higher proportion of persons who are randomized to HIVST will complete HIV testing than those randomized to standard clinic-based testing. Given the randomized nature of the study design, the study team will use a standard comparison approach to assess the outcomes of the 2 intervention arms for this aim. Standard contingency tables with Fisher exact test for significance is used to evaluate the efficacy of the intervention. A comparison of intervention arms (HIVST vs clinic-based) is the primary outcome measure, and balance in potential measured confounders is assessed. Implementation measures of HIV testing include uptake of HIV testing services, fidelity of the implementation of the intervention, and acceptability of HIV testing options.

Attrition analysis is conducted to assess the potential differential loss to follow-up by individual characteristics (demographics, sexual identity, and distance from office/clinic) as well as assigned intervention groups. Where possible, we attempt to recontact participants to understand individual reasons for failed return, which is particularly important during the start-up of the interventions, in which logistical changes can be made to address losses to follow-up. Any logistical changes are documented.

## Aims 2 and 3: CD4 Point-of-Care and Peer Navigation

### Aims 2 and 3 Design

Participants diagnosed with prevalent or incident HIV infection during participation in Aim 1 of the study are offered CD4 POC to assess whether this technology can increase the likelihood that HIV-infected MSM and TW are successfully staged for HIV disease and engaged in care (Aim 2). All persons who accept CD4 POC testing are offered peer navigation and viral load testing in the final stage (Aim 3). Treatment adherence and clinical outcomes, including the proportion of MSM and TW participants who achieve successful viral suppression, is assessed by nonrandomized comparison of participants who accept and decline peer navigation support. Participants of Aims 2 and 3 follow the same procedures; thus, the following section jointly describes the methodology for Aims 2 and 3.

### Aims 2 and 3 Recruitment

Participants who test positive during Aim 1 or who report a previous diagnosis of HIV infection are offered enrollment by the study team into Aims 2 and 3. Separate consent forms are provided for each of these aims. Specifically, the consent form for Aim 2 requests consent to participate in CD4 POC testing, and the consent form for Aim 3 will request consent for participation in peer navigation.

### Aims 2 and 3 Study Sample

Inclusion criteria for Aims 2 and 3 are assigned male gender at birth, aged 18 years or older, reports having had any type of sex with another man in the past 12 months, is mentally sound and capable of providing consent to participate, speaks Myanmar, current resident of the greater Yangon area, diagnosed with HIV infection, not currently engaged in any treatment or care programs, and has provided informed consent to participate in the study. Participants will be excluded from Aims 2 and 3 if they report that they are already linked into an HIV treatment or care program or have tested negative for HIV infection.

The overall study sample size estimate was driven by the numbers needed for the feasibility and acceptability studies of CD4 POC testing, viral load, and peer navigation, with a target

of 54 participants in CD4 POC testing to assess key parameters. Assuming a 10% decline in participation for peer navigation and viral load testing, our target sample for viral load and peer navigation is 49 participants. As data analysis and monitoring are ongoing during data collection, RDS can be extended for additional recruitment should additional recruitment be required to reach targets in Aims 2 or 3. Further, if necessary to reach our desired Aim 2 sample size, additional MSM and TW who are newly HIV-diagnosed can be recruited from partnering organizations for this phase.

### Aim 2 CD4 Point-of-Care

CD4 POC testing capacity is available at the study site. Given the need for CD4 POC testing, there is no randomization of participants during this phase of research. We use the BD FACSPresto Near Patient CD4 Counter (BD Biosciences) system for POC CD4, which is currently available but in limited use in Myanmar. This system uses the BD FACSPresto cartridge, which contains desiccated reagents that eliminate requirements for a cold chain and cold storage and is well-suited to rural areas and settings with unstable power. The BD FACSPresto Near Patient CD4 Counter system was selected given its availability in Myanmar and limited use by local nongovernmental organizations in Myanmar to provide free CD4 POC services to key populations who have been diagnosed with HIV infection. The system is portable and can provide easily read CD4 outputs within 20 minutes, while patients wait to receive their results. The BD FACSPresto machine contains a built-in training module along with a detailed manual for easy training and operation. In addition to this, laboratory staff attended a training provided by Yee Shin Co Ltd, the Yangon-based regional distributer of the machine and cartridges. Yee Shin Co Ltd is also available to the staff for troubleshooting and other maintenance services as needed. Prequalified by WHO, the BD FACSPresto Near Patient CD4 Counter system has demonstrated reliability and accuracy when used in resource-limited settings [45-47]. This innovation can reduce continuum losses through immediate provision of results, post-CD4 stage counseling, and access to treatment for those who meet treatment criteria on the day of testing. Persons with very low CD4s can thereby be immediately engaged with peer navigators (Aim 3) to seek ART access.

### Aim 3 Peer Navigation

If successful, increasing HIV status awareness through HIVST and POC CD4 will identify a significant number of persons in need of health care and ART. All Aim 2 participants are offered enrollment in Aim 3, which intends to address barriers to HIV care and ART adherence by comparing those who opt into peer navigation to those who decline.

Peer navigation is offered to all participants on the account of high rates of existing AIDS-related morbidity and mortality among MSM and TW populations living with HIV in Myanmar. For this phase of the project and given the severity of clinical needs, we will not conduct a randomized assessment of peer navigation. Consequently, we measure actual numbers of persons who successfully start on ART, comparing those who opt into peer navigation to those who decline. We treat this aim as an observational study, with peer navigation assistance as

the exposure of interest and ART uptake as the outcome. All eligible participants are offered peer navigation with approximately 8 participants assigned to each peer navigator.

Trained peer navigators follow and support all clinically staged participants who have accepted navigation support for 12 months. Peer navigators offer focused training on the importance of CD4 and viral load monitoring, self-care when living with HIV, and methods to prevent HIV transmission. Participants are given contact information for their assigned peer navigator and are encouraged to reach out to them for assistance navigating the Myanmar health system. The role of the peer navigator is to provide support and information to HIV-positive MSM and TW who are seeking HIV treatment and care in the Myanmar. In order to maintain confidentiality in this peer relationship, the questionnaire administration and appointment reminders are the responsibility of office staff.

Peer navigators are selected from the MSM and TW population by Alliance and partner CBOs. Ideally, peer navigators will have prior experience working in HIV prevention or other outreach, but this is not required. Peer navigators undergo an intensive training on topics of MSM and TW health, HIV prevention and care, disclosure of HIV status and issues of social support, and other related topics. Training will build on past training used locally as well as in Malawi and South Africa and incorporate key aspects from the Fenway Guide and other validated MSM training materials [48,49]. Local CBOs and MSM and TW participants also provide input to trainings to ensure contextual relevance. Peer navigators are provided with condoms and lubricants for distribution as well as informational materials on where specific (nonstigmatizing) services can be obtained. Peer navigators are overseen by the research coordinator and report on a weekly basis for debriefing. The research coordinator occasionally monitors participant meetings to ensure fidelity to the curriculum and adherence to the study protocol.

### Aims 2 and 3 Data Collection

Upon determination of eligibility and verbal confirmation of informed consent, participants complete a structured 20-minute interviewer-administered questionnaire. Participants are then asked to return to participate in surveys conducted at 6 and 12 months. Surveys assess the primary outcome and initiation of ART as well as ART adherence (among those successfully initiated) and other clinical outcomes, including viral suppression, as measured by HIV viral load assessment at 0, 6, and 12 months. This questionnaire is used to assess the strength of peer navigation in improving access and uptake of viral load by MSM and TW living with HIV in care. Peer navigation implementation data (eg, number of meetings per participant, types of support provided) along with participant perceptions will be collected to understand the benefits and challenges of peer navigation and note opportunities for improvement. Incentives are distributed at the conclusion of each follow-up survey. An electronic data entry and tracking system has been developed for this study and allows for registration, screening, survey data collection, data entry of laboratory results, and participant tracking through a secure, Health Insurance

Portability and Accountability Act–compliant site. This system     is used throughout all phases of the study (Figures 4 and 5).

**Figure 4.** Participant tracking system (English).
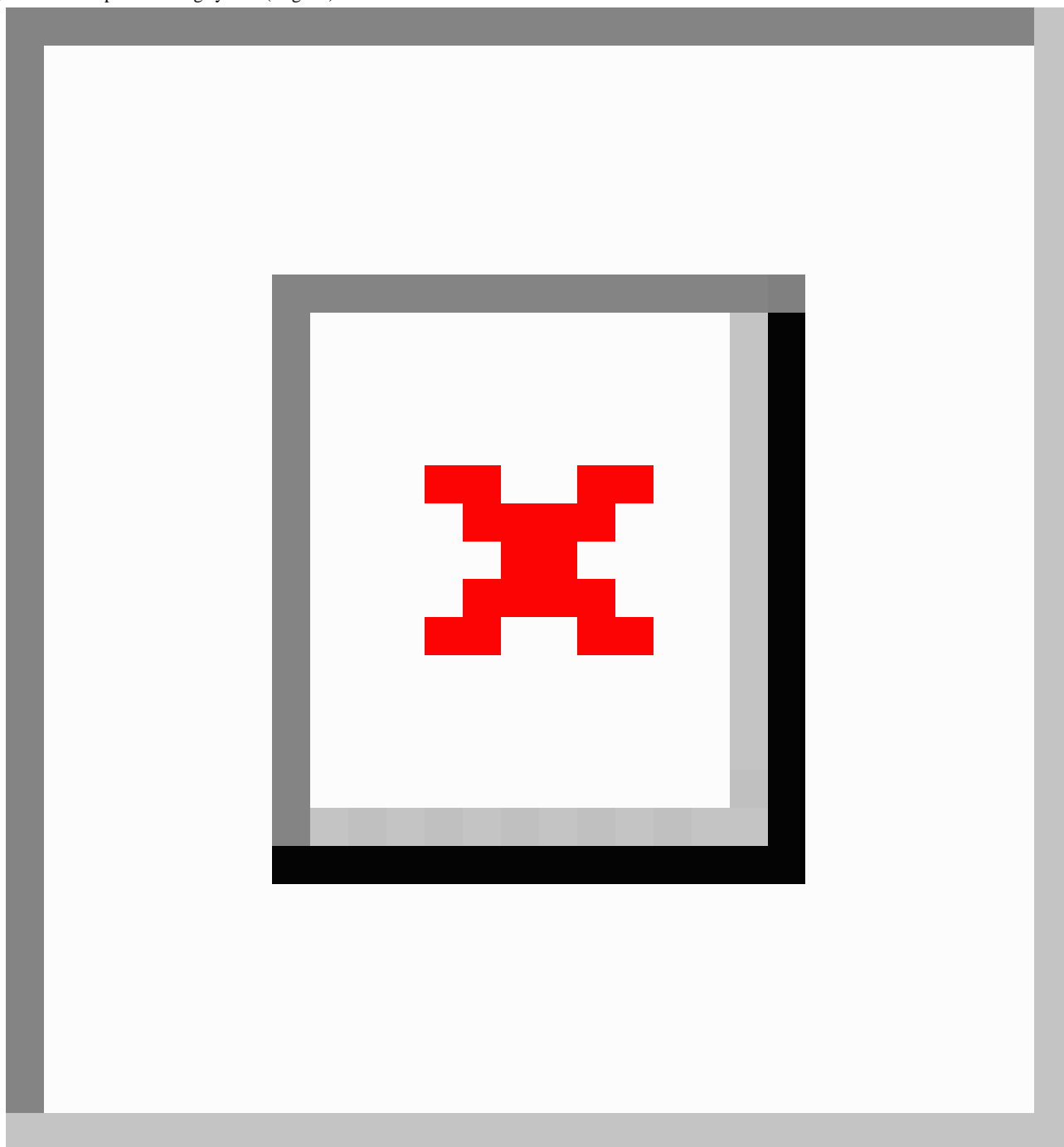
**Figure 5.** Participant tracking system (Burmese).



## Aims 2 and 3 Analytical Approach

The primary hypothesis for Aim 2 is that a higher proportion of MSM and TW living with HIV who accept CD4 POC testing will be successfully staged. The primary hypothesis for Aim 3 is that HIV-positive persons who accept peer navigators will have a higher likelihood of achieving ART treatment access than those who decline peer navigation. Aims 2 and 3 are analyzed as observational studies, with CD4 POC testing and peer navigation assistance as the exposures of interest and ART uptake and viral suppression as the outcomes. Specifically, the primary outcomes of interest follow the HIV care continuum and include the actual numbers of persons who accept CD4 staging, are linked to treatment, successfully initiate ART, accept viral load testing and peer navigation, reach viral suppression, and are lost to follow-up.

We conduct longitudinal analyses to measure the associations between these innovations and impact outcomes, including time to CD4 staging, receipt of CD4 results, time to engagement in HIV care and treatment for those eligible, barriers and facilitators to completing CD4 staging, perceived and experienced stigma in health care settings, and uptake of treatment referrals. Regression analysis controls for potential confounding by participant demographics and behaviors. Additional analyses related to peer navigation assess frequency of peer navigator meetings, types of discussions and HIV prevention materials provided, and associated changes in ART adherence and viral load testing. Statistical analysis to achieve Aims 2 and 3 will be conducted using multilevel logistic regression to allow for exposure to peer navigation to vary by time. This will be implemented using regression models specified for proportions in Stata 14 (StataCorp LLC). Longitudinal analysis compares time to CD4 POC and ART (among those eligible) for participants testing positive for HIV infection, controlling for other potential confounders.

## Human Subjects Considerations

Discussion of HIV and sexuality is inherently sensitive in nature. As such, all study activities are conducted with emphasis on confidentiality and privacy of participants. The study office provides the participants with a safe environment free from outward harassment or discrimination. Our collaboration with the International HIV/AIDS Alliance Myanmar and local CBOs serving the MSM and TW populations ensures that all activities are sensitive to stigma and other challenges faced by MSM and TW and designed interventions are acceptable to the population. The surveys and data collection are conducted in a private room located in the study offices. Study staff members are required to complete human subjects training and provide their certificates of training prior to conducting human subjects research. All study activities are conducted in private with individual participants; no individual other than the interviewer or laboratory technician is permitted in the room at the time of data collection. During data collection, the participant has the right to refuse to answer any questions he or she is not comfortable answering to protect privacy.

Trained Alliance staff working on this project obtain informed consent from participants but allow participants to leave a mark in lieu of their signed name. All consent processes use a Myanmar language consent script, approved by Johns Hopkins School of Public Health Institutional Review Board and the local ethical review board. During the consent process, the staff member explains the study in detail, outlining the purpose, sequence of events, rights, potential risks and benefits to participants, and eligibility criteria. This information, along with a local study phone number that can be called with questions or concerns, is available on a paper version of the approved version of consent script. Study staff read aloud the consent form and will allow participants to ask any questions at any time prior to requesting consent for participation in the

study. The consent process, along with surveys and biologic specimen collection, will be conducted in private offices to maintain participant confidentiality and privacy.

Study staff keep confidential phone numbers and first names of potential participants for scheduling purposes only. One hard copy of the contact list is stored in a locked cabinet and an electronic version is saved in the electronic tracking system, separate from study data. Only staff members tasked with scheduling participants have access to the electronic list, by permission of the in-country principal investigator. The staff are instructed not to leave any voice or text messages with participants, to verify the identity of the individual, and to not mention any potentially stigmatizing behavior or HIV status during the phone conversations. When the study is mentioned over the phone or while reminding participants of an appointment, it is referred to as a health and wellness project.

Unique identifiers will be used to link study data and are constructed for all participants using information known only to the participant; these will be created to link all surveys, specimens, and laboratory results. The code is formulated from questions that are easily answered, reproducible, culturally appropriate, individually unique, and that MSM and TW will be comfortable answering. The unique identifier is an 8-digit reproducible alphanumerical code developed using the using the first 2 letters of the participant's last name, the first 2 letters of the participant's first name, the first 2 letters of the participant's father's first name, and last 2 digits of the participant's birth year. Burmese names are Romanized to English letters based on a transliterated chart of the Myanmar alphabet for purposes of creating a unique ID. During the process of creating the unique ID code with the participant, the study team member indicates that the participant only needs to respond with the appropriate numbers or letters to the question and do not need to give the full response (eg, participant only needs to provide the first letter of the city where he or she currently lives rather than state the full name of the city). Doing so provides an additional layer of privacy for the participants. This unique identifier can be recreated throughout the study and will facilitate linking study participants with biological results while maintaining anonymity. This process has been successfully used in past research studies conducted by this study team [39,50].

All surveys are interviewer-administered and collected using secure, computer-based systems. Anonymous, paper-based surveys are used only as back-up to the computer-based systems. Any anonymous, paper-based data collection forms are secured in a locked cabinet in the project offices. Data entry will take place at the study office, where study data are maintained on designated password-protected computers. Electronic transfer from the study office to JHU occurs only through encrypted files. The JHU principal investigator (CB) and in-country principal investigator (SN) control access to the data. Only relevant study staff who have completed ethical training and have permission from the principal investigator have access to the data.

Following completion of study activities, eligible participants receive 9000 kyat (about US $7) at visit 1 as incentive and

reimbursement of travel costs to the project office. Participants who are ineligible at visit 1 also receive 1000 kyat (about US $0.80) for travel expenses. Participants are provided with another 5000 kyat (US $4) at visit 2 for travel expenses as well as an additional 1000 kyat (about US $0.80) for each RDS recruitee who is eligible and participates in the study (maximum of 3 recruitees). These incentive amounts are consistent with other RDS studies implemented in Myanmar and are determined to encourage recruitment without unduly coercing participation [51]. For eligible participants, subsequent visits at 6 and 12 months upon enrollment into Aims 2 and 3 include 10,000 kyat (about US $8) as incentive and to cover travel expenses.

## Results

Formative, qualitative research was completed between June and September 2015. This included 12 MSM and 13 TW in-depth interview participants, as well as 12 MSM and TW participants and 23 service providers and community leaders participating in focus group discussions [36].

Participants provided logistical input, particularly as it related to location of the study office, recommending that the office be in a neighborhood in the center of the city and directly accessible by most bus lines. Participants also provided insights into social considerations for providing HIV testing, prevention, and care for MSM and TW populations in Yangon; opinions, preferences, and concerns about HIVST; and experiences and perceptions of HIV treatment and care. Generally, both MSM and TW described concerns about discrimination and stigmatization of MSM and TW populations within government health systems, often preferring to use nongovernmental community-based services that are an expanding presence in Yangon. Regardless of general perceptions that MSM and TW were at high risk for HIV acquisition and emerging options for HIV testing and care, MSM and TW participants described hesitation about HIV testing that was often related to fear of being seen in a testing facility that would unintentionally disclose one's HIV status, gender, or sexual identity.

The privacy and convenience offered by HIVST garnered significant interest from a majority of focus group participants, many of whom indicated the appeal of using these kits in the privacy of their own homes. This interest was weighed, however, against concerns that incorrect use could produce an inaccurate result and that lack of pretest counseling could lead to unintended adverse effects such as suicide by someone who receives a positive result. A further concern was that users would not be effectively linked to care following a positive diagnosis. These findings led to concrete protocol changes for the subsequent self-testing intervention. Specifically, in collaboration with OraSure, we developed new Myanmar language instructions for use, included a sticker on all packaging that provided a 24-hour telephone number in the case of questions or concerns, and included provision of pretest counseling for participants that included linkage to services when participants were provided with the self-test at the study office.

MSM and TW qualitative participants also described a variety of challenges in moving through the HIV care continuum.

Despite a significant increase in availability of ART in Myanmar in the past 5 years, the majority of participants reported issues with staging, treatment, and care, which can delay treatment initiation and inhibit adherence. Participants expressed frustration with current health system structure; many described having to visit different clinics and hospitals for testing, staging, treatment, and monitoring as well as having repeated confirmatory tests at each provider they visited.

MSM and TW participants expressed a strong preference for treatment and care services that are friendly, discrete, and convenient. Long travel times and cost, limited clinic hours, and unfriendly staff were described as barriers by many participants, especially when they are required to visit different providers for testing, staging, and treatment. In response, the research protocol was adjusted to include night and weekend office hours, the project office was chosen because of its central location and proximity to bus lines, and MSM and TW office staff were hired to create a nonstigmatizing and welcoming environment.

Qualitative participants also voiced concerns that home visits by peer navigators could expose their HIV status to their family or the community. To protect the privacy of the participants who enroll in peer navigation, we adapted the protocol to allow peer navigators to visit participants in any mutually agreeable location. This flexibility allows the participant to determine if, how, and when they would like to disclose their status to family and friends and minimizes the chance of unintentional disclosure.

Following the qualitative research, Aim 1 recruitment began in November 2015 with subsequent enrollment into Aims 2 and 3, and study activities for the 3 aims are currently ongoing. Broader social changes have since led to further modification of the above protocol. First, during the development of the intervention protocol the government of Myanmar adjusted the ART guidelines to reflect the importance of early detection and treatment in key populations at risk of HIV infection [52]. Recent updates to the WHO guidelines have since prompted the government to change this strategy and promote immediate ART initiation for all key populations, including MSM and TGW, regardless of CD4 count [28,53]. Our protocol had initially focused on the inclusion of ART-eligible MSM and TW in Aims 2 and 3; however, these policy changes made all newly diagnosed participants eligible for ART. Thus, the research plan was adjusted to incorporate this change, and all participants found to be living with HIV are referred to treatment and care programs and offered peer navigation assistance.

Throughout the implementation of this study, many nongovernmental organizations in Yangon have begun to offer home visits and peer support programs for clients who are on ART. Given the recent popularity of such programs and potential competition between this study and ongoing programs, we further altered the procedures in Aim 3, allowing participants to use our peer navigation services or, alternatively, use external peer navigation services from organizations providing the participant's ART. Additional survey items were subsequently developed to capture data about types and frequency of services participants receive from these organizations to use in the comparison of peer navigation versus declined navigation.

## Discussion

This study seeks to identify successful and acceptable methods to address losses in the HIV care continuum among MSM and TW in Myanmar. Formative, qualitative research has been completed and was used to further refine the study protocol and interventions. Qualitative research identified several perceived benefits and concerns related to HIVST, which allowed us to ensure instructions of HIVST were understandable to participants and that participants had appropriate pretest counseling prior to HIVST and were linked to counseling and services following testing. Additional identification of barriers and facilitators to HIV care, ART initiation, and adherence during qualitative research allowed for further refinement of the intervention and study procedures. Following the completion of the formative research, enrollment into Aim 1 began in November 2015 with subsequent enrollment into Aims 2 and 3 with prospective follow-up for participants with biologically confirmed prevalent or incident HIV infection and who had not previously been engaged in care. These participants are being followed to determine the impact of CD4 POC and peer navigation on ART initiation and virologic suppression.

Early identification of HIV infection, engagement in care, and ART adherence are critical components to provide both therapeutic benefits for people living with HIV and to reduce onward transmission of HIV among at-risk populations [54]. The National AIDS Program in Myanmar has recognized the urgent need to respond to the HIV epidemic that is concentrated among MSM, TW, and other key populations; however, innovative methods to overcome stigma and provide access to HIV testing and care services are needed. The growth of the nongovernmental organization community in Myanmar, coupled with the increasing implementation of and capacity for innovative methods, can very well support these national efforts and may have aggregate effects against the HIV epidemic among MSM and TW.

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## Authors' Contributions

CB is the principal investigator of this study. CB, SN, ALW, EC, and SDB collaborated in the design and oversight of the overall study. ALW, EC, and SHHM led trainings for study team members, and KHT, AZP, and ZMT oversee data collection. AW wrote the initial drafts of this manuscript. All authors reviewed and edited the manuscript, and all take responsibility for its integrity as well as the accuracy of the analysis.

## Conflicts of Interest

None declared.

## Multimedia Appendix 1

Reviewers' comments.

[PDF File (Adobe PDF File), 47KB - resprot_v6i5e90_app1.pdf ]

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## Abbreviations

**3 MDG:** Three Millennium Development Goals Fund
**amFAR:** Foundation for AIDS Research
**ART:** antiretroviral therapy
**CBO:** community-based organization
**DBS:** dried capillary blood spot collection
**FDA:** Food and Drug Administration
**HIVST:** HIV self-test
**HPTN:** HIV Prevention Trials Network
**JHU:** Johns Hopkins University
**LGBT:** lesbian, gay, bisexual, and transgender
**MSM:** men who have sex with men
**PEPFAR:** United States President's Emergency Plan for AIDS Relief
**POC:** point-of-care
**RDS:** respondent-driven sampling

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**TW:** transgender women
**VCT:** voluntary counseling and testing
**WHO:** World Health Organization

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Proposal

# Geriatric Patient Safety Indicators Based on Linked Administrative Health Data to Assess Anticoagulant-Related Thromboembolic and Hemorrhagic Adverse Events in Older Inpatients: A Study Proposal

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## *Abstract*

**Background:** Frail older people with multiple interacting conditions, polypharmacy, and complex care needs are particularly exposed to health care-related adverse events. Among these, anticoagulant-related thromboembolic and hemorrhagic events are particularly frequent and serious in older inpatients. The growing use of anticoagulants in this population and their substantial risk of toxicity and inefficacy have therefore become an important patient safety and public health concern worldwide. Anticoagulant-related adverse events and the quality of anticoagulation management should thus be routinely assessed to improve patient safety in vulnerable older inpatients.

**Objective:** This project aims to develop and validate a set of outcome and process indicators based on linked administrative health data (ie, insurance claims data linked to hospital discharge data) assessing older inpatient safety related to anticoagulation in both Switzerland and France, and enabling comparisons across time and among hospitals, health territories, and countries. Geriatric patient safety indicators (GPSIs) will assess anticoagulant-related adverse events. Geriatric quality indicators (GQIs) will evaluate the management of anticoagulants for the prevention and treatment of arterial or venous thromboembolism in older inpatients.

**Methods:** GPSIs will measure cumulative incidences of thromboembolic and bleeding adverse events based on hospital discharge data linked to insurance claims data. Using linked administrative health data will improve GPSI risk adjustment on patients' conditions that are present at admission and will capture in-hospital and postdischarge adverse events. GQIs will estimate the proportion of index hospital stays resulting in recommended anticoagulation at discharge and up to various time frames based on the same electronic health data. The GPSI and GQI development and validation process will comprise 6 stages: (1) selection and specification of candidate indicators, (2) definition of administrative data-based algorithms, (3) empirical measurement of

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indicators using linked administrative health data, (4) validation of indicators, (5) analyses of geographic and temporal variations for reliable and valid indicators, and (6) data visualization.

**Results:**  Study populations will consist of 166,670 Swiss and 5,902,037 French residents aged 65 years and older admitted to an acute care hospital at least once during the 2012-2014 period and insured for at least 1 year before admission and 1 year after discharge. We will extract Swiss data from the Helsana Group data warehouse and French data from the national health insurance information system (SNIIR-AM). The study has been approved by Swiss and French ethics committees and regulatory organizations for data protection.

**Conclusions:**  Validated GPSIs and GQIs should help support and drive quality and safety improvement in older inpatients, inform health care stakeholders, and enable international comparisons. We discuss several limitations relating to the representativeness of study populations, accuracy of administrative health data, methods used for GPSI criterion validity assessment, and potential confounding bias in comparisons based on GQIs, and we address these limitations to strengthen study feasibility and validity.

## Introduction

### Background

People aged 65 years and over are the most frequent users of acute care hospitals in Europe, and aging trends among hospital inpatients are expected to increase dramatically in the next decades [1,2]. However, acute care hospitals often deliver substandard care to older people with complex care needs [3]. Moreover, frailty, chronic multimorbidity, disability, polypharmacy, and the resulting clinical and organizational complexity of care [4] expose older inpatients to an increased risk of hospital care-related adverse events [5-7]. A literature review not only confirmed the high incidence of adverse events among older inpatients, accounting for 5% to 60% of admissions in acute care hospitals, but also highlighted the strong association between adverse events and hospital care quality, with more than 50% of these events being deemed preventable [7]. These adverse events have important consequences for older patients, as they accelerate the aging process and lead to loss of autonomy, frequent and longer hospitalization, institutionalization, and finally death [4,6,7]. Adverse events also worsen patients' experience with hospital care and affect their quality of life [4,8]. Finally, they weigh on health services utilization and costs [4,6].

Like most countries, Switzerland and France have initiated systemic reforms to move toward a more sustainable health care system and meet the challenges of aging and chronic multimorbidity [9]. Both governments give priority to health care quality improvement in older patients and foster the provision of better data to inform health policy, promote transparency, and improve health care efficiency [10-15]. Indeed, quality and safety indicators targeting older inpatients are essential to support and drive quality improvement, as well as inform health care stakeholders. These indicators are also of great interest to compare the performance of various health systems [16]. Some commonly used indicators based on large administrative health databases (eg, hospital discharge and insurance claims databases) could help assess and compare patient safety and health care quality across hospitals and health

territories in both countries. They could also enable comparisons of Swiss and French health systems' performance in providing high-quality, safe care to vulnerable older inpatients [12,15], which are a source of "cross-country learning" and improvement [17,18]. For example, the Patient Safety Indicators (PSIs) [19], which have been developed by the US Agency for Healthcare Research and Quality (AHRQ) [19] and adopted internationally [20,21], could screen acute hospital discharge data for potentially avoidable adverse events occurring during hospitalization. Similarly, PSIs adapted to linked administrative health data (ie, hospital discharge data linked to insurance claims data) could be of use to monitor in-hospital and postdischarge adverse events, as the latter may reflect delayed and poor quality of hospital care or premature discharge from hospital [22]. Finally, some of the Assessing Care of Vulnerable Elders-3 (ACOVE-3) quality indicators could evaluate health care processes and medication management in older inpatients based on administrative data [3,23].

Among adverse events affecting older inpatients, anticoagulant-related thromboembolic and hemorrhagic adverse events are especially frequent and serious; in fact, age is one of the strongest predictors of venous or arterial thromboembolism and bleeding during anticoagulation [24-26]. Furthermore, thromboprophylaxis is frequently suboptimal in older inpatients despite the availability of professional guidelines [27]; many studies have indeed reported recurrent prescriptions of supratherapeutic doses of anticoagulants, as well as frequent underuse and rare risk-benefit assessment of anticoagulation in this population [26-30]. Finally, the growing use of anticoagulants, especially of direct oral anticoagulants, in the geriatric inpatient population and their substantial risk of toxicity and inefficacy have become an important patient safety and public health concern worldwide [25,31]. Anticoagulant-related adverse events and the quality of anticoagulation management should therefore be routinely assessed in older inpatients receiving anticoagulants for the prevention and treatment of arterial or venous thromboembolism.

Two PSIs can be used to monitor potentially avoidable perioperative thromboembolic or bleeding events in older Swiss

and French inpatients: PSI-12, Perioperative Pulmonary Embolism or Deep Vein Thrombosis Rate, and PSI-09, Perioperative Hemorrhage or Hematoma Rate [19,20,32-34]. Indeed, although both indicators target adult inpatients, most corresponding adverse events affect inpatients aged 65 years and over [20]. Moreover, PSI-12 has been adapted to coding systems of various countries, including Switzerland and France [21,35]. Lastly, both algorithms have been extended to capture both in-hospital and postdischarge adverse events based on hospital discharge data linked to outpatient claims data [22]. Besides these perioperative PSIs, others should be developed to monitor adverse events related to venous thromboembolism curative treatments and thromboprophylaxis in at-risk medical conditions such as severe acute infection or atrial fibrillation. Case-mix adjustment of PSIs should also be considered to account for differences in older inpatients' clinical risks or disease severity at admission [4] and enable comparisons across hospitals or geographic areas [36,37]. In particular, PSIs should be adjusted for older inpatients' risk factors for both hospital care-related adverse events (eg, frailty, chronic multimorbidity, disability, or polypharmacy) and thromboembolic or hemorrhagic adverse events (eg, age ≥75 years, renal or liver failure, inherited or acquired disorders of hemostasis, malignancy). Thus, besides the Charlson comorbidity index [38] and the updated chronic disease score [39], which have already been adapted to Swiss and French administrative health data, other comorbidity indexes [40], proxy measures of frailty and disability [41,42], and individual risk scores of thromboembolism or hemorrhage [43,44] should also be developed or adapted [45].

Regarding process quality metrics, three ACOVE-3 indicators may be used to evaluate warfarin prescription and surveillance in older patients with heart failure or atrial fibrillation [23]. Additional indicators should be developed to assess the management of other anticoagulants, including direct oral anticoagulants.

## Objectives

This research project aims to develop and validate a set of outcome and process indicators based on linked administrative health data (ie, insurance claims data linked to hospital discharge data) assessing older inpatient safety related to anticoagulation in both Switzerland and France, and enabling comparisons across time and among hospitals, health territories, and countries.

The project will thus comprise complementary steps aiming to (1) develop and validate a set of geriatric patient safety indicators (GPSIs) assessing in-hospital and postdischarge anticoagulant-related adverse events in older inpatients; (2) adapt the PSI-09 and PSI-12 to Swiss and French linked data; (3) develop a set of geriatric quality indicators (GQIs) assessing the management of anticoagulants for the prevention and treatment of arterial or venous thromboembolism based on Swiss and French data; (4) develop or adapt chronic multimorbidity indexes, proxy measures of frailty and disability, and thromboembolic and bleeding risk scores based on Swiss and French data to adjust GPSIs on case mix; and (5) compare anticoagulation safety within and between Switzerland and France.

## Methods

### Development and Validation Process

We will develop and validate GPSIs according to the methodology used by the AHRQ [46-48], which comprises 6 standardized sequential stages (Figure 1).

### Selection and Specification of Candidate GPSIs

We will use a modified Delphi method [49] combining evidence from a systematic literature review with the collective judgment of clinical experts (clinical panel) to select candidate indicators and define their specifications (numerator, denominator, risk-adjustment factors, and measurement time frame for postdischarge adverse events). These candidate GPSIs will measure the cumulative incidences of thromboembolic and hemorrhagic adverse events for selected surgical procedures or medical conditions (Textbox 1).

**Figure 1.** Summary of the geriatric patient safety indicator (GPSI) development and validation process. GQI: geriatric quality indicator; NPV: negative predictive value; PPV: positive predictive value; Se: sensitivity; Sp: specificity.
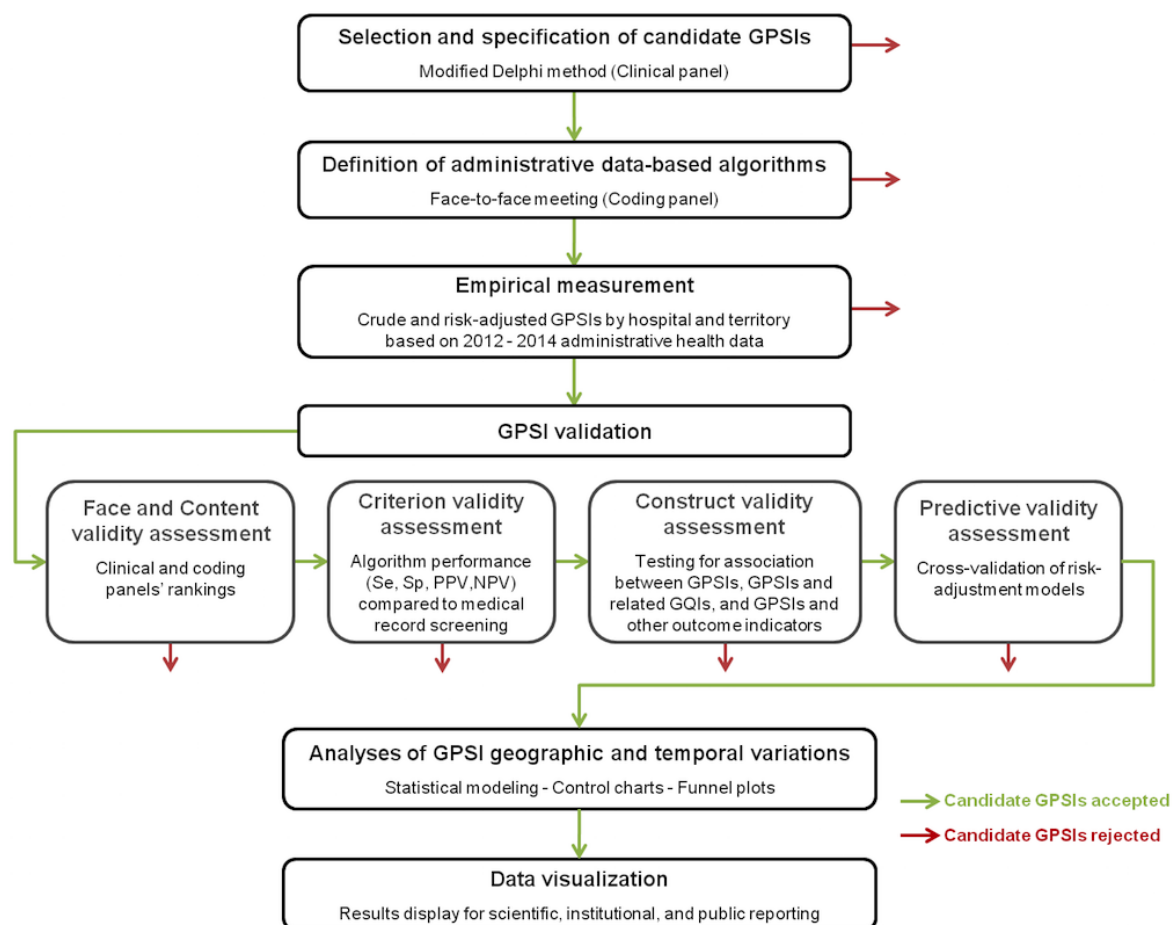


**Textbox 1.** Candidate geriatric patient safety indicators (GPSIs) and geriatric quality indicators (GQIs) assessing older inpatient safety regarding anticoagulation.

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**GPSIs**

Cumulative incidence of in-hospital and postdischarge anticoagulant-related adverse events:

1. Venous thromboembolism or hemorrhagic events in surgical patients

- High-risk surgery (eg, total hip or knee arthroplasty)

- Moderate-risk surgery (eg, abdominal and pelvic surgery)

- Low-risk endoscopic surgery or diagnostic procedures (eg, colonoscopy)

2. Venous thromboembolism or hemorrhagic events in medical patients

- Acute medical conditions (eg, severe acute infection, acute heart failure, nonsurgical trauma)

- Chronic conditions (eg, cancer, chronic inflammatory diseases)

3. Strokes and other systemic arterial embolisms or hemorrhagic events in patients with atrial fibrillation

4. Recurrent venous thromboembolism or hemorrhagic events in patients with venous thromboembolism

5. Adapted Patient Safety Indicator (PSI) -12 (perioperative thromboembolism)

6. Adapted PSI-09 (perioperative hemorrhagic event)

**GQIs**

For each GPSI, 2 GQIs assessing the management of anticoagulant treatments:

1. Proportion of index hospital stays resulting in the recommended anticoagulation (drug, dose, frequency, duration) at and after discharge

2. Median duration of anticoagulant treatment after discharge for index hospital stays

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### Definition of Administrative Data-Based Algorithms

GPSI algorithms will be determined by Swiss and French administrative health data experts (coding panel) during a face-to-face meeting. The coding panel will first determine the feasibility of measuring candidate indicators and risk-adjustment factors using administrative health data, and, second, select the diagnosis, procedure, and drug codes to be included in and excluded from their calculation.

### Empirical Measurement

We will empirically measure crude and risk-adjusted GPSIs retained at the end of the second stage at the hospital, territorial, and national levels for the years 2012 to 2014 using Swiss and French data. We will conduct sensitivity analyses to assess the impact of different definitions and selected codes on the robustness of empirical results. This stage will also aim to explore the consistency of the empirical results with the literature, highlight variations in indicators across hospitals or health territories, and examine potential bias related to insufficient adjustment on patient case mix or variation in coding practices. We will exclude GPSIs not performing well from the validation stage.

### Validation of GPSIs

We will test the reliability and validity of retained GPSIs using a comprehensive validation framework. (1) *Face and content validity assessment*: the apparent and content relevance of GPSIs will be discussed by the clinical and coding panels. (2) *Criterion validity assessment*: we will assess the algorithm accuracy of each retained GPSI by measuring its performance in identifying the corresponding adverse event compared with a reference standard (medical record screening). GPSIs with low sensitivity (<75%) or low positive predictive value (PPV) (<75%) will be excluded from the candidate list [50]. We will similarly assess the accuracy of the algorithm developed for each case-mix factor based on coded administrative health data. (3) *Construct validity assessment*: we will verify statistical associations among unadjusted GPSIs, between unadjusted GPSIs and related process indicators, and between unadjusted GPSIs and other unadjusted outcome indicators assessing the same care processes (eg, mortality rates, length of stay, and potentially avoidable readmissions rates). GPSIs with nonsignificant or inconsistent correlations will be excluded from further development and validation processes. (4) *Predictive validity assessment*: finally, for each remaining GPSI, we will assess the statistical performance of its risk-adjustment model in accounting for actual differences in case mix, and therefore in predicting the related outcome, by measures of its calibration and discriminatory power.

### Analyses of GPSI Geographic and Temporal Variations

(1) We will analyze *geographic variations* at the hospital and territorial levels using funnel plots to identify outliers. Statistical modeling will identify potential causes of systematic variations related to the health system or the quality of care. (2) We will study *temporal variations* in monthly or quarterly measures of GPSIs for the period 2012-2014 at the national and territorial levels using statistical models to identify potential trends and explanatory factors. We will also study temporal variations at

the hospital level, hospital legal status level (ie, public, private not-for-profit, and private for-profit), and hospital volume level (ie, tertiles or quintiles of annual index hospital stays eligible for GPSI denominator) using control charts to identify special causes of variation related to the quality of the health care processes.

### Data Visualization

For both Switzerland and France, we will construct comparative graphic displays of the anonymized results for scientific, public, or institutional reporting. They will comprise (1) a Swiss and French atlas documenting territorial variations in risk-adjusted GPSIs; (2) funnel plots reflecting between-hospital and between-hospital category variations in risk-adjusted GPSIs; (3) individual control charts of risk-adjusted GPSIs displaying temporal variations for each hospital, hospital category, and territory; and (4) national, territorial, and individual temporal trends in GPSIs over the period 2012-2014.

Regarding GQIs, the clinical panel will select candidate indicators among those suggested in Textbox 1. We will then apply a similar development and validation process, except for criterion and predictive validity assessment. Indeed, as anticoagulant treatments (drug, dose, frequency, and duration) coded in insurance claims data reflect quite precisely the ones that were prescribed and reimbursed, GQI algorithms should be accurate for assessing the management of anticoagulants at, and after, discharge. In addition, we will not be able to access outpatient medical records, which would constitute the suitable reference standard for testing the accuracy of GQIs. We will not assess the predictive validity of GQIs because process indicators do not require case-mix adjustment when comparing hospitals or health territories. Indeed, the quality of hospital care processes does not usually depend on inpatient case mix [37,51].

## GPSI and GQI Development

### Study Design

To develop GPSIs or GQIs, we will conduct multicenter retrospective observational cohort studies based on insurance claims data individually linked to hospital discharge data.

### Population Setting

In Switzerland, the study population will consist of all residents aged 65 years and over admitted to a Swiss acute care hospital at least once between 2012 and 2014 (ie, the inclusion period) and insured under the compulsory basic health insurance scheme by Helsana Group for at least 1 year before admission and 1 year after discharge. Helsana is one of the 3 biggest insurance groups in Switzerland, covering approximately one-fifth of the Swiss population aged 65 years and over [52].

Inclusion criteria for the French study population will be similar except that they will target older residents admitted to a French acute care hospital and insured under the general scheme by the National Health Insurance Fund for Salaried Workers (Caisse Nationale d'Assurance Maladie des Travailleurs Salariés [CNAMTS]). This scheme covers approximately 69% of the French population aged 65 years and over (2014 data provided by CNAMTS).

We will exclude from both study populations patients for whom (1) 2012-2014 administrative health data were incomplete, (2) individual data linking was not possible, and (3) hospital length of stay was less than 2 days.

## Candidate GPSIs and GQIs

AHRQ PSIs are measures based on administrative health data that "screen for adverse events that patients experience as a result of exposure to the healthcare system, and that are likely amenable to prevention by changes at the system or provider level" [19]. Likewise, candidate GPSIs will screen Swiss and French linked administrative data for thromboembolic or hemorrhagic adverse events that resulted from exposure to medical or surgical conditions requiring anticoagulant treatments, and occurred during hospital stay or after discharge (Textbox 1). Hospital-level GPSIs will measure, for each acute care hospital, the cumulative incidences of in-hospital and postdischarge anticoagulant-related adverse events and be defined with a denominator (ie, index stays in a given hospital within a 1-year period) and a numerator (ie, denominator stays resulting in the adverse event of interest during hospitalization and up to 30 days, 60 days, 90 days, 6 months, and 1 year after discharge). For example, the denominator of the GPSI that will measure the 2012 cumulative incidence of in-hospital and 30-day postdischarge hemorrhagic events for older patients receiving venous thromboprophylaxis after elective total hip arthroplasty will include any 2012 hospital stay for elective total hip arthroplasty, excluding 1-day surgery, of patients aged 65 years and over. Indeed, older patients undergoing elective total hip arthroplasty are supposed to receive the appropriate venous thromboprophylaxis, as they are considered to be at high risk of thromboembolic and hemorrhagic events [53]. The numerator will comprise any hemorrhage [54] occurring during index hospital stays and up to 30 days after the patients' discharge dates. The hospital that performed the total hip arthroplasty procedure will be held accountable for the index stay and hemorrhage. We will identify index stays and hemorrhages using hospital discharge data and linked administrative health data, respectively.

For each GPSI, 2 GQIs will measure for each hospital (1) the proportion of index hospital stays resulting in the recommended anticoagulation (drug, dose, frequency, and duration) at discharge, and up to 30 days, 60 days, 90 days, 6 months, and 1 year after discharge; and (2) the median duration of recommended anticoagulant treatment after discharge for index hospital stays. For example, the GPSI described above will be completed by the following GQIs: (1) the proportion of 2012 hospital stays for elective total hip arthroplasty in patients aged 65 years and over resulting in the recommended anticoagulation (drug, dose, frequency, and duration) at and up to 30 days after discharge; and (2) the median duration of recommended anticoagulant treatment after discharge for these index stays. We will extract information on anticoagulant treatments after hospital discharge from insurance claims data.

## Administrative Health Data Scope and Time Frame

We will extract Swiss administrative health data from the Helsana Group data warehouse and will include 2010-2015 insurance claims data individually linked to 2012-2015 acute care hospital discharge data and individual measures of dependency for nursing home residents. Since data collection of inpatient diagnosis and procedure codes and dependency measures started in 2012, only insurance claims data will be available for the period 2010-2012.

We will extract French data from the national health insurance information system (Système National d'Information Inter-Régimes de l'Assurance Maladie [SNIIR-AM]) hosted by CNAMTS [55]. Since 2007, SNIIR-AM has included individually linked data from various administrative databases for the entire French population: all hospital discharge data (ie, discharge data from acute, postacute, rehabilitation, psychiatric, and long-term care hospitals and from hospital-at-home facilities); insurance claims data; data on nursing homes residents; and data on health professionals' characteristics. We will include only those patients insured under the general scheme, as vital status and death date are exhaustive only for these patients.

Multimedia Appendix 1 comprehensively describes Swiss and French data, including linkage methods and success rates.

In both countries, we will identify index hospital stays and in-hospital adverse events from 2012-2014 hospital data and adverse events up to 1 year after discharge from 2012-2015 linked hospital and insurance data (Textbox 2). Similarly, we will test anticoagulation management up to 1 year after discharge over the period 2012-2015 using linked data (Textbox 2). GPSI risk-adjustment factors will be estimated using data from 2010-2014 to account for patient conditions up to 2 years before their admission. Since hospital discharge data will not be available for the period 2010-2012 in Switzerland, we will derive risk-adjustment factors from insurance claims data only (Textbox 2).

**Textbox 2.** Geriatric patient safety indicator (GPSI) and geriatric quality indicator (GQI) measurement time frames.

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**GPSIs**

Inclusion period for index hospital stay (denominator)

- Discharge date between January 1, 2012 and December 31, 2014

Follow-up period for adverse event screening (numerator)

- From admission date of index hospital stay up to 1 year after discharge date of index hospital stay

Inclusion period for case-mix factors present at admission (risk adjusters)

- Up to 2 years before admission date of index hospital stay

**GQIs**

1. Proportion of index hospital stays resulting in the recommended anticoagulation at and after discharge

Inclusion period for index hospital stay (denominator)

- Discharge date between January 1, 2012 and December 31, 2014

Follow-up period for prescription of anticoagulant treatment (numerator)

- Up to 1 year after discharge date of index hospital stay

2. Median duration of anticoagulant treatment after discharge for index hospital stays

Follow-up period for prescription of anticoagulant treatment

- Up to 1 year after discharge date of index hospital stay

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## GPSI Criterion Validity Assessment

### Study Designs

The study design considered to assess the criterion validity of each GPSI will be a multicenter cross-sectional study with a test-based enrollment approach [56].

### Population Settings

For each GPSI, the study population will comprise all older insured patients who were admitted to an acute care hospital between 2013 and 2014 and were at risk for the related adverse event (GPSI denominator population). Whereas any acute care hospital may be included in the Swiss validation study, the French study will target acute care hospitals located in the Burgundy-Franche-Comté region, which hosts Dijon University Hospital (ie, the French collaborative research center). Indeed, as these studies are time and resource consuming, it is necessary to balance representativeness against efficiency. For both countries, exclusion criteria will include an insufficient number of at-risk admissions over the 2 years 2013 and 2014 (≤50 stays) and a hospital's refusal to participate.

### Data Source and Criterion Validity Metrics

We will assess GPSI accuracy by measuring the performance of the algorithm in identifying corresponding adverse events based on administrative health data compared with a reference standard (medical record screening). We will identify GPSI+ (ie, complicated) and GPSI– (ie, uncomplicated) hospital stays from administrative data based on the algorithm. Then, we will randomly select a sample of these GPSI+ and GPSI– stays and verify whether an adverse event is recorded in the corresponding medical record. GPSI criterion validity will then be assessed based on the sensitivity, specificity, PPV, and negative predictive value of the algorithm.

## Planned Statistical Analyses and Sample Size Calculation

Statistical analyses will be performed using Stata/MP software version 14 for Windows (StataCorp LLC) or SAS/STAT software, version 9.4 of the SAS system for Windows (SAS Institute Inc).

### Indicator Calculation and Case-Mix Adjustment

GPSIs will provide yearly (2012-2014) observed cumulative incidences of thromboembolic and bleeding adverse events in selected surgical procedures or medical conditions (Textbox 1) for each hospital, hospital legal status, hospital volume category, health territory (ie, Swiss cantons and French departments), and country. We will calculate these incidences as the proportion of at-risk hospital stays resulting in in-hospital or postdischarge adverse events over a year. To allow comparisons across hospitals and health territories, we will adjust GPSIs on patient case mix (eg, age, sex, multimorbidity, frailty, disability, polypharmacy, point of origin for admission, admission mode, thromboembolic or hemorrhagic individual score, and local health care capacity) using multilevel logistic regression modeling accounting for the hierarchical structure of the data. Every GPSI risk-adjustment model will undergo a 3-fold cross-validation, in which we will use a random sample comprising one-third of the whole data to develop the empirical model (development dataset), another one-third to estimate the parameters (estimation dataset), and the remaining one-third to test the predictive validity of the model (validation dataset) [57]. The predictive validity of the model will be assessed by

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measures of its calibration (Hosmer-Lemeshow goodness-of-fit test) and discriminatory power (C statistic) [58]. We will provide expected cumulative incidences with their 95% confidence intervals.

We will calculate GQIs as (1) the proportion of at-risk hospital stays resulting in the recommended anticoagulation (drug, dose, frequency, and duration) at discharge and up to 30 days, 60 days, 90 days, 6 months, and 1 year after discharge; and (2) the median duration of recommended anticoagulant treatment after discharge for index hospital stays. Anticoagulation management for selected at-risk conditions (Textbox 1) will be assessed at the hospital, hospital legal status, hospital volume category, territorial, and national levels and for each year of the inclusion period. Process indicators will not be risk adjusted.

### Case-Mix Factor Calculation

Case-mix factors usually considered for PSI risk adjustment include age, sex, past medical history, point of origin for admission, admission mode, and comorbidity present at admission [19,36]. We will also consider other important predictors of adverse health outcomes, including thromboembolic or hemorrhagic events, in older inpatients. To this end, multimorbidity, polypharmacy, frailty, and disability indexes based on Swiss and French administrative health data will be purposely developed or adapted from already validated ones [38-40,59-62]. Although these conditions are considered as separate clinical entities and independently associated with poor outcomes, they overlap significantly and are causally interrelated [4,41,61,63]. Consequently, risk-adjustment models will also account for possible interactions or associations between these various case-mix variables. We will also consider a single proxy measure of older inpatient complexity—similar to the Charlson and Elixhauser indexes—that could encompass all these conditions. GPSIs will also be adjusted on individual thromboembolic or bleeding risk scores, including venous thromboembolism risk scores for surgical patients (Caprini and Rogers scores) [44], ischemic stroke risk scores for patients with atrial fibrillation ($CHA_2DS_2$-VASc or ATRIA score) [43], and a major bleeding risk score for patients on anticoagulation (HAS-BLED) [43]. $CHA_2DS_2$-VASc and HAS-BLED have already been estimated based on French data [45] and will be adapted to Swiss data. We will develop the remaining scores in both countries.

### Studies of GPSI and GQI Geographic and Temporal Variations

We will study variations across hospitals, hospital legal status, hospital volume categories, and health territories using (1) funnel plots to identify potential outliers [64-66]; (2) hierarchical logistic regression models to identify potential causes of systemic variations related to the health system (eg, health care supply, including specialized geriatric units or professionals in hospitals; availability of integrated care organizations; health policy strategy supporting patient safety) or to the quality of care (eg, availability of professional guidelines, adherence to treatment and surveillance standards regarding anticoagulation); and (3) propensity score-based risk-adjustment models to

estimate the performance of the different hospitals assessed by validated GPSIs or GQIs [67].

We will study monthly or quarterly variations in GPSIs and GQIs over the inclusion period at the national and territorial levels using multilevel logistic regression modeling for repeated measures to identify potential trends and explanatory factors (eg, changes in anticoagulation guidelines, coding rules, or classifications, Diagnosis-Related Group (DRG) system, or drug and procedure reimbursement limits). We will also assess temporal variations at the hospital, hospital legal status, and hospital volume levels using control charts, including p-charts and cumulative sum charts [68-71], to identify special causes of variation related to the quality of health care processes.

### Comparisons of Anticoagulant-Related Safety Between Switzerland and France

We will compare GPSIs measured at the national level between Switzerland and France using direct age and sex standardization, as recommended by the Organisation for Economic Co-operation and Development [16]. Indeed, age and sex standardization enable accounting for between-country differences in population structures, including general and inpatient populations, and practices regarding older inpatients' hospitalization in acute care [21]. For each GPSI, aggregated nationwide counts of index hospital stays stratified by age and sex will define the internal reference population. We will then calculate a comparative morbidity figure (ie, the ratio of directly age- and sex-standardized adverse event rates in Switzerland and France) along with its 95% confidence interval. Moreover, to account for differences in coding systems, we plan to adjust national measures of GPSIs on the mean number of secondary diagnoses among denominator cases [21].

## Results

### Administrative Health Data and Study Populations

After accounting for inclusion and exclusion criteria, we will include 166,670 Swiss and 5,902,037 French residents aged 65 years and over in our study. Multimedia Appendix 1 comprehensively describes Swiss and French data available for our study, along with data linkage methods and success rates.

### Sample Size Calculation for GPSI Criterion Validity Assessment

For sample size calculation, we used a test result-based sampling method [72] to minimize the number of medical records to be abstracted. We estimated optimal sample sizes, as well as sampling fractions of GPSI+ and GPSI– medical records to be abstracted, for prevalence (ie, proportion of medical records in which at least 1 adverse event was recorded) ranging from 0.4% to 5%, a desired algorithm sensitivity of 75%, a 20% width for sensitivity 95% confidence interval, and unknown numbers of at-risk stays (ie, unknown GPSI denominators). We extracted prevalence values and PPVs from the literature [16,24,32-34,44,50,73-75] and calculated sample size using Stata/IC software version 13 (see Multimedia Appendix 2). Thus, assuming a prevalence of 2%, an optimal sample of 3164 medical records should be randomly selected from participating

hospitals and abstracted: 126 GPSI+ and 3038 GPSI– medical records. These results are consistent with the literature [73].

## Ethical and Regulatory Aspects

The research project was approved by the Cantonal Ethics Commission of Vaud (Switzerland) in August 2016 (Decision CER-VD 2016-00508) and by the French data protection authority (Commission National de l'Informatique et des Libertés) in March 2016 (Decision DE-2016-036).

## Timetable of the Project

All administrative health data are now available to the Swiss and French research teams. The research project will run until the end of 2018.

# Discussion

## Main Strengths of the Study

First, to our knowledge, this is the first study aiming at developing and validating a set of geriatric quality and safety indicators based on linked administrative health data, both in Switzerland and in France. Assessing the quality and safety of anticoagulation in older inpatients based on such data is also innovative. Indeed, in addition to using extended PSI-09 and PSI-12, which capture perioperative adverse events up to 30 days after discharge [22], we will develop and validate a set of GPSIs assessing thromboembolic or bleeding adverse events for various surgical procedures or medical conditions requiring curative or prophylactic anticoagulation. Similarly, our set of validated GQIs will complement the ACOVE-3 quality indicators based on administrative health data assessing warfarin prescription and surveillance in older patients with heart failure or atrial fibrillation [23]. In particular, they should provide useful information on direct oral anticoagulant management.

Second, validated GPSIs will account for an older inpatient case mix, which is crucial when comparing hospitals or health territories. Specific indexes based on Swiss and French administrative health data, including multimorbidity, polypharmacy, frailty, and disability indexes, will thus be purposefully developed or adapted from existing ones to target older inpatients' conditions at admission [38-40,59-62]. These important predictors of adverse health outcomes (ie, mortality, morbidity, dependency, and institutionalization), health-related quality of life, and resource use [38,40,59] may be used not only as risk-adjustment factors for other health care quality and safety indicators, but also as screening tools for older patients' vulnerability in various health care settings. Indeed, many countries, including France, try to implement frailty or vulnerability screening and management programs (eg, the French initiative "parcours de santé pour les personnes âgées en risque de perte d'autonomie" [PAERPA]) to avoid institutionalization and hospitalization, improve older citizens' quality of life, and reduce health care costs [76,77]. Finally, assessing patient complexity and vulnerability, both at the individual and population levels, may contribute to better planning of appropriate health and social care services [76,77].

Developing or adapting individual thromboembolic or bleeding risk scores based on administrative health data is the third major strength of our study. These scores will be included in GPSI risk-adjustment models and may also contribute to assessing the quality of anticoagulant management by comparing patients' risks with the treatment they actually received. Indeed, decisions regarding anticoagulant treatments (ie, type, dose, frequency, and duration) and surveillance should be consistent with risk-benefit assessment, especially in the older inpatient population, which is highly exposed to anticoagulant-related thromboembolic or bleeding complications. Furthermore, complementing individual scores with patient outcomes (ie, GPSIs) and data on anticoagulant management (ie, GQIs) should enrich information on effectiveness and safety of anticoagulants in "real life," in particular direct oral anticoagulants, and eventually help improve professional guidelines [25,26,30,31].

Fourth, our project will enable comparisons of GPSIs and GQIs between Switzerland and France, which is a source of cross-country learning and performance improvement [17,18]. Indeed, despite having different organization, governance, and financing, and serving different populations, Swiss and French health systems "have similar goals and face similar challenges, such as demographic change, limited resources and rising costs" [17,18]. Between-country comparisons should thus help study differences in (1) linked administrative health data features, quality, regulation, and coding rules; (2) older inpatients' and health care providers' characteristics; (3) quality standards on and safety of anticoagulant management in older inpatients; and (4) health care policy and reforms toward transparency, accountability, and high-quality safe care to vulnerable older inpatients [12,15].

## Study Limitations

Our study has several limitations that should be considered when interpreting the results. First, our study populations may not be representative of all Swiss and French older inpatients. Indeed, Swiss data cover approximately 18% of the Swiss population aged 65 years and over [52], and policy holders residing in German-speaking cantons are overrepresented compared with others. French data include a very large population of nearly 6 million persons, namely 69% of the French insured aged 65 years and over. However, only salaried or retired employees are represented, while other professional subgroups and enrollees in 1 of the 16 specific insurance schemes (eg, soldiers, miners, ministers of religion, and employees of the French National Railway Company) are excluded from the study population [55]. As insured or cultural groups may differ in their risk factors, compliance with anticoagulant treatments, access to and utilization of health services, and geographic distribution (eg, employees may be underrepresented in rural areas), the internal and external validity of our study might be affected by selection bias [78]. Albeit figuring that this bias should not significantly affect our indicators, we will thus generalize our findings to the study populations and gather information on older inpatients excluded from our study. In particular, we will make a request to CNAMTS to access their data on French residents enrolled in other schemes than the general one. French data will thus cover the entire population.

Second, insurance claims data may also be incomplete or "selected." For example, they will not include coded diagnoses on adverse events occurring in outpatient settings and will not provide information on patients' adherence to treatment and surveillance. However, we expect to capture almost all postdischarge adverse events by screening readmissions, prescriptions or modifications of anticoagulant or antihemorrhagic treatments, outpatient procedures (eg, lower limb venous ultrasonography), and laboratory tests (eg, hemoglobin and international normalized ratio tests). Moreover, we believe that the quality of anticoagulant management is accurately assessed using large administrative databases linked over time. Swiss insurance claims may also be missing differentially according to health insurance deductibles (ie, SwF 300 to 2500 per year) [78-80]. Indeed, policyholders with the highest deductibles tend not to claim reimbursement of medical expenses when their annual amount does not reach the deductible, which leads to missing claims. However, this potential selection bias should not be significant, since health insurers estimate that only 2% to 3% of all invoices are not sent for reimbursement [52]. Finally, French data from SNIIR-AM may also lack some information regarding fully reimbursed long-term conditions. Indeed, long-term conditions are often underreported in patients fully covered for several long-term conditions or benefiting from a complementary insurance, or in nursing home residents [81]. We will overcome this limitation by deducing missing long-term conditions from medications coded in insurance claims or from diagnoses coded in hospital discharge records.

Third, hospital discharge data may also provide incomplete information. For example, data on inpatient medications will be missing for both countries, as they are not mandatory for reimbursement. We will then infer the prescribed anticoagulant treatment during hospital stay from that prescribed just after discharge using insurance claims data. Also, in Switzerland, we will not be able to identify reasons for readmission or retransfer to the same hospital within 18 days after discharge if the second stay is grouped in the same Major Diagnostic Category as the initial one. Indeed, according to the SwissDRG billing rules, such a readmission or retransfer is merged with the initial admission, leading to a single stay and discharge record. Furthermore, Swiss hospital discharge data are limited to acute care hospitals and do not cover hospital-at-home facilities, and rehabilitation or psychiatric hospitals. Thromboembolic and hemorrhagic adverse events occurring in these settings will thus be missed except severe ones that would necessitate transfer to acute care facilities.

Fourth, in both countries, neither hospital discharge data nor insurance claims data contain individual information on causes of death—which could be related to thromboembolic and hemorrhagic adverse events—or on significant factors that should be accounted for in GPSI case-mix adjustment. These factors include, for example, genetic factors, demographic characteristics (eg, ethnicity), clinical factors (eg, vital signs, results from clinical examinations or laboratory tests), health-related behaviors (eg, excessive alcohol consumption, diet, and physical activity), health literacy, and patient preferences or cultural beliefs [36].

Fifth, hospital discharge data may have potential limitations regarding coding accuracy. In particular, the quality of diagnostic and procedure coding may be affected by the quality of patient record documentation, coders' background, training, and experience (eg, clinicians vs professional coders), coding quality controls, and unintentional and intentional coding errors (ie, "gaming" or "upcoding" to increase reimbursement) [36,37,82,83]. Similarly, coding rules and classifications, coders' characteristics, DRG classification systems, and coding quality assurance policies (eg, coding quality controls, incentives for coding, and penalties for inappropriate coding) may vary significantly among health systems [21]. For example, Swiss and French health systems differ on coding rules for the "principal diagnosis" (ie, "condition responsible for resource use" vs "reason for admission") [84], mean numbers of secondary diagnoses coded [21], medical coding classifications for diagnoses (*International Classification of Diseases, 10th Revision [ICD-10], German Modification* vs *ICD-10 France*) and procedures (Swiss operation classification [CHOP] vs French shared classification of medical procedures [CCAM]), DRG classification systems (SwissDRG vs French Groupes Homogènes de Malades), and coders' profiles (professional coders vs mixed profiles, including professional coders and physicians). Limitations in coding quality may introduce systematic bias in GPSI estimates and in comparisons among hospitals, health territories, or countries, which cannot be accounted for by risk adjustment [21,36,37,84,85]. Criterion validity assessment will thus be essential to select valid GPSIs. Moreover, regarding the possible influence of coding practice to increase reimbursement, serious controls and financial penalties are in place in Switzerland to limit this issue. Similarly, serious controls are carried out in France, both at the hospital and at the Technical Agency for Information on Hospital Care (Agence Technique de l'Information sur l'Hospitalisation) levels.

Sixth, we have decided to compare the quality of anticoagulant prescription and surveillance across hospitals without adjusting GQIs for differences in case mix. However, process indicators may require case-mix adjustment when inpatients eligible to receive the related process are not perfectly specified [51] or when the "opportunity for violation of the standards" varies by case mix [37]. Indeed, guidelines related to preventive and curative anticoagulation do not account for older inpatients' heterogeneity regarding their functional, cognitive, or social disability, health conditions, and complexity. We will thus verify that these conditions have no impact on GQI variations across hospitals and health territories.

Seventh, criterion validity assessment based on retrospective review of medical records may be less methodologically robust than assessing GPSIs based on prospectively collected data [86]. Indeed, many adverse events are not recognized during the process of clinical care without dedicated assessment, and they are thus incompletely captured in medical records [87-90]. However, major adverse events will probably be well reported in medical records, as they will contribute to the use of additional resources in the hospital, and need to be reported for appropriate reimbursement. Moreover, Klopotowska et al showed that "[adverse drug events] with evident causality and

with clinically apparent and severe consequences," such as adverse drug events resulting in hemorrhage or raised international normalized ratio, are well recognized and documented by medical teams [89]. In addition, the implementation of more valid, but more resource-intensive, studies would require important financial support that will not be easy to obtain, neither from research agencies nor from health care services.

Eighth, prior validation studies have suggested that, despite good predictive and construct validity, AHRQ PSIs demonstrate moderate sensitivity and PPVs in detecting surgical adverse events [22]. Indeed, PSI algorithms usually favor specificity over sensitivity and PPV [91]. Consequently, unless AHRQ PSI validity is improved, more robust adverse event detection methods (eg, prospective monitoring or voluntary patient safety event reporting) should be preferred for internal quality improvement, performance assessment, public reporting, and, above all, pay for performance [83,91-93]. However, recent validation studies contradict these results, at least for PSI-12 and PSI-09 [33,83,91]. Indeed, Mull et al showed that the sensitivity of a PSI-12 algorithm based on *ICD, 9th Revision, Clinical Modification* (*ICD-9-CM*) diagnosis and procedure codes was 65% (95% CI 63%-67%). He also suggested that PSI-12 sensitivity could be improved by using *ICD-10-CM* codes [91]. Similarly, Utter et al reported that the sensitivity of a PSI-09 algorithm based on *ICD-9-CM* codes could reach 85% (95% CI 67%-94%) [33]. Regarding PPVs, Winters et al found, based on a literature review and meta-analysis, pooled PPVs of 63.5% (95% CI 44.3%-82.7%) for PSI-12 and 78.6% (95% CI 73.2%-84.1%) for PSI-09 [83]. In our study, the detection of anticoagulant-related adverse events should also be improved by using hospital discharge data linked to insurance claims data. Indeed, by adapting PSI-12 and PSI-09 algorithms to linked data, Mull et al were able to capture 72% (with PSI-12) and 77% (with PSI-09) additional events occurring up to 30 days after discharge [22]. Finally, in Switzerland, this research project will be integrated into a larger research program, which will aim to develop measures of anticoagulant-related thromboembolic and hemorrhagic adverse events based on structured (ie, administrative and clinical data) and textual data. These measures should, in the end, have better sensitivity and specificity than AHRQ PSIs. The larger research program has just been funded by the Swiss National Fund.

## Conclusions and Perspectives

This innovative study, which is part of a larger research program aiming to develop and validate GPSIs and GQIs in both hospital and ambulatory care settings, will provide valid and reliable outcome and process indicators to assess older inpatient safety related to anticoagulants. It should also provide new information on real-life prevention and treatment of thromboembolism, direct oral anticoagulant prescription and monitoring, and hemorrhagic adverse events related to direct oral anticoagulants in older patients. It should additionally contribute to describing older inpatients' characteristics and health professionals' practices in Swiss and French hospital and ambulatory care settings, and help identify geographic and temporal variations in older patient safety related to the health system. Moreover, within the frameworks of the Swiss Health 2020 policy agenda and the French National Health Strategy, the comparative assessment of hospitals and health territories using validated GPSIs and GQIs could help inform health policies, promote transparency, and improve health care efficiency.

## Authors' Contributions

The study was conceptualized by MALP and BB. The protocol and funding applications were written by MALP, enriched by BB, and reviewed by FP, IPB, CQ, OR, PT, and AFC. MALP and CQ are the coprimary investigators. BB, FP, PT, and AFC supported the project-facing health insurance managers (data owners). OR provided information regarding Swiss data and the Helsana data warehouse. PT and AFC provided information regarding French data and SNIIR-AM. MALP and BB planned the statistical analysis. MALP drafted the manuscript. All authors reviewed the draft version, made suggestions, and approved the final version.

## Conflicts of Interest

None declared. Helsana Health Sciences department is a research unit of the Helsana Insurance Group, which is a not-for-profit insurance. CNAMTS is the public national health insurance. Researchers from the Institute of Social and Preventive Medicine

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at Lausanne University Hospital or from the Department of Biostatistics and Bioinformatics at Dijon University Hospital will only be funded by public grants and by their institution.

## Multimedia Appendix 1

Detailed description of Swiss and French health administrative data used in the research project.

[PDF File (Adobe PDF File), 70KB - resprot_v6i5e82_app1.pdf ]

## Multimedia Appendix 2

Optimal sample size according to proportions of adverse events based on medical record and administrative health data screenings.

[PDF File (Adobe PDF File), 33KB - resprot_v6i5e82_app2.pdf ]

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## Abbreviations

**ACOVE-3:** Assessing Care of Vulnerable Elders-3

**AHRQ:** Agency for Healthcare Research and Quality

**CCAM:** classification commune des actes médicaux (French shared classification of medical procedures)

**CHOP:** Swiss operation classification

**CNAMTS:** Caisse Nationale d'Assurance Maladie des Travailleurs Salariés

**DRG:** Diagnosis-Related Group

**GPSI:** geriatric patient safety indicator

**GQI:** geriatric quality indicator

**ICD-9-CM:** International Classification of Diseases, 9th Revision, Clinical Modification

**ICD-10:** International Classification of Diseases, 10th Revision

**PAERPA:** Parcours de santé pour les personnes âgées en risque de perte d'autonomie (French Healthcare Pathway for frail elderly people)

**PPV:** positive predictive value

**PSI:** Patient Safety Indicator

**SNIIR-AM:** Système National d'Information Inter-Régimes de l'Assurance Maladie

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Protocol

# The SENSOR Study: Protocol for a Mixed-Methods Study of Self-Management Checks to Predict Exacerbations of Pseudomonas Aeruginosa in Patients with Long-Term Respiratory Conditions

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## Abstract

**Background:**   There are an estimated three million people in the United Kingdom with chronic obstructive pulmonary disease (COPD), and the incidence of bronchiectasis is estimated at around 0.1% but is more common in COPD and severe asthma. Both COPD and bronchiectasis are characterized by exacerbations in which bacteria play a central role. Pseudomonas aeruginosa is isolated from sputum samples from 4% to 15% of adults with COPD and is more likely to be isolated from patients with severe disease. Earlier detection of exacerbations may improve morbidity and mortality by expediting treatment. Aseptika Ltd has developed a system for patients to self-monitor important physiological measurements including levels of physical activity, peak flow, forced expiratory volume (FEV1), and biomarkers for P aeruginosa in sputum.

**Objective:**   We aim to test this system in 20 participants with *P aeruginosa* colonization and 10 controls with *Haemophilus influenzae*.

**Methods:**   We plan to recruit 30 adult participants with COPD or non-CF bronchiectasis who have cultured *P aeruginosa* or *H influenzae* during an exacerbation in the last 6 months. They must produce sputum on most days and should have been stable for 4 weeks prior to entry. Daily data collected will include symptoms, health care usage, medication, weight, FEV1, physical activity level, blood pressure, oxygen saturation, and temperature. Sputum and urine samples will be provided daily. These data will be analyzed to assess predictive value in detecting upcoming exacerbations. Qualitative data will be gathered through self-administered questionnaires and semistructured interviews to gather information on participant coping and their use of the technology involved.

**Results:**   Recruitment has been completed and results from the study should be available at the end of 2017.

**Conclusions:**   The SENSOR study aims to test a home-monitoring system in people with chronic airway infection and is currently underway.

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## KEYWORDS

COPD; bronchiectasis; pseudomonas; self-management

## Introduction

### Overview

#### Burden of Respiratory Disease With Pseudomonas Aeruginosa

There are an estimated 3 million people in the United Kingdom with chronic obstructive pulmonary disease (COPD) [1]. Bacteria cause acute exacerbations that characterize the course of COPD, and these exacerbations are associated with substantial morbidity and mortality. In addition, bacteria are present in the lower airways of many adults with COPD, even during clinically stable periods, contributing to the airway inflammation that is a hallmark of COPD.

The observation that *Pseudomonas aeruginosa* is isolated from sputum samples from 4% to 15% of adults with COPD in many cross-sectional studies [2-4] suggests that the bacterium is a relatively common cause of infection in this clinical context. *P aeruginosa* is more likely to be isolated from patients with severe disease [4], particularly among patients who require mechanical ventilation for severe exacerbations.

*P aeruginosa* may cause chronic infections in patients with COPD that are similar to those seen in patients with cystic fibrosis (CF). Strains of *P aeruginosa* that persist in the airways of adults with COPD demonstrate changes characteristic of chronic infection that are similar to changes observed in CF, supporting the conclusion that chronic *P aeruginosa* infection occurs in the context of COPD.

The incidence of bronchiectasis in the United Kingdom is not certain. Chest x-ray reviews in the 1950s suggested an incidence of 100/100,000 with an increase in prevalence with age [5]. With the advent of advanced imaging techniques, up to 30% of patients with COPD and severe asthma are found to have features of bronchiectasis on computed tomography.

Within our center, exacerbations of COPD and bronchiectasis are managed through a combination of admission to a dedicated 76-bed unit and self-management by the patient/carer at home. Patients are provided educational literature, a care plan, and supplies of antibiotics and steroids for use at home. Patients are encouraged to recognize signs of exacerbation and to begin immediate treatment with antibiotics. They are requested to report when they have initiated antimicrobial therapy at home so this can be followed up within 2 days (but often do not report because they feel better). Best practice recommends that patients are followed up within 3 weeks after being admitted for exacerbation [1].

The Portsmouth Hospitals Trust (PHT) Respiratory Centre has created a culture of empowering patients through education and by transferring the skills required for self-management so as to reduce rates of admission [6]. The costs of providing skilled community staff for home visits has proved uneconomic but the cost burden of unscheduled admissions is equally high, necessitating innovative solutions to assist patients to self-manage.

Aseptika Ltd has developed a system for patients to self-monitor important physiological measurements including levels of physical activity, weight, peak flow, forced expiratory volume ($FEV_1$) blood oxygenation, heart rate, wellness scores, clinical contacts diary, start of antibiotics and steroids, and 1 to 3 biomarkers of virulence of *P aeruginosa* in sputum. In a clinical trial sponsored by Papworth Hospital during 2013, data were collected by 15 CF participants and uploaded electronically to Activ8rlives, a Web-based data collection and viewing system developed by Aseptika. The study indicated that clinical parameters and sputum biomarker changes are likely to enable early detection of exacerbations in CF patients and have a role in highlighting treatment failure [7]. The Self-Management Checks to Predict Exacerbations of *Pseudomonas Aeruginosa* in Patients with Long-Term Respiratory Conditions (SENSOR) study aims to investigate if these tools can be more widely applied to other respiratory conditions such as COPD and non-CF bronchiectasis (NCFB). The Activ8rlives app operated from an iPad tablet uses wireless connectivity to home-use monitors to upload physiological and subjective scores and diary information directly to the Cloud-based Activ8rlives solution. The differing demographics between this study population and the Papworth population (ie, the older age of the Portsmouth population) will enable us to learn whether older patients with long-term conditions can be trained to use these monitoring devices.

### Rationale for Study and Potential Impact

As described above, initial trials with Activ8rlives system with CF patients indicated a potential role of this technology in improving patient monitoring and self-management. This is particularly important in patients with chronic respiratory conditions for whom the staff-to-patient ratio is typically much lower than CF and for whom innovative solutions to better enable patients to monitor and self-manage their own condition are key to keeping their illness under control.

It is hoped that the results of this study will enable the self-care planning process that currently exists at PHT to be supported with the Activ8rlives technology to extend the effectiveness of our home hospital concept. Qualitative feedback from patients and carers will contribute to the continuing improvement and adaptation of the system.

The eventual addition of the Activ8rlives self-monitoring solution (including tests for sputum *P aeruginosa* virulence) as an assist for the patients and clinical staff and the provision of an information technology (IT) infrastructure for staff, which could simultaneously monitor and mentor many thousands of patients with respiratory conditions in the Portsmouth area without the costs incurred through undertaking face-to-face home visits, would have a significant impact both on patient health and National Health Service (NHS) costs. The development of this infrastructure and subsequent assessment

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of the effectiveness and cost effectiveness of the system would be assessed in a further large-scale randomized controlled trial.

## Aims and Objectives

### Primary Objective

- To use longitudinal *P aeruginosa* sputum biomarker, telemetry, and symptom data to develop individualizable models to predict a *P aeruginosa* exacerbation in chronic non-CF respiratory disease

### Secondary Objectives

- To investigate the correlation between *P aeruginosa* biomarkers and telemetry with clinical outcomes during and after treatment of an exacerbation with antibiotics
- To describe rates of adherence to data input by participants/carers
- To explore whether the self-management platform provided for data upload is feasible and acceptable for daily use in this clinical population
- To pilot questionnaires to collect data on health care use in this population

### Exploratory Objectives

- To collect urine samples for future studies that may explore whether biomarkers present in urine can also contribute additional information to the exacerbation prediction model
- To perform molecular analysis for the *Haemophilus influenzae* group to corroborate microbiological tests in control groups.

## Methods

### Overview

In a mixed methods study, a longitudinal cohort of participants and their carers (where appropriate) will be asked to collect physiological, biological, and disease outcome data over a 6-month period. Neither participants nor the clinicians responsible for participant care will have access to the longitudinal data, and this information will not be used to make clinical decisions. The laboratory samples will be analyzed in a blinded manner. These data will then be analyzed to develop a model for predicting onset of exacerbations that can be built into a self-monitoring system.

Qualitative methods will be used to explore participant and carer experiences of using the technology and performing daily self-monitoring assessments. The expected duration of participation in the cohort will be 6 months, with an invitation to complete a self-administered questionnaire at baseline to inform a face-to-face semistructured interview with patients with or without carer joint participation at the end of the follow-up period.

### Primary and Secondary Endpoints and Outcome Measures

### Primary Endpoint

An exacerbation will be defined as the initiation of antimicrobial therapy for respiratory symptoms either at home or on admission, with or without concomitant steroids or admission.

For participants who are already on continuous antibiotics, an exacerbation will be defined as starting a course of different antibiotics or increasing the dose or frequency of existing antibiotics due to increased symptoms.

### Secondary Endpoints

Treatment efficacy will be defined as the day at which antibiotic treatment for that episode is completed.

## Study Participants

### Inclusion Criteria

The participant must meet all of the following criteria to be considered eligible for the study:

- Male or female, aged 18 years or above
- Diagnosed with at least one (or a combination) of COPD and non-CF bronchiectasis
- Two or more exacerbations with the same pathogen (*P aeruginosa* or *H influenzae*) proven on culture and treated with antibiotics within the last 12 months, one of which must have been within the last 6 months
- Exacerbation-free for the previous 4 weeks
- Producing at least 1 mL of sputum daily
- Must be capable of operating the self-monitoring devices and tablet-based IT system or have a carer capable of undertaking the measurements and collection, storage, and transport of samples
- Willing and able to give informed consent for participation in the study

### Exclusion Criteria

The participant may not enter the study if any of the following apply:

- Suspected or confirmed diagnosis of CF
- Any condition likely to limit participant survival or adherence during the study period in the judgement of the clinician (eg, malignancy, cirrhosis of the liver)
- Currently taking part in any other research study

Carers will also be included in the qualitative interview and to aid participants with data upload. A carer in this study is defined as an adult (18 years or older) relative or friend who has frequent contact with the participant and will assist the participant to perform measurements or use the iPad tablet to upload data.

### Sampling and Sample Size

Using the sputum biomarkers to predict exacerbations, we based the sample size on the difference in exacerbation frequency in time periods when an exacerbation was predicted compared to time periods when no exacerbation was predicted. This will give an odds ratio of exacerbation following detection of sputum biomarkers.

Time periods will consist of approximately 10 days, of which it will be estimated that there may be on average 12 per participant (assuming an average of 4 months of follow-up). It is estimated that an exacerbation will occur in 60% of time periods in which it is predicted and 10% of time periods in which it is not predicted. It is also assumed that a predicted exacerbation will be made in only 1 in 12 time points (8% of

all time points). Using a 5% significance level and 90% power, it is calculated a total of 120 time periods will be required.

However, as there are multiple time periods from the same participant, the data values are unlikely to be independent of each other and thus the sample size requires inflating. Assuming intraclass correlation of 0.18, a design effect of approximately 3 is calculated. This implies that 360 time periods are required for the analysis. This equates to a total of 30 participants for the study. The proposed 30 participants will consist of 20 participants with chronic *P aeruginosa* infection (10 with primarily COPD and 10 with NCFB) and 10 participants with *H influenzae* infection.

## Study Procedures

### Recruitment

Potentially eligible patients, identified from clinical databases, will be contacted by a member of the research team and invited to attend an information event or specialist research recruitment clinic. The information event will be held locally on a Saturday or in the evening to make the event more convenient for patients and their carers. The event will allow patients to meet the research team, have an educational talk, and find out about the study. They will also be able to look at the devices and iPad app as well as ask any questions. Patients interested in participating in the study will be given a participant information sheet (PIS) and invited to come to a research clinic for screening and enrollment.

At the research clinic, patients will be reviewed by a clinical research fellow and screened for suitability for the study by the research team. Patients and carers will be able to view and try out the self-monitoring devices and tablet-based IT system. Capacity to operate these systems will be assessed as part of screening using a checklist, assessing the patient/carer confidence in using the devices and ability to perform the measurements. Those who meet eligibility criteria will be given a PIS and a carer information sheet if necessary. After adequate time to read, understand, and ask questions (at least 24 hours), patients will be invited back to the research clinic to give informed consent. Baseline data will be captured on paper case report forms (CRFs) and uploaded to a local study database, separate from the self-monitoring database held by Aseptika.

### Participant and Carer Training

Volunteers will be trained by a research nurse and Aseptika personnel during a visit to the participant's home. A home visit will clarify which 3G cellular network is available in their location (for Internet access) and will ensure that the participant has space to install a small dedicated freezer and that there is access for delivery.

Each participant will be provided with the following items and participant and carer will be trained on their use:

- Physical activity tracker: this will be set up for them and they will be shown how and when to wear it.
- Smart scale: the participant will be instructed how to weigh themselves and how this measures their body composition (they will be instructed to perform this in bare feet).
- Blood pressure cuff: the participant will be instructed how to take their own blood pressure and what the results mean.
- Pulse oximeter: the use of a pulse oximeter and how it works will be explained.
- Thermometer: the participant will be provided with a noncontact infrared thermometer and will be shown how to take their temperature.
- Peak flow meter: participants will be shown by the research nurse how to measure their peak flow and $FEV_1$ using a simple, automated device.
- Sputum and urine samples: participant will be taught how and when to take a sample and how to store the sample in the containers provided in the freezer that will be supplied.
- iPad mini and questionnaires: participant will be trained on how to charge the iPad mini, how to switch it on and off, etc. A short questionnaire about symptoms, medications, and health care usage will be completed on the iPad mini using colorful self-explanatory series of screens within the Activ8rlives App. The display will be brightly colored, and any text (which will be kept to a minimum) will be large in size.

Participants will be able to use the iPad mini for personal use as well as for daily study use within the limits specified and agreed to in the participant consent form. Participants will be requested to take this equipment with them to the hospital if they are admitted and to continue recording these data in the hospital. Initial training will take approximately 60 minutes.

Following training, questions about use of the equipment will be answered by the research nurse and referred to the company in the event of technical difficulties with the IT system. The iPads will be supplied preconfigured with all software installed and an account for the volunteer already created and defined. A remote access technical support solution will also be preinstalled allowing the company to remotely access the iPad to resolve problems in the event of significant failures. If required, follow-up visits to the participants will be undertaken. Every effort will be made to ensure that the volunteer is adequately trained and supported for the duration of the study.

### Study Assessments

Participants will be asked to undertake the following once a day every day during a 6-month follow-up period, with assistance from carers as appropriate. Figure 1 illustrates the equipment that will be provided to the participant to facilitate these assessments.

**Figure 1.** Equipment provided to participant to complete the assessments.



Each participant will be provided with a 3G-enabled tablet (iPad) and will upload peak flow, $FEV_1$, pulse rate, oxygen saturation, blood pressure, temperature, and physical activity data on a daily basis. The participants will be provided with a set of instructions about uploading the data onto the iPad. The participants will be blind to their continuous data over the duration of the study but will see the values generated daily on the screens of the devices. There will be no requirement for the participant to enter numerical values into the software as all monitoring devices connect directly reducing the risk of inaccurate data entry. The data collected on the iPad is automatically transmitted to the Cloud databases. No information is stored on the iPad and if the iPad is lost, there is no risk that these data could be accessed. The company is able to track the iPad's location in the event that it is stolen or lost.

The information uploaded by the volunteers will be remotely reviewed daily by Aseptika's Directors to ensure that data has been uploaded on a daily basis and there are no technical problems. Technical problems will be remedied remotely by the Aseptika technical staff. In the case of information not being uploaded, Aseptika's investigator will initially inform the research nurse who will contact the volunteer by telephone to enquire if there have been any difficulties. Should any volunteers find the technology difficult to manage, they will be offered a further home visit for instructions and training.

## Sample Production and Home Storage for Sputum and Urine Samples

- Containers will be prelabeled with the participant study number, expected contents (sputum or urine), and the day and date.
- Participants will be asked to fill the supplied pot with sputum and ensure the lid is correctly sealed.
- Participants will be asked to collect urine in the bulk container and secure the lid.
- They will then connect the Vacutainer to the cap of the urine container (as per supplied instructions), and the Vacutainer will begin to fill with urine.
- Bulk urine collection pot is to be discarded.
- Store both containers in sputum and urine collection bags inside of the supplied –20°C freezer.
- After 1 month, these will be transferred for bulk storage at the Queen Alexandra Hospital in a designated –70°C freezer and a new batch of containers will be provided.

## Clinic Visits

Participants will be required to attend the clinic for a follow-up visit at months 3 and 6 (study completion) ± 2 weeks. Participants will attend their normal review with the medical team that usually involves lung function, sputum sample for culture, and clinical review. They will then have a research visit which will involve disease-specific control and quality of life questionnaires (Quality of Life–Bronchiectasis, Short Form Health Survey, St. George's Respiratory Questionnaire, EuroQol 5-Dimension Questionnaire) as well as noting any changes to treatment and exacerbations. The data collected from these visits

will be recorded on paper CRFs which will then be uploaded by a member of the research team to a local study database with restricted access.

### Health Economics

In preparation for a future cost-effectiveness trial of the self-management system, a questionnaire to collect health care use data will be piloted to capture resource use. These data will be analyzed descriptively. The daily questionnaire within the Activ8rlives app asks if participants have been in contact with a health professional or been in hospital in the last 24 hours. If they answer yes, they will be prompted to give more information about who they saw and for what reason. This will capture data on the participants' health care use for their respiratory condition as well as other conditions.

### Qualitative Methods

Qualitative methodology will be used to explore the psychosocial questions: How do the participant and main carer experience self-managing their condition under routine care? What is the participant's expectation of taking part in the study? How does the participant experience collecting daily self-monitoring data and using the devices provided? Qualitative research seeks to describe, understand, and explain a particular phenomenon to make explicit the experiences and perceptions of the research subjects [8,9]. This is achieved by exploring the data (usually words) for conceptual definitions on how people perceive situations to provide explanations of why something happens in a particular way as well as looking for typologies or classifications of grouping of people (or situations) that tend to have common characteristics, opinions, and experience. Qualitative data will be collected at the end of the study (6 months) through face-to-face semistructured interviews with participants or paired interviews with carers, based on participant preference. Carers will not be interviewed separately.

All interviews will be guided by a semistructured topic guide although free discussion of experiences and ideas will also be encouraged. The semistructured interviews will be audiotaped and field notes taken to describe context, interview process, and initial theme development. A choice of venue, either at home or suitable hospital room, will be used. All qualitative interviews will be conducted by the same trained research fellow supported and supervised by another experienced qualitative researcher.

It is anticipated that the semistructured face-to-face interviews will take between 45 minutes to 1 hour to complete, depending on what the participant wishes to share. The interview will be terminated at any point the participant wishes to stop and this will not influence their subsequent treatment. As a small token of appreciation for time given to take part in the interviews, each participant will be offered a £10 (US $13) gift voucher on completion.

The interviews will be digitally recorded, transcribed verbatim, and entered into NVivo 10 (QSR International), a qualitative software package for systematic and transparent data management. All participant names will be removed from the transcripts to retain confidentiality. Care will be taken to always ensure any direct quotes used in study reports or papers to illustrate the findings will not be directly attributable to individuals.

### Self-Administered Questionnaire

After consent and on entry to the main study, all patients but not carers will be asked to complete a self-administered questionnaire (to be developed with advice from the Patient Public Involvement [PPI] team members) with open and closed questions regarding self-awareness/perception of burden of disease, self-management including use of medication, identifying signs and symptoms of deterioration, problem-solving, seeking support/health care professional input during usual care as well as rationale and expectation of participation in the study and perceived barriers and enablers to successful completion in the study. We anticipate that this short self-administered questionnaire will take approximately 30 minutes to complete. The purpose of this self-administered questionnaire is to use individual responses to act as an "aide memoire" at the follow-up interviews.

### Analysis

Data analysis will use the framework approach which provides a systematic, auditable, and rigorous analysis of qualitative data [10]. It is also more deductive than other thematic analysis approaches and ensures that focused data are collected to answer the clear research objectives of the study. Experienced facilitators will independently code all data. Scrutiny of the framework matrix will be sought to see if there is agreement with the categories generated. In addition, a member of the steering group not involved in data collection will be asked to independently read through a sample of the transcripts to generate a preliminary framework without seeing the original researchers' list. In the case of disagreement, a solution will be sought to clarify the meaning of a code/theme developed until mutual consent is reached. The aim of this stage is to enhance the validity of the development of the conceptual framework and to guard against researcher bias. A narrative summary will be developed from the findings which includes comparison within case and across patient and carer's perception and experience.

### Discontinuation or Withdrawal of Participants From Study

Participants not complying with study requirements or failing to upload data or collect a sample will be retrained. Significant nonadherence (eg, noncollection of data and samples for a period of several weeks) may lead to withdrawal of the participant from the study by the study team. If participants and carers are not willing to continue data collection, they may decide to withdraw from the study and will be requested to return all the equipment.

### Definition of End of Study

The end of study is the date of the last sample and data upload of the last participant follow-up date or the last qualitative interview, whichever comes last.

## Assessment of Safety

This is a noninterventional study and is therefore considered to be of no additional safety risk compared with usual clinical

practice. All patients are expected to have a number of comorbidities and on-going symptoms due to their illness. All study procedures in use are the usual standard of care for this population and are not novel. The test used to observe the variation in levels of Exotoxin A is a new test but one that is validated and in itself provides no risk of harm to the participants; it is not performed on the participants themselves but on their sputum, which they would ordinarily be producing daily, and it will not change any clinical treatment as the results will not be available to the participant or their clinical team.

There is therefore no clear rationale for additional safety monitoring during the study period or for the expedited reporting of any serious adverse events. However, as study procedures are being conducted more frequently by the patients in their homes (as part of their daily routine), there may be an increased frequency of expected side effects or adverse events for some patients. The most likely adverse event during procedures is an increased risk of fainting for those participants who are susceptible to fainting during spirometry (specifically daily peak flow, which requires blowing rapidly and forcefully into a spirometer). Therefore, the following risk-adapted safety monitoring procedures are to be followed during the study period.

Participants will be asked to report any of the expected adverse events (dizziness or light-headedness and fainting) to the research team if they occur at a level which causes significant discomfort to the participant so that the research team can provide any further training or adjustments to the way in which the measurements are taken or reduce the frequency at which the participant is to take the measurement.

The chief investigator and study team will record and monitor any adverse events caused due to the increased frequency of the self-monitoring assessments. If there is any concern over these events or if they become unacceptable and in any circumstance cause the risk-to-benefit ratio to tip, they should be expedited to the sponsor and may be subsequently reviewed by the Research Quality Committee.

## Data Handling and Record Keeping

### Data Collection Forms

The anonymous daily data generated by participants using the technology provided to them will be uploaded directly to the Web servers of Aseptika via 3G built into the iPad tablets provided to the participants. The anonymized data collected at the hospital visits at baseline, 3, and 6 months will be recorded on study-specific CRFs. The data recorded on these forms will then be uploaded by a member of the research team onto the local study database held at Portsmouth Hospitals Trust. This database will be password protected and kept on a secure NHS server with restricted access on a computer with restricted access in a locked room.

### Data Management

Each volunteer will be given an account within Activ8rlives online system. Their name, NHS number, address, or any other identifying information will not be entered. Anonymity will be assured by giving each participant a unique study ID which will

not be traceable to the participant. The unique study ID will be formed from 2 letters and 2 numbers (eg, SE01 for the first participant recruited into the study, SE02 for the second participant recruited).

Aseptika's servers are located in the United Kingdom and have appropriate security measures. Access to these data will be restricted to Director-level personnel within Aseptika and to the research nurse for the purposes of technical support and to track progress of the study. Patients and carers, clinical staff, and laboratory staff will have no access to these data.

Data generated from sputum and urine analysis will be output to Excel (Microsoft Corp) spreadsheets and will be imported into the account for each volunteer to be correlated with other telemetry data. Other clinically relevant information (start of antimicrobial therapy, admission or other treatment) which is associated with an endpoint will be entered into the Activ8rlives system.

## Data Analysis

### Description of Analysis Populations

The study is a nonrandomised cohort of a single group of patients. All subjects recruited into the study will be included in the data analysis.

### Analysis of Endpoints

The first stage of the data analysis is to use data on the collected parameters (eg, peak flow, pulse rate, oxygen saturation, activity data) to predict when an exacerbation is likely. Control charts will be used to determine the boundaries of normal behavior for each parameter. Separate control charts will be used for each participant, as what constitutes normal behavior will vary from participant to participant. When a parameter strays from normal behavior (eg, exceeds 99% control limits), an exacerbation will be predicted.

To examine the association between predicted exacerbation and actual exacerbation, participant follow-up will be divided into periods of time (eg, 7-10 days). A comparison of actual exacerbation when exacerbation has and has not been predicted will be made. To allow for the repeat measurements over time from the same participants, the analysis will be performed using multilevel logistic regression. Additionally, the sensitivity and positive predictive value of the predictions will also be calculated. Estimated values will be presented along with corresponding confidence intervals. Further exploratory analysis using novel computing methods will be conducted.

Health care use data will be presented descriptively (eg, the frequency and type of health care contacts over the study period for different participant groups).

### Procedure for Dealing with Missing, Unused, and Spurious Data

The primary analysis will be restricted to collected data only, without any data imputation. The distributions of the parameters collected will be assessed, and implausible values may be excluded from the analysis. Any data exclusions will be justified both clinically and statistically.

## Procedures for Reporting any Deviations From the Original Statistical Analysis

Any deviations to the statistical analysis plan will be carefully documented and justified.

## Ethics

### Overview

The study will not be initiated before the protocol and all study-relevant material such as informed consent forms and participant and general practitioner information sheets have received approval or favorable opinion from the Research Ethics Committee (REC) and the respective NHS research and development department. Any changes to protocol or relevant study documents will be approved by the sponsor. Should an amendment be made that requires REC approval, defined by REC as a substantial amendment, the changes will not be instituted until the amendment has been reviewed and received approval or favorable opinion from the REC and research and development departments. A protocol amendment intended to eliminate an apparent immediate hazard to participants may be implemented immediately providing that the REC is notified as soon as possible and an approval is requested. Minor amendments, defined by REC as nonsubstantial amendments, may be implemented immediately and the REC will be informed.

### Participant Confidentiality

Study staff will ensure that participant anonymity is maintained. The participants will be identified only by initials and participant ID number on the CRF and any electronic database. All documents will be stored securely and only accessible by study staff and authorized personnel. The study will comply with the Data Protection Act which requires data to be anonymized as soon as it is practical to do so.

### Benefits and Burdens to Participants

This study requires a high engagement and compliance rate from the study participants. The additional daily measurements, monitoring, and uploading of the information onto the study's website for 6 months will be an additional time burden for the participants and may add significantly to their already onerous treatment burden. Clear instruction, in-depth training, and on-going technical support for all of the study equipment along with regular input from an experienced and committed research team will help to mitigate any burden.

Participants will be required to store the various study equipment including a small study freezer, iPad mini, and self-monitoring gadgets in their own homes which may be a burden for some participants, especially those living in smaller properties. Participants will be made aware of the equipment they will be provided with and information on how much space they will need to store the equipment prior to consent. The capability to store the study equipment will be evaluated as part of a participant eligibility assessment prior to giving out participant information.

A research nurse and Aseptika trainer will need to complete a one-off visit to participants' homes to deliver, install, and train the participant in the various study technology. To minimize the burden of this visit, participants will only ever be contacted by the research team, not the company, and a visit time will be scheduled in advance at a time that is convenient to the participant.

On completion of the entire study, each participant and their carer will be shown the data and what has been learned from their participation in the study. Participant benefits include being compensated £1 (US $1.30) a day for successfully completing the measurements and collecting samples, retaining the iPad mini and freezer, being provided with 3G connectivity for 6 months following completion of the study, and retaining ownership of the monitoring devices. Participants will be encouraged to continue the self-monitoring process unblinded thereafter and will have full access to the data they generate. The study will be reviewed by the Research Quality Committee at regular intervals.

## Patient Public Involvement

The study design is similar to that of a previous study carried out with 15 CF patients in Cambridge. Adaptations of the content and methods of data collection and the final design of the questionnaire on the iPad will be informed by a group of PPI members convened for the purposes of this study. These members will be patients at PHT with similar respiratory conditions and will be invited to attend the group by their respective clinicians. PPI members have also given input on the study design and implementation issues and reviewed the PIS and informed consent form. Some key issues raised by the group are listed below, and these will be addressed in the preparation of study implementation:

- How big is the freezer (concern over space at home)?
- How often will samples be collected (concern about storage of samples and consumables and possible expenses to bring samples to the hospital, plus ensuring that any staff who collect samples from the house will have appropriate ID)?
- Ease of use of the Vacutainer urine collection system for participants with comorbidities such as arthritis
- Recommended preprinting of labels
- Some apprehension about using an iPad
- Whether the participants who take part will get to know the results of the study
- What happens if participants wish to go on holiday?

## Results

The SENSOR study is now in data analysis. It is anticipated results will be available by the end of 2017. The use of technology by study participants was successful with high upload figures and product reliability.

## Discussion

The SENSOR study will provide a prospective evaluation of the efficacy of this home self-monitoring system in people with chronic airway infection. The data collected will allow us to determine the key elements of the self-monitoring system for prediction of exacerbations in order to reduce the burden on monitoring on patients in future.

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## Acknowledgments

## Conflicts of Interest

None declared.

## Multimedia Appendix 1

Original peer review report (Portsmouth Hospitals NHS Trust).

[PDF File (Adobe PDF File), 87KB - resprot_v6i5e89_app1.pdf ]

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## Abbreviations

**CF:** cystic fibrosis
**COPD:** chronic obstructive pulmonary disease
**CRF:** case report form
**FEV1:** forced expiratory volume in one second
**IT:** information technology
**NCFB:** non-cystic fibrosis bronchiectasis
**NHS:** National Health Service
**PHT:** Portsmouth Hospitals Trust
**PIS:** participant information sheet
**PPI:** public patient involvement
**REC:** Research Ethics Committee
**SENSOR study:** Self-Management Checks to Predict Exacerbations of Pseudomonas Aeruginosa in Patients with Long-Term Respiratory Conditions

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Protocol

# Evaluation of Mechanisms to Improve Performance of Mobile Phone Surveys in Low- and Middle-Income Countries: Research Protocol

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## Abstract

**Background:** Mobile phone ownership and access have increased rapidly across low- and middle-income countries (LMICs) within the last decade. Concomitantly, LMICs are experiencing demographic and epidemiologic transitions, where non-communicable diseases (NCDs) are increasingly becoming leading causes of morbidity and mortality. Mobile phone surveys could aid data collection for prevention and control of these NCDs but limited evidence of their feasibility exists.

**Objective:** The objective of this paper is to describe a series of sub-studies aimed at optimizing the delivery of interactive voice response (IVR) and computer-assisted telephone interviews (CATI) for NCD risk factor data collection in LMICs. These sub-studies are designed to assess the effect of factors such as airtime incentive timing, amount, and structure, survey introduction characteristics, different sampling frames, and survey modality on key survey metrics, such as survey response, completion, and attrition rates.

**Methods:** In a series of sub-studies, participants will be randomly assigned to receive different airtime incentive amounts (eg, 10 minutes of airtime versus 20 minutes of airtime), different incentive delivery timings (airtime delivered before survey begins versus delivery upon completion of survey), different survey introductions (informational versus motivational), different narrative voices (male versus female), and different sampling frames (random digit dialing versus mobile network operator-provided numbers) to examine which study arms will yield the highest response and completion rates. Furthermore, response and completion rates and the inter-modal reliability of the IVR and CATI delivery methods will be compared.

**Results:** Research activities are expected to be completed in Bangladesh, Tanzania, and Uganda in 2017.

**Conclusions:** This is one of the first studies to examine the feasibility of using IVR and CATI for systematic collection of NCD risk factor information in LMICs. Our findings will inform the future design and implementation of mobile phone surveys in LMICs.

## KEYWORDS

IVR; CATI; Bangladesh; Tanzania; Uganda; mHealth; mobile phone survey; noncommunicable diseases; survey methodology

## Introduction

Effective prevention and control of non-communicable diseases (NCDs) centers on surveillance and reduction of exposure to risk factors that give rise to these conditions. Four behavioral, and largely modifiable, risk factors account for the majority of NCDs: unhealthy diet, tobacco use, inadequate physical activity, and excessive use of alcohol [1]. Surveillance provides crucial information on disease burden to guide resource planning and allocation and evaluation of public health interventions and programs [2]. Unfortunately, many low- and middle-income countries (LMICs) face the challenge of implementing effective and systematic ways of tracking NCD risk factors and collecting timely and high-quality data. The rise of mobile phones in LMICs presents an opportunity to use this technology to aid NCD risk factor data collection. Currently, worldwide mobile phone subscriptions have reached 99.7 subscriptions per 100 persons, with 94.1 subscriptions per 100 persons in LMICs [3].

High levels of mobile phone access and ownership afford new opportunities to conduct surveys. As a complement to household surveys, respondents can be interviewed over their personal mobile phones. The most common types of mobile phone surveys (MPSs) are short message service (SMS), computer-assisted telephone interview (CATI), and interactive voice response (IVR). In CATI, an interviewer questions the respondent over the phone. With SMS, brief text messages are used to communicate between devices [4]. In IVR, users interact with a database programmed with questions and a series of pre-recorded answers to the questions, linked to a specific numeric key or numeric response on a touch-tone phone keypad (eg, "Press 1 if you are male, press 3 if you are female").

The use of MPSs to collect population health estimates in LMICs is in its early stages [5]. Similarly, there is little evidence on the usability and reliability of MPSs and mechanisms to improve survey response, completion and representativeness in LMIC settings. Through a series of 7 sub-studies, this protocol seeks to address the following specific objectives: (1) evaluate the impact of incentive amount, timing, and structure on response, completion, and refusal rates of an IVR-administered NCD risk factor survey; (2) assess the effect of different survey introduction content (eg, informational versus motivational introduction) and modality on response, completion, and refusal rates of an IVR-administered NCD risk factor survey; (3) examine the differences in survey metrics, such as representativeness, completeness, and response rate between different sampling frames of mobile phone numbers; and (4) evaluate the differences in response, completion, and refusal

rates between IVR and CATI surveys and establish the inter-modal reliability.

The research studies described in this protocol are part of the NCD research and development arm of the Bloomberg Data for Health Initiative (BD4HI). The BD4HI is an effort led by Bloomberg Philanthropies to improve health by improving the quality and availability of public health data across the globe. The motivation, key goals, partners, and components of this initiative have been described in another paper by our research team [6]. Briefly, the BD4HI NCD research and development agenda includes assessing ways to optimize MPS for NCD risk factor data collection in LMICs.

## Methods

### Formative Phase

Prior to the implementation of the sub-studies, a number of formative activities will be conducted to contextualize the use of MPSs for optimal performance in each country. Briefly, a 3-pronged, standardized approach is used to inform the design and adapt a centrally developed NCD questionnaire for IVR delivery in each country. This includes key informant interviews (KII) with personnel (eg, in government, regulatory agencies, and academic experts) who have in-depth knowledge of relevance to NCDs or the conduct of mobile phone surveys. Additionally, we will conduct focus group discussions (FGDs) to explore community perceptions and willingness to participate in a MPS and identify potential challenges, barriers, and solutions. Finally, user-group testing will be carried out where community members complete an IVR survey in the presence of study staff. These formative activities will be used to create a revised questionnaire containing appropriate local examples, terminologies, and measurements. The country-adapted questionnaire and response options will be used in each of the 7 sub-studies.

### Evaluation Phase

#### Setting and Participants

The research activities will be implemented in Bangladesh, Tanzania, and Uganda. Information on collaborating partners, mobile phone subscription rates [7], mobile network operators (MNOs), and survey languages is summarized in Table 1. The term "subscription" in Table 1, and throughout this protocol, refers to different forms of mobile phone ownership including monthly subscriptions and pre-payment options which are common in LMICs.

**Table 1.** Country partners, survey languages, and mobile phone subscriptions in each country.

| Country | Mobile phone subscriptions per 100 people, n | Mobile network operators in country, n | Implementing partner | Languages for mobile phone survey |
|---|---|---|---|---|
| Bangladesh | 83 | 5 | Institute of Epidemiology, Disease Control and Research (IEDCR) | Bangla, English |
| Tanzania | 76 | 5 | Ifakara Health Institute (IHI) | Kiswahili, English |
| Uganda | 50 | 6 | Makerere University School of Public Health (MakSPH) | Luganda, Runyakitara, Luo, English |

In each of the 3 countries, participants for the MPS, except for sub-study 6, will be selected through random digit dialing (RDD) [8]. For each country, we will identify all active MNOs and their respective prefixes that lead a 10-digit mobile phone number. Using these unique prefixes, the remaining digits will then be randomly generated via a computer to create a random sample of mobile phone numbers to which the surveys will be delivered (Table 2). Participants that are selected using RDD will be asked to provide consent and their age. Participants who do not indicate their age or report being less than 18 years old will be excluded from the study.

### Study Design

The 7 sub-studies that evaluate mechanisms to improve survey response and cooperation rates of an IVR-administered NCD risk factor survey or compare differences in survey performance between IVR and CATI surveys will be conducted in the 3 countries. The description of each sub-study and a summary of their activities are provided in Table 3. The outcome for every sub-study will be contact, response, completion and refusal rates, and demographic representativeness. In addition, sub-study 7 will include the inter-modal reliability between IVR and CATI-administered surveys.

**Table 2.** Generating a sample through random digit dialing.

| Mobile network operator | Unique prefixes[a] | Examples of RDD[b] phone numbers[c] |
|---|---|---|
| A | | |
| | 0772-XXX-XXX | 0772-111-222, 0772-111-222 |
| | 0773-XXX-XXX | 0773-234-567, 0773-234-567 |
| | 0774-XXX-XXX | 0774-743-128, 0774-743-128 |
| B | | |
| | 0791-XXX-XXX | 0791-381-123, 0791-237-268 |
| | 0792-XXX-XXX | 0792-326-888, 0792-666-418 |
| C | | |
| | 0745-XXX-XXX | 0745-674-190, 0745-552-383 |
| | 0746-XXX-XXX | 0746-901-643, 0746-434-122 |
| | 0720-XXX-XXX | 0720-023-528, 0720-712-090 |
| | 0721-XXX-XXX | 0721-057-444, 0721-723-889 |

[a]Following the unique prefixes, the remaining digits ("X") are randomly generated using a computer to produce a 10-digit phone number.

[b]RDD: random digit dialing.

[c]The telephone numbers that appear in this table were randomly generated and any similarity with an actual subscriber's number is purely coincidental.

**Table 3.** Summary description of the sub-studies.

| Sub-study | Name | Study arms | Sampling | Country |
|---|---|---|---|---|
| 1 | Incentive amount | No airtime | RDD[a] | Bangladesh, Uganda |
| | | X airtime post-IVR[b] | | |
| | | 2X airtime post-IVR | | |
| 2 | Incentive timing | No airtime | RDD | Bangladesh, Uganda |
| | | Approximately 20% airtime pre-IVR; approximately 80% airtime post | | |
| | | 100% airtime post-IVR | | |
| 3 | Incentive structure | No airtime | RDD | Bangladesh, Uganda |
| | | Fixed X airtime post-IVR | | |
| | | Lottery airtime of at least 5X post-IVR | | |
| 4 | Introduction phrasing and voice | Male voice, informational introduction | RDD | Bangladesh, Uganda |
| | | Female voice, informational introduction | | |
| | | Male voice, motivational introduction | | |
| | | Female Voice, motivational introduction | | |
| 5 | Introduction modality | IVR introduction, IVR survey | RDD | Bangladesh, Tanzania |
| | | CATI[c] introduction, IVR survey | | |
| 6 | Sampling frame | IVR survey | MNO[d]-provided numbers | Bangladesh |
| 7 | Survey modality | CATI survey first, IVR survey 7 days later | RDD | Bangladesh, Tanzania |
| | | IVR survey first, CATI survey 7 days later | | |

[a]RDD: random digit dialing.

[b]IVR: interactive voice response.

[c]CATI: computer-assisted telephone interview.

[d]MNO: mobile network operator.

### Sub-Study 1: Incentive Amount

This sub-study evaluates whether there is a differential effect in completion rates of an IVR-administered survey based on the incentive amount. Participants will be randomized to receive 1 of 3 incentive amounts, in the form of airtime, which will be sent to participants upon completion of the IVR survey. The study arms are (1) no incentive; (2) X US dollar airtime incentive, where X is commensurate with the expected time commitment as a function of daily wages (the exact amount will be guided by FGDs and in consultation with country partners); and (3) 2X airtime incentive transferred after survey completion (where 2X is twice the amount of the incentive in arm 2). This sub-study will be conducted in Bangladesh and Uganda.

### Sub-Study 2: Incentive Timing

This sub-study examines whether the timing of incentive delivery (either pre-survey or post-survey) has an effect on survey response and completion rates of an IVR-administered survey. Participants will be randomized to 1 of the following 3 study arms: (1) no incentive; (2) an airtime incentive sent before the survey, where 10% to 40% of the total incentive (X) is sent to the respondent's mobile phone prior to initiation of the survey, and with the remaining 60% to 90% being sent after all questions

answered; or (3) a promised incentive where 100% of the incentive amount is sent to the respondent's mobile phone only after the IVR survey is completed. This sub-study will be conducted in Bangladesh and Uganda.

### Sub-Study 3: Incentive Structure

This sub-study evaluates whether the incentive structure (a fixed incentive amount or a lottery-based incentive) has an effect on completion rate of an IVR-administered survey. Respondents will be randomized to 1 of the following 3 study arms: (1) no incentive; (2) a fixed airtime incentive delivered after survey completion (where the amount of the incentive is guided by sub-study 1); or (3) a lottery airtime incentive of an amount at least 5 times greater than the amount in the second study arm, where the odds of winning the lottery are 1 to 20 (the lottery incentive will be delivered upon completion of the survey and the precise odds for winning will be guided by formative work conducted in each country). This sub-study will be conducted in Bangladesh and Uganda.

### Sub-Study 4: Introduction Phrasing and Survey Voice

This sub-study assesses whether the content of the IVR survey's introduction (motivational versus informational) and the survey's narrative voice (male versus female) has an effect on contact, response, and/or completion rates. Participants will be

randomized to 1 of 4 study arms with varying survey introduction content and voices: (1) male survey narrator with an informational survey introduction; (2) male survey narrator with a motivational survey introduction; (3) female survey narrator with an informational survey introduction; or (4) female survey narrator with a motivational survey introduction. The content of the survey's motivational and informational introductions will be guided by formative work conducted in each country. Participants in each study arm will receive the same airtime incentive. This sub-study will be conducted in Bangladesh and Uganda.

### Sub-Study 5: Survey Introduction Modality

This sub-study evaluates the effect of the survey introduction's modality (human operator versus IVR introduction) on survey completion rates. Participants will be randomized to 1 of 2 arms: (1) a CATI-administered introduction with an IVR survey or (2) a full IVR survey. In the first arm, a human will call the RDD-generated mobile phone number, read the survey's introduction, and the operator will answer any questions the participant may have. Respondents that agree to participate will then be sent an IVR survey. In the second arm, participants will not receive this human introduction. Participants in each study arm will receive the same airtime incentive. This sub-study will be conducted in Bangladesh and Tanzania.

### Sub-Study 6: Sampling Frame

This sub-study examines whether the source of the mobile phone numbers has a differential effect on IVR survey response and completion rates. The previous sub-studies and sub-Study 7 rely on an RDD sampling frame. In this sub-study, we will obtain a de-identified list of mobile phone numbers from a MNO where participants have consented to be contacted for additional studies. This sub-study will be conducted in Bangladesh.

### Sub-Study 7: Survey Modality

This sub-study evaluates the effect of the survey modality (IVR versus CATI) on the survey's response and completion rates and assesses the inter-modal reliability. Participants will be randomized to 1 of 2 arms: (1) IVR then CATI; or (2) CATI

then IVR. Participants in the first study arm will receive an IVR survey first, followed by a CATI survey 7 days later (Figure 1). Participants in the second study arm will receive a CATI survey first followed by an IVR survey 7 days later. At initial enrollment, it will be clearly explained to participants that they are being enrolled in a study where they will be contacted twice. The questionnaires used in both study arms will be the same. This crossover design will allow for an assessment of response consistency, adjusted for the risk of "priming" after exposure to the prior modality. This is the only sub-study that will require participants to answer the NCD survey twice. The amount, timing, and structure of incentive will be guided by the first 3 sub-studies where the incentive that yielded the highest response and completion rates will be provided to all participants in sub-study 7. This sub-study will be conducted in Bangladesh and Tanzania.

### Follow-Up of Study Participants

In order to better understand reasons for refusal and survey attrition, to assess the usability of the IVR platform, and to receive feedback on the incentives and survey introductions, we will call a sub-sample of participants from each sub-study and administer a short MPS. For each of these sub-studies, we will call back a random sample of 30 individuals who (1) were age-eligible and consented but did not complete the survey; (2) refused to consent to the survey; and (3) were identified as non-responders (ie, listened to a portion of the survey introduction but disconnected from the survey).

## Questionnaire

Experts in NCDs, mobile health, and survey methodology convened in 2015 to develop a NCD risk factor questionnaire that could be adapted to a MPS. Questions were selected from standardized surveys such as World Health Organization (WHO) STEPwise Surveillance and Tobacco Questions for Surveys [9,10]. Question selection was guided by the Global Monitoring Framework for NCDs, which included the main behavioral NCD risk factors (physical activity, alcohol consumption, tobacco use, and diet) [11]. Questions were selected independent of their perceived adaptability to an IVR platform.

**Figure 1.** Study design for sub-study 7.
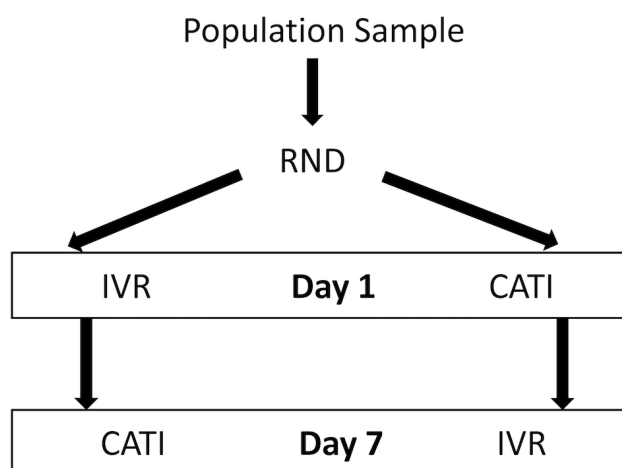
The questionnaire is comprised of the following parts: (1) language selection, (2) introduction, (3) age screening, (4) consent, (5) demographic questions, (6) NCD modules, and (7) airtime delivery, as applicable (Figure 2). NCD modules are groups of topically similar NCD risk factor questions (eg, tobacco, alcohol, diet, physical activity, etc). The order of the modules will be randomly assigned. For example, one participant may be presented with questions on diet first, followed by tobacco, then alcohol, and finishing with physical activity; another respondent may be presented alcohol questions first, and then diet, then physical activity, and finally tobacco.

However, the questions within each module will not be randomized.

The questionnaire will be translated into local languages with input from members of local collaborators and communities to help ensure appropriate syntax and semantics and then back-translated to ensure accuracy. After the questionnaire's translation has been deemed acceptable, country residents fluent in the survey languages will narrate and audio record the survey. The audio recording of the survey will be uploaded into VOTOmobile's IVR platform. VOTOmobile is a Ghana-based organization that works to develop mobile phone survey systems.

**Figure 2.** Sequence of the mobile phone survey.
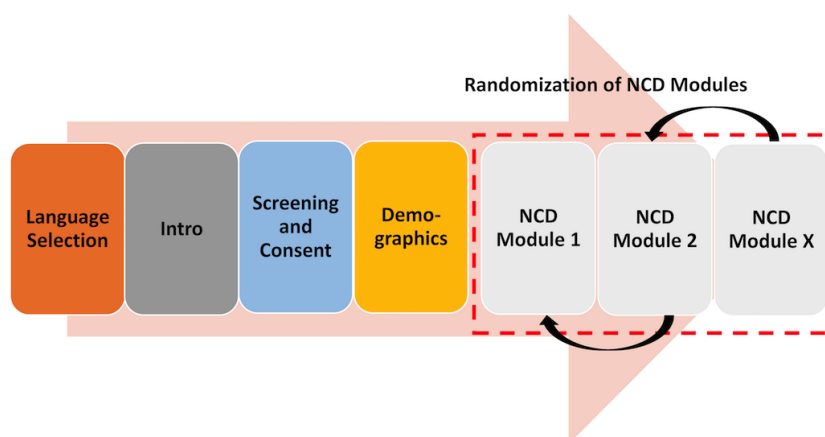


**Survey Delivery and Data Collection**

Unless otherwise indicated, the logistics and timing of MPS delivery will be similar for all sub-studies. When a randomly dialed number is connected (ie, a respondent picks up the phone), the respondent will be presented with a brief pre-recorded introduction to the study and provided an opportunity to select the survey's language. For IVR sub-studies, respondents will select a language by entering their response on their mobile phone keypad (eg, "If you would like to listen in English, press 1").

After the language selection, the speaker will provide a more detailed description of the study that includes the purpose, duration, risks, benefits, sponsoring agency, and requirements to receive an incentive. For sub-study 4, participants in the motivational introduction arm will receive added sentences and language expressions that may further motivate them to participate in the survey. After hearing the survey's introduction, participants will be screened for eligibility based on their age; those who indicate being less than 18 years old will be thanked for their interest and the survey will be terminated. Participants will then be asked to press a number on their keypad to indicate their willingness to continue (eg, "Press 1 if you would like to participate in this survey, press 3 if you do not want to participate in the survey"). Respondents will be asked a series

of demographic questions followed by NCD modules whose order of presentation is randomized as described above.

Surveys will only be sent to participants once. Participants who were ineligible due to age, refused consent, or opted out during the survey will not have an additional survey sent. The MPS will be delivered at random times ranging from 8:00 AM to 8:00 PM local time. The exact time window to deliver the MPS will be determined by each country during the formative phase.

**Proposed Sample Sizes**

Assuming a baseline survey completion percentage of 30%, in order to detect an absolute 10% difference in survey completion between two study arms at an alpha of .05 and power of 80%, it is calculated that 376 individuals who have completed an IVR survey will be needed in each study arm for each sub-study. With a completion percentage of 30%, we calculated that 1254 participants would be required to consent to the survey per study arm in each country. With 16 study arms total in these 6 sub-studies, 20,064 participants will be enrolled in each country (Table 4). We have not inflated the sample size for multiple comparisons as per the recommendation by Rothman [12]. We chose a 10% difference between study arms as our preliminary analysis indicated that a 1 dollar incentive becomes cost-neutral at this cut-off point.

**Table 4.** Number of participants needed to complete a mobile phone survey per country.

| Sub-study | Study arms | Participants who completed survey per study arm, n | Total participants who completed the survey, n |
|---|---|---|---|
| Sub-study 1 | 3 | 376 | 1128 |
| Sub-study 2 | 3 | 376 | 1128 |
| Sub-study 3 | 3 | 376 | 1128 |
| Sub-study 4 | 4 | 376 | 1504 |
| Sub-study 5 | 2 | 376 | 752 |
| Sub-study 6 | 1 | 376 | 376 |
| Sub-study 7[a] | 2 | 405 | 810 |
| Total | | | 6826 |

[a]For sub-study 7, we adjust for a 20% loss to follow-up from the first and second mobile phone survey.

For sub-study 7, the sample size is calculated based on the kappa statistic [13]. With assumption of kappa .75, a margin of error of 0.05%, an alpha of .05, and the proportion of positive responses of 0.3, 405 participants who have completed the survey per study arm are needed. Adjusting for a 20% loss to follow-up from the first and second mobile phone survey and a 30% baseline completion percentage, 1688 participants who consented will be enrolled per arm, for a total of 3376 participants across the two arms for each country.

### Data Management and Analysis

The main outcomes in this study are contact, response, refusal, and completion proportions. Our outcomes are defined based on standard definitions from the 9th edition of the American Association for Public Opinion Research (AAPOR) [14], with some modifications to accommodate our RDD MPS design. Eligible individuals will be defined as persons who confirm that they are at least 18 years old.

Complete interviews (CI) are defined as age-eligible respondents who answer 5 or more modules. Partial interviews (PI) are defined as age-eligible respondents who answer between 2 and 4 modules. Participants who are age-eligible but answer less than 2 modules will be classified as a refusal/break-off (R). Non-contacts (NC) are defined as a confirmed number where respondent never picks up (this classification only applies to sub-studies 6 and 7). The main outcomes will be calculated using the equations in Figure 3.

Outcomes will be tabulated and stratified by both the question number and the question content due to the randomization of NCD topic modules. As a secondary analysis, we will conduct Kaplan-Meier curves to plot survey attrition by time spent on survey. For sub-study 7, test for agreement in survey responses between the survey modalities will be assessed using Cohen kappa. Statistical significance will be determined at an alpha of .05.

**Figure 3.** Equations used to calculate the main outcomes.

$$\text{Response rate} = \frac{CI + PI}{CI + PI + NR}$$

$$\text{Completion rate} = \frac{CI}{CI + PI + NR}$$

$$\text{Refusal rate} = \frac{R}{CI + PI + NR}$$

$$\text{Contact rate} = \frac{CI + PI + R + O}{CI + PI + NR}$$

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## Ethical Considerations

The research protocol will receive ethical approval from the institutional review boards of the following institutions: Johns Hopkins University Bloomberg School of Public Health (JHSPH); Makerere University School of Public Health (MakSPH), Uganda; the Uganda National Council for Science and Technology; the Medical Research Coordinating Council (MRCC); the Ifakara Health Institute (IHI), Tanzania; and the Institute of Epidemiology Disease Control and Research (IEDCR), Bangladesh.

## Results

Research activities are expected to be completed in 2017.

## Discussion

National public health surveillance in many LMICs have typically centered on communicable diseases [9]. The emerging burden of NCDs means that many LMICs have to work quickly to set up effective surveillance systems to curb the epidemic. Faced with greater resource constraints than high-income countries, there is need for cost-effective and timely surveillance methods in LMICs. MPSs have the potential to enhance current efforts for systematic collection of NCD risk factor data to identify national trends, as well as to identify segments of the population at particularly high risk for NCDs. If properly harnessed, MPSs have potential to assist LMIC policy makers with resource allocation and choice of NCD prevention and control interventions, among other decisions [15].

The systematic examination of selected incentive characteristics has two potential benefits. First, the optimization of incentive structure and amounts will increase the survey's contact, response, and completion rates; thereby reducing the number of calls needed to achieve the desired sample size. Second, and only if incentives do not have a differential effect on sub-groups of respondents (ie, incentives increase response in those with more education or of higher socio-economic status), higher response and completion rates may potentially reduce non-response bias.

## Conclusion

The studies discussed in this protocol will evaluate the impact of different strategies to improve IVR survey response and completion rates and to identify the combinations of incentive timing and structure, introduction characteristics, and sampling frames that provide highest yield. Though this protocol centers on NCD risk factors, our findings could potentially be used to inform surveys using IVR methodology for other conditions or aspects such as governance and public opinion.

## Conflicts of Interest

None declared.

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## Abbreviations

**BD4HI:** Bloomberg Philanthropies Data for Health Initiative
**CATI:** computer-assisted telephone interview
**FGD:** focus group discussion
**IEDCR:** Institute of Epidemiology, Disease Control and Research
**IHI:** Ifakara Health Institute
**IVR:** interactive voice response
**KII:** key informant interview
**JHSPH:** Johns Hopkins Bloomberg School of Public Health
**LMICs:** low- and middle-income countries
**MakSPH:** Makerere University School of Public Health
**MNO:** mobile network operator
**MPS:** mobile phone survey
**MRCC:** Medical Research Coordinating Council
**NCD:** non-communicable disease
**RDD:** random digit dialing
**SMS:** short message service

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Protocol

# The Development of a Web-Based Program to Reduce Dietary Salt Intake in Schoolchildren: Study Protocol

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## Abstract

**Background:**   Salt intake of schoolchildren in the Australian state of Victoria is high. To protect future cardiovascular health, interventions that seek to reduce the amount of salt in children's diets are required.

**Objective:**   We sought to develop and pilot test a Web-based program (Digital Education to Limit Salt Intake in the Home [DELISH]) that aims to reduce dietary salt intake among schoolchildren and to improve child and parent knowledge, attitudes, and behaviors related to salt intake. This paper presents the DELISH study protocol, along with pilot findings used to inform the development of the program.

**Methods:**   The DELISH program is a 5-week Web-based intervention that targets schoolchildren aged 7-10 years and their parents. This is a single-arm study with a pretest and posttest design. We will assess change in salt intake through analysis of 24-hour urinary sodium excretion. Children and parents will complete online surveys assessing knowledge, attitudes, and behaviors related to salt intake. We will assess feasibility of the program via process measures, which include metrics to describe intervention uptake (eg, number of children who complete Web-based sessions and of parents who view online newsletters) and evaluation surveys and interviews conducted with children, parents, and schoolteachers. The first 2 Web sessions developed for children were pilot tested in 19 children aged 8-12 years.

**Results:**   Findings from pilot testing indicated that most children (session 1: 18/19, 95%; and session 2: 19/19, 100%) enjoyed completing each session and liked the inclusion of comic strips and interactive games. Commonly reported areas of improvement related to sessions being text and content heavy. Based on these findings, we simplified sessions and developed 3 additional sessions for use in the DELISH program. The DELISH program was implemented during June-December 2016. We expect to have results from this study at the end of 2017.

**Conclusions:**   To our knowledge, this is the first Australian study to examine the effectiveness of a Web-based program to reduce salt intake among children in primary school. If shown to be acceptable and effective in lowering salt intake, the DELISH program could be tested using a more rigorous randomized controlled trial design.

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## Introduction

In adults, excess salt intake is associated with high blood pressure [1], which is a major risk factor for cardiovascular disease [2]. It has been predicted that lowering population salt intake would substantially reduce morbidity, mortality, and public health care costs [3,4]. As part of the global action plan to reduce noncommunicable diseases, the World Health Organization has recommended a 30% reduction in global salt intake by 2025 [5].

As in adulthood, childhood dietary salt intake is positively associated with blood pressure [1,6]. Findings from a meta-analysis of 10 controlled salt-reduction trials found that a 42% reduction in salt intake predicted a significant reduction in both systolic (–1.17 mm Hg) and diastolic (–1.29 mm Hg) blood pressure [7]. Although the magnitude of the association between salt reduction and blood pressure in children is relatively modest, blood pressure follows a tracking pattern from childhood into adulthood [8]; therefore, the public health benefits of shifting the distribution of population blood pressure levels is important [9]. Additional consequences of excess salt intake during early life include increased risk of obesity [10,11] and the development of taste preferences for saltier foods [12,13].

The most recent (2011-2012) Australian national estimates of sodium intake, determined via 24-hour dietary recall, showed that average intakes were 2058 mg/day (salt equivalent 5.2 g/day) among 4- to 8-year-old children and 2462 mg/day (salt 6.3 g/day) among 9- to 13-year-old children [14]. This is in excess of dietary recommendations, which specify daily intakes of no more than 1400 mg/day (salt equivalent 3.5 g/day) and 2000 mg/day (salt 5 g/day) for each respective age group [15]. Using the reference standard measure of 24-hour urinary sodium excretion, we have previously reported an average salt intake of 6.1 g/day among 4- to 12-year-old schoolchildren in Victoria, Australia, with 72% of children exceeding the age-specific guideline for salt intake [16]. These findings demonstrate the need for strategies that seek to reduce salt intake among Australian schoolchildren.

Past evidence indicated that educational messages targeting the key sources of salt in the diet [17] and behavioral skills, such as reading food labels to select lower-salt foods [18] or using herbs and spices instead of salt to flavor food [19], are key components of effective programs to reduce salt intake in adults. However, there is little evidence of effective behavioral-based strategies for reducing salt intake in schoolchildren. The expansion of Internet technologies within the home in Australia [20] provides an important opportunity to deliver public health interventions. In 2014-2015, 97% of Australian households with children aged under 15 years had access to the Internet [20]. Although there is a social gradient for Internet access in Australia, access among more marginalized groups is still relatively common (eg, 77% of those educated to grade 12 or below have Internet access) [20]. Research suggests that online technologies can be used to engage children to achieve positive changes in dietary behaviors [21,22], for example, improved intakes of fruit and vegetables [23]. To date, no Web-based

behavioral intervention targeting salt reduction in Australian schoolchildren has been trialed. Hence, we sought to develop and pilot test a Web-based salt-reduction program that targets primary school children and their parents. The primary objective of the program is to reduce salt intake among children by 20% and improve child and parent knowledge, attitudes, and behaviors related to salt intake. Secondary objectives relate to taste preferences in children; these include (1) assessing their salt preference for commercially available foods of varying salt concentration, (2) assessing the association between salt preference and salt intake, and (3) assessing whether participation in the program alters salt preference.

The purpose of this paper is to describe the Digital Education to Limit Salt Intake in the Home (DELISH) program and data collection methods that we will use in the study. In addition, we report on findings related to the development of the program, which includes pilot testing of educational materials among a sample of children aged 8-12 years.

## Methods

### Study Design and Participants

The DELISH program is a 5-week Web-based intervention that targets schoolchildren in years 2-4 of schooling (ages 7-10 years) and their parents. This is a single-arm study with a pretest and posttest design. The age range of participants is restricted to facilitate the design of appropriate intervention materials with respect to reading ability and comprehension. Children and parents are targeted, as research suggests that interventions that target the whole family, as opposed to only the parent or child, are more effective for achieving dietary changes [24]. Ethics approval has been granted by the Deakin University Health Human Ethics Advisory Group (Project No. HEAG-H 37/2016) and the Department of Education and Training, Victoria State Government (2015_002884). We will obtain written informed consent from the primary caregiver and assent from the child before their participation. This study is supported by a Heart Foundation Vanguard grant (Application ID: 100574).

### Recruitment Procedures

We will recruit children from government primary schools located in the Greater Geelong Region of Victoria, Australia. We will use a Web-based school locater search engine to identify schools with enrollments for primary school children [25]. The school's postcode and corresponding Index of Relative Socio-economic Advantage and Disadvantage [26] will be used to group each school into low-, medium-, and high-socioeconomic areas of Victoria. Following this, we will randomly select schools from each tertile and invite each school's principal to participate in the study via an email invitation and a follow-up courtesy call reminder. Classroom teachers will be provided with information about the study. Prior to school participation, written consent will be obtained from the school principal and classroom teachers. Following this, children in school grades 2-4 (7-10 years of age) will receive a study information pack, which will include an invitation letter addressed to parents, and a parental and child plain language brochure and consent forms. We will also advertise the study through the schools' newsletters.

## Inclusion Criteria

Inclusion criteria are that children (1) will be required to have a parent with an email address and have access to a computer or tablet at home with an Internet connection, and (2) must be attending a Victorian government primary school in years (ie, grade) 2-4.

## Intervention Overview

The Web-based program will be delivered over a 5-week period. Children will actively participate in weekly Web-based sessions designed to take approximately 20-30 minutes each to complete. Parents will receive concurrent educational materials through weekly online newsletters sent via email and short message service (SMS) text messages. In addition, there will be a central study website, where resources for children and parents will be posted.

## Sample Size Calculations

We designed the intervention to reduce salt intake by 20% (ie, 1.2 g/day of salt). Using a random intercept multilevel model (with salt intake outcome allowed to vary randomly at both the individual and the school level) to estimate the change in salt intake over time (pre vs post as a fixed effect) and assuming a mean baseline salt intake of 6.0 (SD 2.5) g/day and intraclass coefficient of 0.04 (school clusters), we require a sample size of 102 children to detect a difference of 1.2 g/day of salt with 90% power at $P<.05$. Anticipating a 20% rate of dropout or incomplete urine samples returned, we aim to recruit 122 children across 6 schools.

## Intervention Development

### Behavioral Objectives of the Intervention

We developed 3 key behavioral messages to reduce salt intake in 7- to 10-year-olds: (1) *stop* using the salt shaker during cooking and at the table, (2) *switch* to lower-salt foods by checking food labels (focus on bread, breakfast cereal, and cheese), and (3) *swap* processed salty foods (eg, processed meats, take-out pizzas and burgers, savory sauces, and snack foods) with healthier alternatives.

We assessed the potential effectiveness of these strategies to meet the primary outcome of a 20% reduction in salt intake via dietary modelling and deemed them as suitable (Multimedia Appendix 1 [27-31]). The rationale for the development of these messages is described below.

The selection of food groups to target within the intervention was informed by our previous work, which identified the main dietary sources of salt among Australian children [32]. These are bread (15%); processed meat (9%); savory sauces and condiments (6%); mixed cereal dishes (7%), which include pizza, sandwiches, and hamburgers; cheese (5%); breakfast cereals (4%); pastries (4%), which include meat pies and sausage rolls; and snack foods (4%). As sodium is widespread within the food supply [33], the main sources of dietary salt are diverse in their nutritional composition and include discretionary options, which should be limited in the diet (eg, processed meats and pastries), as well as core foods, which should form the basis of a healthy dietary pattern (eg, bread and cheese) [34]. We have previously reported that core foods provided more than

half of all salt consumed (55%) by schoolchildren, with the remaining 45% provided by discretionary foods (unpublished data, 2017). Hence, to reduce salt intake, there is a need for strategies that incorporate messages related to overall healthy eating principles, such as limiting the consumption of discretionary foods, as well as messages related to the consumption of core foods that have lower levels of salt. The large variability of salt content within core foods [33,35] makes finding lower-salt options feasible. On this background, we used the *Australian Guide to Healthy Eating* (AGTHE) as an evidence-based healthy eating tool to embed salt-specific messages in the intervention. The AGTHE is a food selection guide that groups foods as core or discretionary choices and provides a visual representation of the proportion of the 5 food groups recommended for consumption each day [34].

We also considered the contribution of discretionary salt use to intake. While no data for Australian children are available, in Western countries it is estimated that approximately 6% of sodium consumed comes from salt added at the table and 5% is added during cooking [30,36]. Previously, we have shown in Victorian schoolchildren that reported table salt use was related to overall higher salt intake, as measured by 24-hour urinary sodium excretion [37]. In addition, we have previously reported that the use of table and cooking salt is relatively common among Victorian schoolchildren and their parents (eg, 40% of children reported using table salt and 66% of parents reported using cooking salt) [31]. These findings demonstrate the importance of targeting discretionary salt use.

Finally, to aid in the development of tailored strategies, we considered the contribution of salt from different meals as consumed by Australian children participating in the 2007 Australian National Children's Nutrition and Physical Activity Survey [27]. We found that foods consumed at dinner contributed the most to daily salt intake (35%) (Multimedia Appendix 2 [27]). Although foods consumed during lunch provided less salt overall (25% of daily intake), these foods had the highest sodium density, indicating the consumption of particularly salty foods at lunch. These findings indicate the importance of targeting lunchtime and dinnertime food intake to help reduce daily salt intake.

### Theoretical Framework

Social cognitive theory is frequently used in dietary interventions targeting children [24], and it informed the development of this intervention. Social cognitive theory stipulates that behavior is determined by the reciprocal interaction of personal cognitive factors (eg, self-efficacy, outcome expectations, and knowledge), socioenvironmental factors (eg, observational learning, normative beliefs, social support, barriers, and opportunities), and behavioral factors (eg, behavioral capability, intentions, and reinforcement) [38].Developing strategies that address the constructs within social cognitive theory increases the likelihood of influencing behavior change [38]. In particular, we focused on those constructs previously shown to be related to dietary intake in children. These include self-efficacy [39], intentions (ie, goal setting) [40,41], reinforcements [42], and knowledge [43]. We developed strategies to address the intervention content with

reference to Michie and colleagues' [44] taxonomy of behavior change techniques. We selected behavior change techniques for inclusion in the intervention considering what was appropriate given the intervention mode of delivery (ie, Web based, with no face-to-face contact) and what behavior change techniques have previously been used in effective interventions targeting children's eating behaviors [24,45]. In addition, we considered previous reports of what behavioral-based strategies were effective in reducing salt intakes. For example, in adults and children, effective strategies to reduce salt intake include providing education on reading sodium information included on food labels, cooking recipes with spices and herbs, information on selecting lower-sodium foods when eating out, and goal setting [18,19,46,47]. Multimedia Appendix 3 shows a list of strategies included in the intervention, mapped to behavior change techniques and social cognitive theory constructs.

### Intervention Content

Storytelling can be used as a means to communicate health messages and facilitate learning outcomes in children [48,49]. In conjunction with a creative writer and illustrator (Ben Pearmain Illustration, Melbourne, Australia) we created a narrative within which to embed the intervention content. To help engage children, we selected a detective theme as a basis of the story, with a personified dog as the protagonist [49,50]. Comic strips will deliver the story at the beginning of each Web session (Multimedia Appendix 4), which will set the scene for the weekly learning activities for the children to complete.

### DELISH Starter Pack

Following the collection of baseline data, we will mail a starter pack to the family home. The pack will include a 1-page overview of the program; a fridge magnet outlining the 3 key behavioral objectives of the program; AGTHE educational resources (including fridge magnet and pamphlets); a cheat sheet shopping card outlining sodium content targets for bread, breakfast cereal, and cheese; a detective logbook for the child to record weekly goals and stick badges in; and a "stop using the salt shaker" sticker and stickers of badges for completing case files and meeting goals.

### Web-Based Sessions

Parents will receive a weekly email with access to the Web-based session; alternatively, children will be able to access each session via the study website. We developed the Web sessions using the e-learning software Articulate Storyline 2 (Articulate Global, Inc). To facilitate engagement and learning, the sessions will be packaged as a series of detective case files for the child to solve. Each case file targets key learning objectives related to the behavioral messages of the intervention (outlined in detail in Multimedia Appendix 3). Table 1 provides an overview of each session. Sessions we developed are interactive and include comic strips, characters to introduce key concepts (Figure 1), activities and games, video content, and sound effects. Multimedia Appendix 4 presents the basic format of the sessions. If the child completes the session and solves the case file, a badge is awarded (Figure 2).

**Table 1.** Overview of weekly Web-based sessions for children.

| Week | Session name | Session overview |
|---|---|---|
| 1 | Salty Business | Background narrative is introduced, child signs up to detective program, and program structure is outlined. Key information related to salt is presented: difference between salt and sodium, the function of salt in the body, the link between excess salt and health, and dietary recommendations for salt. |
| 2 | Hidden & Visible Salt | Dietary sources of salt, including processed foods and discretionary salt, are outlined. Concept that fresh, unprocessed foods do not contain added salt is introduced (ie, "Salt Free Champions"). Key message 1, "Stop using the salt shaker," is introduced. |
| 3 | Sneaky Salt | AGTHE[a] is introduced, as well as the concept that some core foods contain added salt (ie, "Sneaky Salties"). Information on reading food labels to find foods with less salt is provided. Key message 2, "Switch to lower salt foods by checking food labels," is introduced. |
| 4 | Salt Swaps | AGTHE is used to provide information on discretionary foods and "Salt Offenders" are introduced. Key message 3, "Swap processed salty foods with healthier alternatives," is introduced. |
| 5 | Wrap-up session | The story concludes, and the 3 key messages to reduce salt intake (ie, Stop, Switch, and Swap) are reiterated. As child has solved all 4 case files, they are promoted to a chief investigator. |

[a]AGTHE: *Australian Guide to Healthy Eating*.

**Figure 1.** Characters used to convey key messages to children.
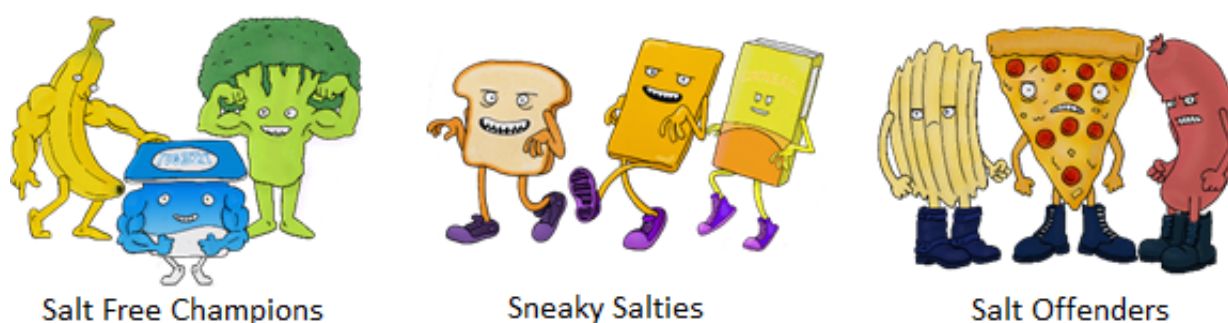


**Figure 2.** Badges provided for completing Web-based sessions and meeting goals.



### Goal Setting

At the end of each session (weeks 2, 3, and 4), the child will be asked to set a goal that is related to the key behavioral message for that week. Given the ages of the children, we created predefined options for goals from which the child could select [51]. We will provide information on possible barriers to meeting the goal and solutions to overcome. Children will be encouraged to record their goal in the detective logbook and discuss this with their parent. If the child reports meeting their goal in the following week, they will be awarded a bonus badge (Figure 2).

### Pilot Testing of Web-Based Sessions

The first 2 Web sessions that were developed were pilot tested in children aged 8 to 12 years. We recruited children via advertisements and email invitations that we distributed among networks at our workplace (ie, Deakin University). Parent and child consent was provided and ethical approval was granted by the Deakin University Health Human Ethics Advisory Group (Project No. HEAG-H 142_2014). Parents were emailed

hyperlinks for their child to access the 2 Web-based sessions. At the end of each Web session, a hyperlink was provided to access an evaluation survey to determine the acceptability and appeal of each session. We invited a subsample of children to participate in a face-to-face interview to provide more detailed feedback on each session. The results section below presents findings from this evaluation.

### Parent Newsletters

Parents will receive weekly emails with hyperlinks to access the online newsletter. The newsletters include educational materials relevant to the week of the program and information on the child's weekly goal (Figure 3). Additional hyperlinks will be embedded within newsletters directing parents to extra resources, such as a video for reading food labels, supermarket cheat sheets for top picks for foods with less salt, and an herbs and spice resource for cooking without salt. The content of newsletters has been reviewed by a dietitian and tested with 2 mothers, and where necessary changes were made to the language, layout, and graphics.

**Figure 3.** Example from online newsletter for parents.
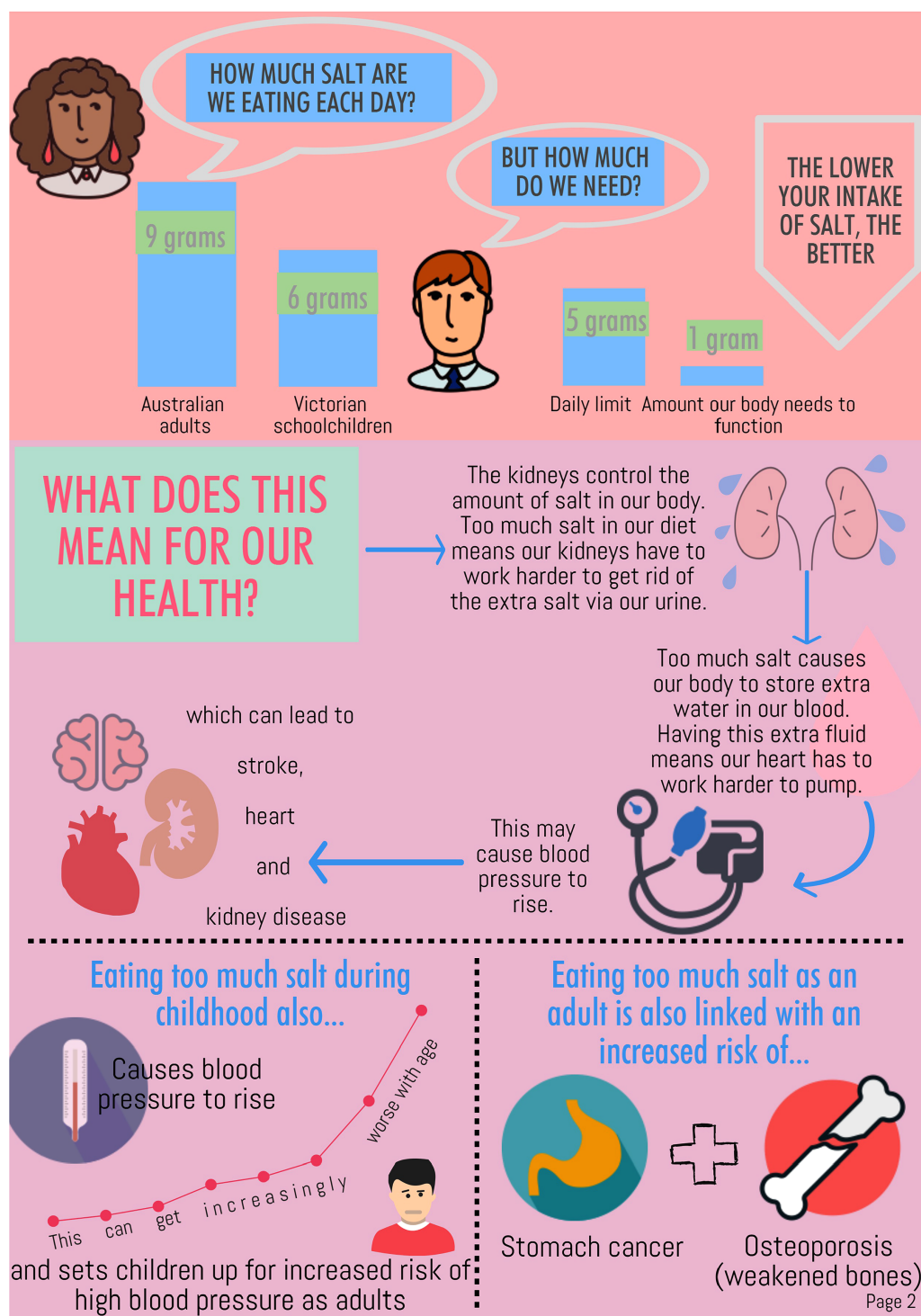
### Study Website

A password-protected study website will be accessible during the intervention and will provide resources for children and parents. We will update the website weekly with relevant resources. The children's section will include access to the detective case files (ie, Web-based sessions), downloadable versions of the comics, weekly case badges, bonus badges, and handouts describing potential barriers to meeting weekly goals with suggested solutions. The parent's section will contain access to online newsletters, also available to download in PDF format, as well as other key resources (Figure 4). In relation to recipe resources, we used existing recipes from health agencies, such as the National Heart Foundation of Australia and World Action on Salt & Health, and where appropriate we provide information for modifying the recipe to reduce salt.

**Figure 4.** Parents' section of the study website.



### SMS Text Messages

We will send 2 to 3 reminder SMS text messages to the parent during each week of the intervention. The messages will provide information related to weekly key messages and goal setting, and will include hyperlinks to access intervention resources, such as online newsletters and materials posted on the website.

### Data Collection Methods

Table 2 provides an overview of measures to be completed before and after the intervention.

### Urine Collection

The primary outcome of the DELISH program is the change in the child's salt intake assessed via a 24-hour urine collection. To engage parents, we will provide them with the option of completing a 24-hour urine collection; however, this will not be mandatory. We will follow our previous protocol for collecting 24-hour urine samples in schoolchildren [52]. Briefly, the first morning urine will be voided, and this will be recorded as the 24-hour urine start time. Following this, all urine will be collected, finishing with a final collection at the corresponding 24-hour finish time. Participants will be able to commence the 24-hour urine collection either at school or at home over the weekend. We will instruct participants to complete the postintervention 24-hour urine collection on the same type of day (ie, school or nonschool day) as the baseline assessment. Children will be provided with a 2.5-L widemouthed, rimmed polypropylene bottle to collect urine. To assist with urine collection, we will provide an additional 500-mL plastic handled jug. Verbal and written instructions will be provided. Children will be asked to report any missed collections or spillages on a urine collection slip, which will be returned with the 24-hour urine sample. We will standardize urine volume and electrolytes to a 24-hour period; for example, [24 hours/urine duration (hours)] × urinary measure. We will consider 24-hour urine samples to be complete if no more than 1 collection is reported as missing (provided that we find no differences in urinary sodium by sex between those who report 1 missed collection and those who report no missed collections), duration of

collection is within 18-34 hours, total volume is 300 mL or more, and urinary creatinine excretion (mmol/kg body weight/day) is greater than the fifth percentile cutoff point obtained from previous reference data among Victorian schoolchildren (ie, 7-8 years, ≥0.1 mmol/kg body weight/day; and 9-10 years, ≥0.1 mmol/kg body weight/day [52]).

The first morning void of the 24-hour urine collection will be collected in a separate container, before the start of the 24-hour collection, and will be assessed for sodium concentration [53]. Research staff will visit the school on the day preceding the scheduled testing to provide those children completing a school-day 24-hour urine collection with a 500-mL plastic collection container and carry bag, along with verbal and written instructions, so the child can collect the overnight urine sample on waking on the day before starting the 24-hour urine sample at school. Children who complete weekend-day 24-hour urine collections will be provided with the collection materials and instructions for both the 24-hour urine collection and overnight collection on the day of testing at the school. Children will be asked to report onto a urine collection slip any spillages while collecting the overnight urine.

Urine samples will be transported to a commercial pathology company for urinalysis. Total volume of both urine samples will be measured, and each will be assessed for sodium and potassium concentrations using indirect ion-selective electrodes and for urinary creatinine concentration using the Jaffe reaction [54] on the Siemens Advia 2400 analyzer (Siemens Healthcare GmbH, Erlangen, Germany). Per participant, 2×10-mL aliquots will be taken from the 24-hour urine collection for storage and transferred to –80°C conditions. We will use the molecular weights of sodium (23 g/mol), sodium chloride (58.5 g/mol), and potassium (39.1 g/mol) to convert laboratory values of millimoles to milligrams [55].

## Anthropometry (Child)

Trained research staff will collect anthropometric measurements at the school site on the day of testing. Height will be measured to the nearest 0.1 cm using a calibrated portable stadiometer, seca model 220 (Hamburg, Germany). Weight will be measured to the nearest 0.1 kg using a calibrated UC-321 portable electronic scale (A&D Medical, San Jose, CA, USA). Waist circumference will be measured to the nearest 0.1 cm using a Lufkin Executive Thinline W606PM pocket tape (Sparks, MD, USA). Waist circumference will be measured at the end of a normal expiration at the narrowest point between the lower costal border and the top of the iliac crest. For all anthropometric measures, 2 measurements will be taken. If these 2 measures differ by more than 5 mm for height, 0.1 kg for weight, or 10 mm for waist circumference, a third measurement will be taken. Where 2 measurements are taken we will use the mean in the analysis, and where 3 measurements are taken we will use the median value. We will calculate body mass index as body weight (kg) divided by the square of body height (m$^2$). Age- and sex-adjusted body mass index $z$ scores will be calculated using the LMS method [56] with the 2000 US Centers for Disease Control and Prevention growth charts acting as the reference population [57]. Participants will be grouped into weight categories (very underweight, underweight, healthy weight, overweight, obese) using the age- and sex-specific International Obesity Task Force body mass index reference cutoffs for children [58,59].

## Dietary intake (Child)

To assess the dietary intake of children at baseline, the parent will complete an online version of the validated Australian Child and Adolescent Eating Survey (ACAES) [60]. The ACAES is a 120-item, semiquantitative food frequency questionnaire that includes a comprehensive list of foods, enabling the estimation of all macronutrients and key micronutrients. We will compute the nutrient data from the ACAES using FoodWorks (version 3.02.581; Xyris Software [Australia] Pty Ltd). Parents will be instructed to report on their child's dietary intake for the previous month. The purpose of collecting information from the ACAES is to provide background information on overall dietary intake within the group.

## Online Salt Survey (Child)

We developed a 29-item online survey assessing the constructs of knowledge (20 questions), attitudes (2 questions), behaviors (4 questions), and self-efficacy (3 questions) related to dietary salt. To simplify the survey and help with readability, we incorporated images into response options. The survey instrument was pilot tested with 3 schoolchildren aged 7-9 years, 2 mothers, 1 primary school teacher, and 2 dietitians to check for readability, age appropriateness, and content. Following this testing, we made small modifications to the survey. An online readability tool graded the survey instrument as "easy to read" and appropriate for 8- to 9-year-olds [61]. We will assess test-retest reliability of the questionnaire in a separate sample of 45 schoolchildren.

The knowledge questions include declarative (eg, food sources of salt, relationship between salt) and procedural knowledge (eg, reading food labels to pick foods with less salt). Response scales include multiple choice options, along with "true," "false," and "not sure" responses, with the latter included to discourage guessing. Correct answers will be scored 1 point and incorrect answers, including "not sure," will be scored as 0, with a total maximum knowledge score of 20. Attitude questions assess the importance of salt in food to make it tasty (eg, "Salt makes food tasty"), and these questions were modelled from a previous survey conducted in adults [62] and were simplified for use with children (eg, the response scale was modified to a 5-point Likert smiley-face scale). Responses will be scored as "agree a lot"=3 points, "agree"=2 points, "I'm not sure"=0 points, "disagree"=0 points, and "disagree a lot"=0 points; hence, higher scores will reflect stronger beliefs about the importance of salt in food for taste. Behavior questions are related to discretionary salt use, previously used in children [52], and specific behaviors targeted within the intervention, such as talking to parents about salt use at home. Behavior question response items will be scored from 0 to 3, or 0 to 1 in the case of 2-item responses, with a higher score indicating better adherence to targeted salt-related behaviors. Self-efficacy questions were based on those used in previous studies in children [63] and examined key behaviors targeted within the intervention. The 3 response item will be scored as 0 to 2 ("not

sure at all," "a little sure I can," and "very sure I can") indicating     low, medium, and high self-efficacy, respectively.

**Table 2.** Overview of data collection procedures.

| Participants | | | Baseline | Postintervention |
|---|---|---|---|---|
| **Child** | | | | |
| | **Face-to-face school measures** | | | |
| | | 1 × 24-hour urine sample | ✓ | ✓ |
| | | 1 × overnight urine sample | ✓ | ✓ |
| | | Weight, height, and waist circumference | ✓ | ✓ |
| | | Taste-testing session | ✓ | ✓ |
| | **Online measures** | | | |
| | | Australian Child and Adolescent Eating Survey (completed by parent proxy) | ✓ | |
| | | Child salt survey to assess knowledge, attitudes, and behaviors | ✓ | |
| | | Program evaluation questionnaire | | ✓ |
| | | Evaluation interview (subsample n=10) | | ✓ |
| **Parent** | | | | |
| | | 1 × 24-hour urine sample (optional) | ✓ | ✓ |
| | | Parent salt survey to assess knowledge, attitudes, behaviors, and demographic characteristics | ✓ | ✓ |
| | | Program evaluation questionnaire | | ✓ |
| | | Evaluation interview (subsample n=10) | | ✓ |
| **Teachers/principals** | | | | |
| | | Evaluation interview | | ✓ |

### Online Salt Survey (Parent)

The study parent will complete an online questionnaire, containing 34 questions (baseline) and 21 questions (postintervention) assessing sociodemographic characteristics such as age, sex, and education level (13 questions) and knowledge, attitudes, and behaviors related to salt intake. The survey was based on a previously validated salt knowledge questionnaire [62,64], while other questions were modelled on those used in past surveys [65-67], and was tested for readability in 5 parents from varying demographic backgrounds. The pre- and postintervention surveys for parents were identical, with the exception of excluding demographic information on the follow-up survey.

We included 14 knowledge questions assessing declarative (ie, relationship between salt and sodium, current recommendation, main sources, health conditions related to excessive salt intake) and procedural knowledge (interpreting sodium information on food labels). These question responses are in the form of multiple choice and 5-point Likert scale ("strongly disagree" to "strongly agree"). All correct responses will be scored as 1, while incorrect responses, including "don't know" and "not sure," will be scored as 0. Responses to Likert scale questions will be scored as a 2 for "certainly true," 1 for "probably true," and 0 for incorrect answers, including "not sure" and "don't know" responses. Negative statements will be reversed prior to scoring. The salt knowledge questions will be summed to generate scores for each question, and a total salt knowledge

score will be derived by summing all the knowledge questions. The minimum and maximum salt knowledge scores are 0 and 32, respectively. We added some additional questions assessing knowledge specific to salt consumption in children, as the original validated questionnaire was not directed to parents.

We assessed 3 attitude questions (ie, parents' personal attitude toward their own salt intakes, salt as a flavor enhancer, taste of low-salt foods, and importance of reducing salt) using 5-point Likert scales ("strongly disagree" to "strongly agree"). Scores will be assigned from 1 ("strongly disagree") to 5 ("strongly agree"). The scores will be summed to derive a total beliefs score. The minimum and maximum attitude scores will be 0 and 6, respectively, with a score of 3 assigned for "strongly agree," 2 for "agree," 1 for "neither agree nor disagree," 0 for "disagree" or "strongly disagree." Higher scores will indicate stronger beliefs about the importance of the salt in food for taste. Some questions regarding attitudes related to salt intake will be presented as percentages.

We assessed 4 behavior questions regarding discretionary salt use (ie, adding salt to food during cooking [parent] or at the table [child and parent], and placing a salt shaker on the table [child and parent]) using 5-point Likert scales. Scores will be assigned from 0 for "always" to 4 for "never." Parents will report the frequency of current actions taken to reduce their child's salt intake (and actions taken in the past 1 month in the follow-up survey) using a 7-point Likert scale. The scores will be summed to derive a total behaviors score according to frequency of engaging in behavior (6 for "never," 4 for "2-3

times/week," etc). The minimum and maximum behavior score will be 0-53, respectively. Higher scores will indicate a higher frequency in engaging in positive salt related behaviors.

### Taste-Testing Procedures

Tastings will be conducted with 2 commercially available food products, 1 snack food (potato chips) and 1 staple food (cornflakes), both of which are important sources of dietary salt

for children [32]. We used the sodium content listed on packaged nutrient information panels to select 3 products of varying salt content for each food (Table 3). Nutrient profiles, particularly sugar and fat, were matched as closely as possible between samples of the same food type, as was visual appearance. Children will complete 2 taste tests for each food type during the testing session completed at schools (1) preference tests and (2) ability to rank samples according to salt content.

**Table 3.** Sodium content of chip and cornflake samples.

| Food products | | Sodium (mg/100 g) | Salt equivalent (g/100 g) |
| --- | --- | --- | --- |
| **Chips** | | | |
| | No added salt | 14 | 0.04 |
| | Mid salt | 200 | 0.5 |
| | High salt | 486 | 1.2 |
| **Cornflakes** | | | |
| | Low salt | 90 | 0.2 |
| | Mid salt | 390 | 1.0 |
| | High salt | 590 | 1.5 |

All samples of chips and cornflakes will be presented in plain containers in a predetermined randomized sequence. Children will be asked to have a drink of water between tasting each food sample. On completion of tasting the 3 samples, children will be asked which one they liked the most (ie, preference). The most liked sample will be removed from sight and the question repeated for the remaining 2 food samples. This forced-choice rank-order method means that each child will rank the 3 samples from most to least preferred. Following the same procedure, the child will then be asked which sample they think tastes the saltiest (ie, ability to rank samples). This rank-order method is based on previous methods [68] and has been successfully used in a similar sample of children ranking sour intensities and preference [69].

### Data Analysis

We will use Stata SE 14 (StataCorp LP) for all statistical analyses. Descriptive statistics will describe continuous (mean, SD) and categorical (n, %) measures. McNemar test will assess the change in proportion of responses in the pretest and posttest surveys. Multilevel regression models will assess the change in salt intake among children, as well as child and parent salt survey scores (knowledge, attitudes, and behaviors). Models will adjust for potential confounders (ie, age, sex, and parental level of education). To assess whether participation in the program alters salt preference, we will group participants based on the sample they most preferred, and we will use the McNemar test to assess the change in proportion of children's preferences before and after the intervention. Statistical significance will be set at $P<.05$.

### Process Evaluation

To assess the feasibility and acceptability of the program, we will collect a range of process evaluation measures. To assess the extent of the intervention delivered to children and parents, we will collate metrics for use of the study website (ie, page

views and unique visitors), including the number of views for each week's online newsletter provided to parents. For the weekly Web session for children, we will record the number of unique visitors, number of views, proportion of the session completed, and duration to complete the session. The number of children who report setting weekly goals, as well as whether those goals were met will be recorded. At the end of the intervention, we will ask parents and children to complete an anonymous online evaluation questionnaire to assess the acceptability of materials and assess any barriers that may have limited engagement. Interviews will be held with a subsample of children (n=10) and the primary caregiver (n=10) to assess their overall enjoyment of the program and materials. For children, this will be a face-to-face interview completed at the child's school. For parents, this will be a telephone interview. We will invite participating teachers and principals to a short interview to assess their thoughts on the feasibility of incorporating a salt education program within their current curriculum and about their use of existing food or nutrition-related programs within their teaching. The interviews will take place either face-to-face or over the phone. All interviews will be audio recorded, transcribed verbatim, and analyzed for themes using NVivo software version 11.3.1 (QSR International).

## Results

### Developmental Phase of Intervention: Pilot Testing of 2 Web-Based Sessions

A total of 19 children between the ages of 8 and 12 years (n=12, 63% boys) completed both of the Web-based sessions and corresponding evaluation surveys. Of these children, 5 (3 boys) completed the additional interview. Overall, the sessions were well received. Most children (session 1: 18/19, 95%; and session 2: 19/19, 100%) reported that they liked completing the sessions, as well as the inclusion of the comic strips and the dog

protagonist. All children liked the interactive games (Table 4). When children were asked to list one thing they liked most about each session, the most common responses related to the dog character, being a detective, the comic strips, and the incorporation of activities (such as using a salt detector to find out what foods have salt) and games. Children also reported that they liked learning things about salt that they didn't know. When children were asked to list one thing they did not like about each session, some children (n=4 in session 1, n=8 in session 2) reported nothing; other responses related to technical glitches, text (eg, too many words, text changing too quickly, small font size), the speed at which children had to complete some activities, and a limited selection of avatars. More than half of the children found the activities included in each session easy to complete; however, some did report having difficulties (Table 4). When asked to specify why they found any part of the activities difficult, their responses related to use of small text that progressed quickly, hence making content difficult to read, and the inclusion of too many questions to answer.

With relation to findings from the interviews, overall, children indicated that they liked completing the sessions and found the format of the information presented to be interesting and engaging. Some children indicated that there was too much information in session 1 and that they could not understand some words used. Overall, children reported that they liked the overall look and layout of the sessions, along with the detective theme and background story. Multimedia Appendix 5 provides a selection of quotes from the interviews.

Based on findings from pilot testing, the first 2 Web sessions were modified and the remaining 3 sessions were created. Modifications related to using less text to deliver content and instead using more pictures, using a larger text font, including a seek bar to enable children to replay text and access the content delivered, testing further to remove technical glitches, and slowing down and simplifying activities (eg, foods moving across a conveyor belt to test salt levels). While we noted that children wanted more variety and interesting avatars to select from, we made no changes due to limitations in access to artwork. All of the final Web sessions used in the DELISH program were reviewed for developmental appropriateness and comprehension by a primary school teacher and were further tested with 2 primary school children. Where necessary, we made minor changes to language.

## Data Collection in the Main DELISH Study

Data collection was completed in December 2016. We are now collating and cleaning the data. Analysis will be conducted in June 2017 and we expect to have results at the end of 2017.

**Table 4.** Quantitative findings from pilot testing of 2 Web-based sessions.

| Question | First session | | Second session | |
|---|---|---|---|---|
| | n | % | n | % |
| **Did you watch the education session until the end?** | | | | |
| Yes | 19 | 100 | 19 | 100 |
| No | 0 | 0 | 0 | 0 |
| **Did you like completing the online education session?** | | | | |
| Didn't like it at all | 0 | 0 | 0 | 0 |
| Didn't like it | 1 | 5 | 0 | 0 |
| Don't know | 0 | 0 | 0 | 0 |
| Liked it | 8 | 42 | 9 | 47 |
| Liked it very much | 10 | 53 | 10 | 53 |
| **Did you like the comic strip at the start of the education session?** | | | | |
| Didn't like it at all | 1 | 5 | 0 | 0 |
| Didn't like it | 1 | 5 | 1 | 5 |
| Don't know | 0 | 0 | 2 | 11 |
| Liked it | 8 | 42 | 5 | 26 |
| Liked it very much | 9 | 47 | 11 | 58 |
| **Did you like the detective dog, Banjo, that led you through the education session?** | | | | |
| Didn't like it at all | 1 | 6 | 2 | 11 |
| Didn't like it | 2 | 11 | 0 | 0 |
| Don't know | 0 | 0 | 1 | 5 |
| Liked it | 4 | 22 | 5 | 26 |
| Liked it very much | 11 | 61 | 11 | 58 |
| **How difficult was it to complete the activities included in the education session?** | | | | |
| Very easy | 3 | 16 | 4 | 21 |
| Easy | 10 | 53 | 11 | 57 |
| Difficult | 3 | 16 | 2 | 11 |
| Very difficult | 1 | 5 | 0 | 0 |
| Not sure | 2 | 11 | 2 | 11 |
| **Did you enjoy completing the quiz/game at the end of the session?** | | | | |
| Didn't like it at all | 0 | 0 | 0 | 0 |
| Didn't like it | 0 | 0 | 0 | 0 |
| Don't know | 0 | 0 | 0 | 0 |
| Liked it | 13 | 68 | 4 | 21 |
| Liked it very much | 6 | 32 | 15 | 79 |
| **Did you find the information included within the education session interesting?** | | | | |
| Didn't like it at all | 0 | 0 | 0 | 0 |
| Didn't like it | 1 | 5 | 1 | 5 |
| Don't know | 0 | 0 | 1 | 5 |
| Liked it | 8 | 42 | 7 | 37 |
| Liked it very much | 10 | 53 | 10 | 53 |
| **Are you looking forward to completing the 2nd education session?** | | | | |
| Not really looking forward to it at all | 2 | 11 | N/A[a] | N/A |

| Question | First session | | Second session | |
|---|---|---|---|---|
| | n | % | n | % |
| Not really looking forward to it | 0 | 0 | N/A | N/A |
| Don't know | 1 | 5 | N/A | N/A |
| Looking forward to it a little bit | 5 | 26 | N/A | N/A |
| Yes really looking forward to it | 11 | 58 | N/A | N/A |

[a]N/A: not applicable.

## Discussion

Lowering exposure to dietary salt during childhood is likely to have important cardiovascular health benefits [70]. In Australia, no Web-based behavioral programs to reduce salt intake among schoolchildren have been developed or tested. The process findings related to usability and acceptability of the DELISH program by parents and children, along with teachers' views on incorporating salt-reduction messages within school nutrition programs, can be used to refine and modify the program as necessary. We acknowledge that the study is limited by the pretest and posttest design; as such, any reported changes in outcomes could be due to other confounding factors, such as wider health-related initiatives conducted at the participating schools. If shown to be acceptable and effective in lowering salt intake, the DELISH program could be tested using a more rigorous randomized controlled trial design.

## Authors' Contributions

CAG, AB, KC, and CN conceived the project and designed the study. CAG wrote the manuscript, and DK and MW contributed to the parent salt survey and taste-testing sections. CAG was primarily responsible for the development of all intervention content with input from the other coauthors. All authors read and approved the final manuscript.

## Multimedia Appendix 1

Dietary modelling to assess impact of intervention strategies on sodium (ie, salt) intake.

[PDF File (Adobe PDF File), 25KB - resprot_v6i5e103_app1.pdf ]

## Multimedia Appendix 2

Sodium intake in Australian schoolchildren aged 6-16 years by eating occasion (n=2921).

[PDF File (Adobe PDF File), 28KB - resprot_v6i5e103_app2.pdf ]

## Multimedia Appendix 3

Overview of intervention objectives, content, and strategies mapped to behavior change techniques and social cognitive theory construct.

[PDF File (Adobe PDF File), 90KB - resprot_v6i5e103_app3.pdf ]

## Multimedia Appendix 4

Overview of format for weekly Web-based sessions for children.

[PDF File (Adobe PDF File), 818KB - resprot_v6i5e103_app4.pdf ]

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## Multimedia Appendix 5

Selection of quotes from interviews during pilot testing of 2 Web sessions.

[PDF File (Adobe PDF File), 19KB - resprot_v6i5e103_app5.pdf ]

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## Abbreviations

**ACAES:** Australian Child and Adolescent Eating Survey
**AGTHE:** Australian Guide to Healthy Eating
**DELISH:** Digital Education to Limit Salt Intake in the Home
**SMS:** short message service

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Protocol

# Neoadjuvant Hypofractionated Radiotherapy and Chemotherapy in High-Grade Extremity Soft Tissue Sarcomas: Phase 2 Clinical Trial Protocol

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## Abstract

**Background:** Neoadjuvant radiotherapy (RT) and chemotherapy are applied to large, high-grade extremity soft tissue sarcomas to treat metastatic disease earlier and sterilize margins to perform R0 surgery. However, preoperative RT increases wound complication rates (rWC), delaying adjuvant chemotherapy or preventing it from being administered altogether. Hypofractionated neoadjuvant RT can be offered in this situation, concomitant to chemotherapy, allowing patients to receive chemotherapy as a preoperative treatment in less time with an acceptable rWC.

**Objective:** The objectives of this protocol are to maintain low rates of morbidity and mortality compared to literature data, improving survival rates and avoiding poor responders from receiving unnecessary adjuvant chemotherapy.

**Methods:** This noncontrolled, single-arm, phase 2 clinical trial recruited patients aged over 18 years with high-grade soft tissue sarcomas in the girdles or extremities. Three neoadjuvant chemotherapy (ifosfamide and doxorubicin) cycles were administered with 5 days of hypofractionated RT (25 Gy in 5 fractions) in the second cycle of doxorubicin only. Viable cell counts in the surgical specimen were measured, and patients in whom this value was less than 30% continued to receive an additional 3 full chemotherapy cycles as adjuvant treatment.

**Results:** Primary endpoint will be disease-specific survival measured by the evaluation of local and distant recurrence after neoadjuvant treatment. The secondary endpoints will be wound complication and amputation rates and chemotherapy toxicity. We also will record the viable cell rates after the schema and correlate this with survival.

**Conclusions:** As seems with other solid tumors, hypofractionated RT has comparable efficacy and safety as conventional fractionation. This modality of treatment combined with chemotherapy could increase the pathological response rates and improve the outcomes of select patients.

**Trial Registration:** ClinicalTrials.gov NCT02812654; https://clinicaltrials.gov/ct2/show/NCT02812654 (Archived by WebCite at http://www.webcitation.org/6qC3puBOy)

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## KEYWORDS

soft tissue sarcoma; neoadjuvant treatment; hypofractionated doses; radiotherapy; dose fractionation; toxicity

## Introduction

Soft tissue sarcomas (STSs) are rare neoplasms and account for 1% of all solid tumors in adults. In 2013, there were 11,410 new cases diagnosed in adults and children in the United States, with 4390 expected deaths [1]. There are no data on such estimates in Brazil. By inference, using the American population, we have predicted an annual incidence of 7060 cases for 2013.

Approximately 50% to 60% of cases develop in the limbs, which can differentiate into more than 50 histological subtypes [2]. High-grade sarcomas, which are deep and larger than 5 cm, are locally aggressive and cause distant metastases, primarily to the lungs. The risk of lung metastasis from high-grade tumors ranges from 34% in 5- to 10-cm lesions to 43% for those over 10 cm [3].

The treatment for STSs, which are localized but not amenable to adequate resection, is multimodal in most cases and often involves surgery, chemotherapy, and radiotherapy (RT) [3]. Nevertheless, selecting patients to receive chemotherapy as adjuvant treatment is an option to avoid unnecessary toxic treatment in cases that are considered to be nonresponsive; this approach increases the rates of limb sparing but fails to improve overall survival (OS)—patients continue to die of metastatic disease, especially in the lung. Further, choosing an RT scheme that reduces wound complication rates might increase the number of patients who receive chemotherapy when it is indicated.

To increase the tumor necrosis rate in patients with STSs of the extremities that are not amenable to adequate resection, with regard to their survival, we have proposed a treatment regimen in which neoadjuvant chemotherapy is administered with concomitant hypofractionated RT and adjuvant chemotherapy for select cases, depending on the viable cell count. Our aim is to maintain morbidity and mortality rates compared with the current regimen, improve survival, and spare patients who are considered to be poor responders from unnecessary chemotherapy.

## Methods

### Overview

This prospective, uncontrolled, phase 2 study began in February 2015. Recruitment is expected to be completed by December 2018. A total of 70 patients are to be recruited in this period, based on the demographics of new cases that enter our service per year and the criteria for compatibility with the study. For a rise in disease-free survival from 50% to 70%, we calculate that we will need 70 patients, with an alpha error of .05 and statistical power of 80% (1-tailed test). These parameters are also considered for increasing the response rate from 15% to 20%.

The recruitment will target patients aged 18 to 75 years with nonmetastatic STSs of the extremities with high histological grade, including the pelvic and shoulder girdles, as confirmed by an anatomopathological exam. These patients must have primary or recurrent tumors that are not amenable to resection, with an adequate 3-dimensional margin of 1.0 to 2.0 cm or, in those in whom preservation of the limb is not possible, must not have undergone chemotherapy or prior RT before the clinical trial. The Karnofsky index [4] should be greater than 70%, and the following criteria must be met: leukocyte count >3500/mm$^3$, neutrophil value >1500/mm$^3$, platelet count >100,000/mm$^3$, serum creatinine <1.5 mg/dL, bilirubin serum concentrations within normal limits, transaminase levels up to twice normal values, and no signs of coronary artery disease as determined by ejection fraction.

Patients who have been diagnosed with embryonal rhabdomyosarcoma, primitive neuroectodermal tumors, chondrosarcomas, osteosarcomas, or HIV infection or have refused to sign the informed consent form, as approved by the Research Ethics Committee, will be excluded from the study. Patients with pelvic or thoracic organs in the radiation field are also excluded.

Recent resection was defined as surgery up to 3 months before admission to our service, whereas relapsed tumor was considered a tumor that appeared after 3 months of any prior surgical treatment.

### Toxicity

Treatment will be continued until disease progression (according to Response Evaluation Criteria In Solid Tumors [RECIST], version 1.0) [5], unacceptable toxic effects, withdrawal of consent, or death. Adverse events will be graded per the National Cancer Institute Common Toxicity Criteria for Adverse Events (version 5.0) [6].

All patients will be staged with regard to local disease by magnetic resonance imaging (MRI). Chest computed tomography (CT) will be used to evaluate the presence of distant disease. For patients with liposarcoma of the extremities, CT or ultrasonography of the total abdomen with the pelvis will be performed. All tumors, including recurrent tumors, will be classified per the American Joint Committee on Cancer Cancer Staging Manual, 7$^{th}$ Edition [7].

### Chemotherapy and Radiotherapy

The treatment plan comprises 1 cycle every 21 days for a total of 3 preoperative cycles in conjunction with hypofractionated RT. Doxorubicin 75 mg/m$^2$ will be administered intravenously over 30 minutes, day 1, in cycles 1, 2, and 3; ifosfamide 9.0 g/m$^2$ will be delivered intravenously over 2 hours, days 1 to 5 in cycles 1 and 3; mesna will be given at 100% of the ifosfamide dose, with half infused 15 minutes prior to and half infused 4 hours after beginning the infusion of ifosfamide; and filgrastim 300 mcg will be administered subcutaneously, days 6 to 10 in cycles 1, 2, and 3.

Surgery will then be performed 4 to 6 weeks after the end of the third cycle. Three additional cycles of chemotherapy, similar to cycle 1, will be offered to cases with ≤30% viable cells in the surgical specimens (thus considered to be good responders). RT (intensity-modulated radiation therapy or 3-dimensional) will be performed with the following doses and fractions: 25 Gy/5 fractions of 500 cGy on consecutive days from Monday to Friday, starting on day 1 of the second chemotherapy cycle (C2) (see Figure 1).

After the phase RT/induction chemotherapy, the patients are examined after 3 weeks of each chemotherapy cycle by the responsible surgeon. Imaging, MRI of the local tumor, and chest CT are repeated 3 weeks after the last chemotherapy cycle. RECIST criteria will be used to evaluate clinical responses [5].

The surgery will be performed 4 to 6 weeks after the end of the third chemotherapy cycle, totaling 7 to 9 weeks after RT. If large dermal-adipose flaps must be fashioned, the aid of a skilled plastic surgeon can be requested to reduce wound morbidity. Figure 1 shows treatment schedule.

**Figure 1.** Scheme and treatment schedule illustration.
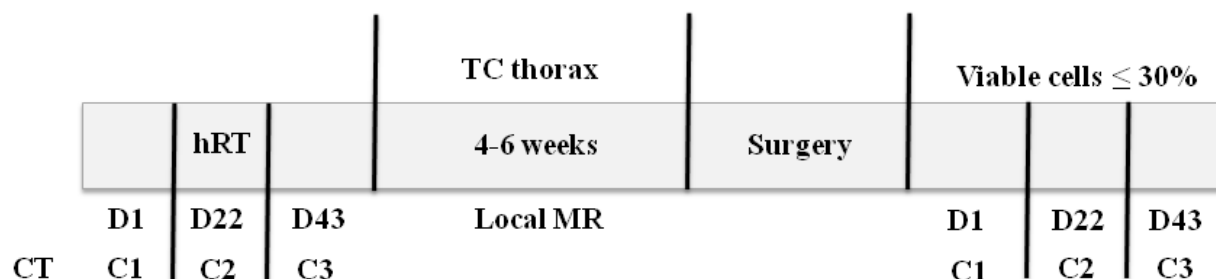


## Wound Complications

All cases are examined by a committee (including a nurse, surgeon, and oncologist) to evaluate and rate wound complications according to the criteria used by O'Sullivan et al in 2002; major wound complications were defined as a "secondary operation under general or regional anesthesia for wound repair or management" [8]. Late radiation toxicity grade will be reported according to the Radiation Therapy Oncology Group (RTOG-0630) [9].

## Pathological Anatomy

All cases are assessed by a single pathologist from the Department of Pathological Anatomy of AC Camargo Cancer Center (IWC) who will diagnose and grade the tumors per the World Health Organization Blue Books [2]. Tumor grades II and III are jointly considered to be high-grade for therapeutic purposes. The collection of clinical data and complementary exams will be obtained from medical records.

From each surgical specimen that is resected after preoperative chemotherapy treatment, a representative slice of the entire specimen with less visible macroscopic necrosis will be obtained. A mapping image will be generated from this slice with 1.0- to 2.0-cm$^2$ cuts. Next, blocks and slides will be prepared for microscopic study. On microscopic examination, the percentage of viable cells, fibrosis, and necrosis in each slide will be determined. Ultimately, the sum of the percentages of viable cells in each slide will be divided by the number of slides evaluated. Based on this calculation, the mean value (as a percentage) of the viable cells that are present in the surgical specimen will be calculated.

## Statistical Analysis

SPSS version 18.0 (IBM Corp) will be used for all calculations. The variables and clinical outcomes of the study will be descriptive and will be determined based on simple frequencies

of the variables themselves and the outcomes. McNemar tests will be used for paired categorical variables, and chi-square or Fisher exact tests will be used for unpaired categorical variables.

Measures of central tendency (mean and median) and variability (variance and standard deviation) will be used to describe numerical variables, whereas frequency distribution will be used for categorical variables. Mean and median follow-up times will be calculated from the date of the first cycle of chemotherapy until the date of the last consultation, loss to follow-up, or death. The level of significance for the statistical tests will be 5% ($P$<.05). Survival calculations and survival curves will be generated by the Kaplan-Meier method (Mantel-Cox) and log-rank test.

## Endpoints

The primary endpoints regard disease-specific survival and will be measured by the evaluation of local and distant disease-free survival after neoadjuvant treatment. Secondary endpoints are wound complication rates, amputation rates, and chemotherapy toxicity. We also will record the necrosis or viable cell rates after the schema and try to correlate with survival.

## Results

Patients have been recruited since February 2015, and recruitment is expected to be finished by the end of 2018. We are trying to change this protocol to a multicenter study in order to have 70 patients, based on the sample size calculation.

After the enrollment of the first 20 patients, an interim analysis is planned that focuses on side effects. The follow-up period will be at least 3 years after treatment, and it will include metastatic patients depending on the early results.

The main hypothesis is that the addition of hypofractionated RT can increase the necrosis rate, and we expect to have a higher rate of complete pathological response than in our previous 16%

(data not shown), that was achieved using only chemotherapy. Whether this mechanism is related to survival remains unclear.

## Discussion

The prognosis of patients with high-grade STS remains poor, primarily due to relapses at distant sites [3]. Because STSs are rare, cases in most studies are separated into high-grade and low-grade tumors. This classification guides the therapy in most patients, although other factors such as tumor size and depth also correlate with relapse and death [1]. Tumor severity is another predictor of the response to cytotoxic therapies, wherein better response rates are observed with high-grade tumors. Thus, chemotherapy remains warranted for patients with high-grade tumors, irrespective of histological type, although some of them might respond differently to specific drugs [10,11].

Neoadjuvant chemotherapy,despite being a nonstandard treatment, can theoretically facilitate tumor resection with adequate margins and combat micrometastatic disease early and allow in vivo verification of the clinical or pathological response to chemotherapy after surgery. The pathological response that is induced by the treatment and the subsequent effects on survival have been the subjects of many studies [12-14], such as Gomez et al [15]. This group performed a retrospective study of patients with extremity high-grade sarcomas who underwent neoadjuvant treatment with RT and chemotherapy. Local disease-free survival and OS were significantly better in patients who exhibited more than 95% necrosis in the surgical specimen. The addition of ifosfamide to the regimen increased the percentage of patients with ≥95% necrosis from 13% to 48%, improving survival rates [16].

We used the standardized RECIST criteria [5] to evaluate the clinical response to preoperative treatment. The main limitation of this method is that it is one-dimensional with respect to the assessment of the primary lesion, because shrinkage of the tumor might be absent, but we believe that it is simple to implement and interpret. Consequently, the RECIST criteria remain widely used in measuring the clinical response to treatment for solid tumors [17].

Our previous results showed a wound complication rate (rWC) of nearly 42% using conventional chemotherapy/RT preoperatively, indicating that approximately 70% of patients failed to receive or were delayed in receiving adjuvant chemotherapy. Thus, in 2005, we began a new prospective phase 2 study using preoperative chemotherapy and relegating RT to the adjuvant scenario to reduce the surgical rWC. It was imperative to evaluate whether this preoperative chemotherapy regimen lowered the rWC without altering local control or amputation rates. Our group proposed that the action of systemic chemotherapy and its effect on the tumor, as a neoadjuvant treatment, be examined measuring the pathological response based on the quantification of necrosis, fibrosis, and the percentage of viable cells in surgical specimens.

From April 2005 to July 2012, 48 patients with high-grade extremity STSs were assessed; the median follow-up time was 40 months. The OS rates for nonmetastatic patients were 86.3% and 74.1% at 3 and 5 years, respectively, with an rWC of 19.5%.

The analysis of surgical specimens showed that 6 patients (15%) had 5% (or less) viable cells in the sample, for whom the estimated OS and relapse-free survival (RFS) at 5 years were 100%. With a cutoff of 30% or less, 15 patients (37.5%) had an RFS of 82% and an OS of 90.9%.

Despite the favorable results with regard to avoiding the conventional preoperative RT scheme, the use of neoadjuvant chemotherapy alone has not effected better outcomes and subjects patients to higher doses due to larger fields of radiation postoperatively, correlating with late functional complications such as fibrosis and joint limitations. A different RT modality might solve or minimize this problem.

Hypofractionated treatment has comparable efficacy and safety as conventional fractionation in other solid tumors, such as those of the breast, prostate, and rectum. The usual dose for neoadjuvant RT in sarcomas is 50 Gy/25 fractions of 2 Gy. Radiobiology studies have shown that the sarcoma alpha/beta relationship is less than 10 Gy, which favors hypofractionated treatment [18]. Despite chemotherapy sometime being used concomitantly with RT, there is no standard treatment for hypofractionated RT. Ryan et al [19] prospectively treated 25 patients with hypofractionated RT (28 Gy/8 fractions) concomitant with chemotherapy with epirubicin and ifosfamide (3 cycles each pre- and postoperatively). This group reported high rates of hematological toxicity, with 64% of patients completing all chemotherapy cycles. Overall and disease-free survival was 84% and 62%, respectively.

More recently, a prospective study reported the results on 272 patients who were treated with an RT regimen that was similar to that in our study, with 25 Gy/5 fractions followed by immediate surgery (3 to 7 days after the end of RT) [20]. Some patients (22%) also underwent neoadjuvant chemotherapy. The OS rate at 3 years was 72%, with 42% of patients experiencing some acute toxicity and 7% requiring surgical intervention. The authors concluded that hypofractionated treatment generates similar results in terms of local control and OS compared with conventional treatment, with acceptable toxicity.

A criticism of chemotherapy for sarcomas is that histological types respond differently to several types of drugs. According to a multivariate analysis by the Italian and Spanish Sarcoma Group [21], histological subtype was associated with a difference in survival after chemotherapy, and patients with leiomyosarcoma had the worst prognosis. However, most studies claim that chemotherapy with doxorubicin must be maintained for most tumors of this type [22].

In this study, we added chemotherapy preoperatively to combat micrometastatic disease early and identify patients who were good responders (ie, harboring fewer than 30% viable cells in surgical specimens). For these responders who have received chemotherapy and hypofractionated RT, we offer 3 additional cycles of chemotherapy as an adjuvant treatment, avoiding chemotherapy for patients who theoretically do not need it.

Our main concerns are related to recruitment issues. Because STS is a rare condition, attaining the calculated sample size will be difficult. Most patients with high-grade STS are metastatic at the diagnosis, which is an exclusion criterion. However, as

a cancer center, our institution receives patients from throughout Brazil, despite the lack of a specific government program.

Hypofractionated RT plus adjuvant chemotherapy can increase the pathological response and improve the outcomes of select patients, avoiding unnecessary chemotherapy and instead offering more chemotherapy to good responders. This approach is a rational use of adjuvant chemotherapy, despite the many histological types of sarcoma and limited chemotherapy schemes for sarcomas. We are confident that adding hypofractionated RT in the neoadjuvant scenario can shorten treatment times and lower costs without increasing the rWC compared with conventional RT.

## Conflicts of Interest

None declared.

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## Abbreviations

**CT:** computed tomography
**MRI:** magnetic resonance imaging
**OS:** overall survival
**RECIST:** Response Evaluation Criteria in Solid Tumors
**RFS:** relapse-free survival
**RT:** radiotherapy
**rWC:** wound complication rate
**STS:** soft tissue sarcoma

Original Paper

# Meeting the Needs of Mothers During the Postpartum Period: Using Co-Creation Workshops to Find Technological Solutions

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## Abstract

**Background:** The postnatal period is associated with many new needs for mothers.

**Objective:** The aim of this study was to find technological solutions that meet the needs of mothers during the year following childbirth.

**Methods:** Two co-creation workshops were undertaken with parents and professionals. The aim of the first workshop was to create a list of all the criteria the proposed solution would have to address to meet the needs of mothers after childbirth. The aim of the second workshop was to create solutions in response to the criteria selected during the first workshop.

**Results:** Parents and health professionals want solutions that include empathy (ie, to help fight against the feelings of abnormality and loneliness), that help mothers in daily life, that are personalized and adapted to different situations, that are educational, and that assures some continuity in their contact with health professionals. In practice, we found that parents and professionals think the solution should be accessible to everyone and available at all times. To address these criteria, technology experts proposed different solutions, such as a forum dedicated to the postpartum period that is supervised by professionals, a centralized website, a system of videoconferencing, an online exchange group, a "gift voucher" system, a virtual reality app, or a companion robot.

**Conclusions:** The human component seems to be very important during the postnatal period. Nevertheless, technology could be a great ally in helping mothers during the postpartum period. Technology can help reliably inform parents and may also give them the right tools to find supportive people. However, these technologies should be tested in clinical trials.

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## Introduction

Pregnancy and childbirth are two critical stages in a woman's life. The postnatal period is associated with many new needs for mothers, and several studies have demonstrated a great need for information after childbirth [1,2]. Many mothers search for reliable and realistic information and want to be better prepared for the realities of motherhood (especially women having their

first baby) [3,4]. Many also have anxieties and fears around early parenting and their changing roles [5]. Women are generally concerned about the safety of their new baby, and they lack self-confidence as new mothers and in their own ability to care for their baby. Women need to be surrounded by those who will emotionally support them in this transition to parenthood [6,7].

A previous unpublished study in our department (Department of Public Health, Epidemiology and Health Economics, Liège, Belgium) has evaluated the needs of mothers in the year after childbirth and listed them in four categories: (1) a need for information (women seemed to require medical, practical, and administrative information); (2) a need for psychological support (women want to be surrounded, reassured, and understood in this difficult period of life); (3) a need to share experiences (women liked having the possibility of discussing issues with other mothers, especially to find out if what they are experiencing is normal); and (4) a need for practical and material support (women remained preoccupied by housework and appreciated help with household chores, ironing, etc).

Today, the Internet and new technologies are a constant feature in daily life [8]. For example, in 2015, 75.0% of Belgian people (vs 61.7% in 2014) said that they used the Internet at home to get information [9]. Be it for private or professional purposes, connecting to the Internet to communicate or seek information is now part of our daily life. Innovations in mobile and electronic health care are revolutionizing the involvement of both patients and doctors in the modern health care system, creating new opportunities for patients to participate actively in monitoring and improving their own health, and for doctors to supervise their patients' health. During the perinatal period, (future) mothers are turning more frequently to the Internet to satisfy their need for information [10,11] but also to help them make decisions [12-14]. In addition, studies have already demonstrated the effectiveness of interventions based on new technologies during the postpartum period (eg, an Internet-based intervention enhancing Finnish parents' parenting satisfaction and parenting self-efficacy [15], telemedicine after early postnatal discharge [16], and videoconferencing as a support in early discharge after childbirth [17]). Therefore, following a previous exploration of mothers' needs during the postpartum period, the aim of this study was to find one or more adapted technological solutions to meet the needs of mothers during the year following childbirth.

## Methods

To find technological solutions that meet mothers' needs after childbirth, two co-creation workshops were organized. The study was approved by the Comité d'Ethique Hospitalo-Facultaire Universitaire de Liège, Belgium (#2015/48).

### Step 1: Make a List of Criteria for Proposed Solutions

The aim of the first co-created workshop was to bring parents and health professionals together to list criteria that proposed solutions must meet to address the needs of mothers during the year following childbirth. We chose to focus on the year

following childbirth as similar to the perinatal period, which is defined as from conception to 1 year after birth [18,19]. In addition, postnatal depression is common during this period. Its incidence does not necessarily decline over the first year following childbirth, and it is associated with physical symptoms, especially tiredness or even exhaustion [20,21].

Our inclusion criteria were women or men, who had a child under 2 years and who agreed to participate in the study; and any professionals involved in the postnatal period (ie, gynecologists, midwives, pediatricians, general practitioners, psychologists, medical-social workers of the Office de la Naissance et de l'Enfance [Belgian Office of Birth and Childhood], and nursery nurses). We chose to include fathers because they are well placed to give information about their wife's experience. In addition, our previous study, which evaluated the needs of mothers after childbirth, showed that fathers play a central role in the psychological well-being of their partner and that health professionals consider fathers as real partners in care. Exclusion criteria for mothers and fathers were the following: multiple gestation pregnancy, fetal death in utero, very premature childbirth (<34 weeks of gestation), and fetal pathologies. There were no exclusion criteria for professionals.

The recruitment of participants was mainly done through social networks: Facebook and the websites of the Wallonia e-health Living Lab (WeLL) and of the AlterNative (platform for a respected birth). Individuals who had already been in contact with our research team and who matched the inclusion criteria were contacted to participate in these focus groups. Professionals were also contacted based on their specialty. During the first workshop, 12 participants were present: 3 midwives (one of them was also a young mother), 1 gynecologist, 1 psychologist, 1 medical-social worker from Office de la Naissance et de l'Enfance, 5 mothers, and 1 father. Two work groups were formed.

The workshop was held at WeLL on December 16, 2015. The workshop protocols were drafted by the research team in collaboration with a group of experts for the co-created study design at WeLL. First, participants were asked to introduce themselves to each other, and the search topic (including the four needs previously identified) was presented. Participants were given the opportunity to ask questions about the study and their involvement before the session started. Then, two work groups were formed. Three of the four needs previously identified were explored in this first workshop: the need for information, psychological support, and shared experiences.

Exploration of the need for information was done by the two work groups. It consisted of listing all the criteria that participants liked (for the first group) and did not like (for the second group) in the actual dissemination of information system. To do this, participants had to come up with "pros" letters ("I am completely in love with you because …") for the first group, and "cons" letters ("I do not love you because …") for the second group.

Exploration of the need for psychological support was made with a mind map with the first group only. The mind map consisted of mapping participants' thoughts on a large sheet of

paper. Participants were asked to think about the terms that mothers had linked with psychological support, namely, "surrounded," "understood," and "reassured". Those three words were written on the sheet at the start. Participants could then write down the first word they thought of when reading one of the three words above. Participants could then bounce off their own words or words written by others.

Finally, the need to share experiences was explored by the Chinese portrait method. The principle of the Chinese portrait method is to respond to the question "If I were …, I would be …". Participants had to respond to the following questions: "If I were a dish, an exotic pet, a song, an object, a perfume, a town, an actor, I would be …". After each response, participants had to explain why they chose their response.

The need for practical and material support was not explored because there are very few possible technological solutions to meet this need.

Each stage of the workshop highlighted some criteria required for the development of potential solutions. Some illustrative examples of the co-creative methods used in the first workshop and how we extracted the most important criteria required for the development of potential solutions from each method are presented in Table 1. After each step, participants had to choose four criteria that they found essential for the development of potential solutions. Therefore, each participant had to place four stickers next to their most important criteria: the more important the criteria, the more stickers there were.

**Table 1.** Illustrative examples of the co-creative methods used in the first workshop of the study.

| Need | Exploration methods | Examples from the first co-created workshop[a] |
|---|---|---|
| Need for information | Pros (I am completely in love with you because …) | … You understand that our demand evolves with the development of our child and you can even anticipate it. |
| | | … You are free and sexy, you attract me and you are available at all times. |
| | | … You allow me to be consistent with myself and you comfort me on the legitimacy of my requests which are common to other mothers. |
| | Cons (I do not love you because …) | … You are too informative and not enough educational: I am drowning and I feel alone! |
| | | … You're always arriving at the wrong time; or too early or too late! |
| | | … You've maintained the myth of the ideal motherhood for too long and you lack realism, liar! Keep your false advertising for you! |
| Need for psychological support | Mind map (surrounded) | Listening |
| | | Be helped |
| | | Heat |
| | | Without prejudice |
| | | Presence[a]: if needed[a]; on demand[a]; to be heard |
| | | Non-judgment |
| | | Don't forget yourself |
| | | Find time for yourself |
| | | To be understood/supported in their own experience |
| Need to share experience | Chinese portrait | "If I were a dish, I would be Spaghetti or Pizza because they are easy to prepare and shared in community, they require few dishes, they are not expensive ... This helps to lighten the daily life." |
| | | "If I were an exotic pet, I would be a penguin because penguins shuffle in circles, staying tightly packed to keep everyone of the huddle, warm (comfort, protection, and the weakest in the middle). This could inspire us in the care of mothers." |

[a]The most important criteria required for the development of potential solutions.

## Step 2: Propose Solutions to Meet Participants' Criteria

The aim of the second co-created workshop was to bring together technology experts (technology professionals and enthusiasts) to devise solutions in response to the different criteria selected during the first workshop. All technology professionals or people with a particular interest in technology who agreed to participate were eligible for this study. There were no exclusion criteria.

The recruitment of participants was mainly done through social networks (Facebook and the WeLL and AlterNative websites) and by word of mouth. The technology experts, who already worked with WeLL, were contacted to participate in the second workshop. The second workshop was composed of 8 technology experts (5 men and 3 women, all parents). Two work groups were then formed.

The second workshop was also held on the WeLL premises on February 22, 2016. The workshop protocols were drafted by the research team in collaboration with WeLL. First, participants were asked to introduce themselves to each other, and two work groups were formed. The research problem (the needs of mothers during the postpartum period) was presented, and participants were given the opportunity to ask questions about the study and their involvement before the session started. The experts discussed and shared their understanding of the context. Then, all the criteria found to be essential for parents and professionals in the previous step were presented to the experts. The experts had to brainstorm many technological solutions for addressing the needs of mothers and to match at least one of the criterion required for the development of potential solutions (=co-creating stage). All solutions using technology, in any manner whatsoever, were welcomed. It was not necessary to have revolutionary ideas but to have, above all, ideas that could meet the criteria previously highlighted. Finally, role-playing exercises (situations that mothers may encounter in the postpartum period) were presented to the experts, who then explained how the solutions that they brainstormed could help mothers in those situations. The role-playing exercises are presented in Table 2.

### Analyses

With the agreement of the participants, the two workshops were audio-recorded using a Dictaphone and then transcribed verbatim. To ensure confidentiality, all information allowing identification was removed from the transcripts. Management of the data and analyses were made manually. Transcripts were systematically coded by topic and classified into groups of similar issues. To help identify the different themes, handwritten notes were made during the workshops and analyzed afterwards. The thematic content analysis used the analytical method of thematic framework (developed by the National Centre for Social Research [22]). This systematic data extraction created a thematic network, which illustrated the relationship between the themes addressed. In the results section, some direct quotes, which were extracted from the workshops, are provided to illustrate each theme.

## *Results*

A diagram illustrating the progression from the first workshop comments to the second workshop solutions is presented in Figure 1.

### Step 1: Make a List of Criteria for Proposed Solutions

The criteria that participants selected during the first workshop are presented in Table 3. The number of stickers assigned to the different criteria is also presented (shown as bullets). The number of stickers demonstrated the importance of the criteria for parents and professionals: the more a criterion had stickers, the more it was considered important.

In addition, several times during the first workshop, parents and professionals insisted on the fact that the fathers' involvement was beneficial to the development of solutions because they also experience the important transition to fatherhood.

**Table 2.** Role-playing exercises used during the second workshop.

| Scenario | Case | | |
|---|---|---|---|
| | 1: Lea, 22 years old, living with her partner, gave birth to her first child 3 weeks ago. She is a nurse in a nursing home and does a lot of sport. | 2: Marie, 34 years old, is married and has 2 children including one of 6 years. She gave birth 6 weeks ago. She works as an employee in a pharmaceutical company. She feels alone during her maternity leave. | 3: Melissa, 30 years old, living with her partner, gave birth 2.5 months ago. She works as a waitress in a restaurant chain. |
| 1 | She would like to share her experience to see if other women are in the same situation and see if what she is experiencing is normal. | | |
| 2 | She needs information about breastfeeding because her baby does not drink enough. | | |
| 3 | She feels overwhelmed by all the tasks of daily life and she is no longer able to take some time for herself. | | |
| 4 | She feels that her husband is not paying enough attention to her and that he is not invested enough since the birth of the baby. | | |
| 5 | She finds that the opinions of the different professionals she consults are different (sometimes even opposed). She tries to apply exactly everything they said (changing at each consultation) and therefore, she feels completely lost. | | |
| 6 | She must start working in 3 weeks but has not found a childcare system yet. She is panicking about the idea of leaving her baby to someone. | | |
| 7 | Her gynecologist advised her to do postnatal physiotherapy, but she does not know any physiotherapist in this field. Her friends have no children yet and do not know how to help her. | | |

**Figure 1.** Diagram of the progression from the workshop 1 comments to the workshop 2 solutions.
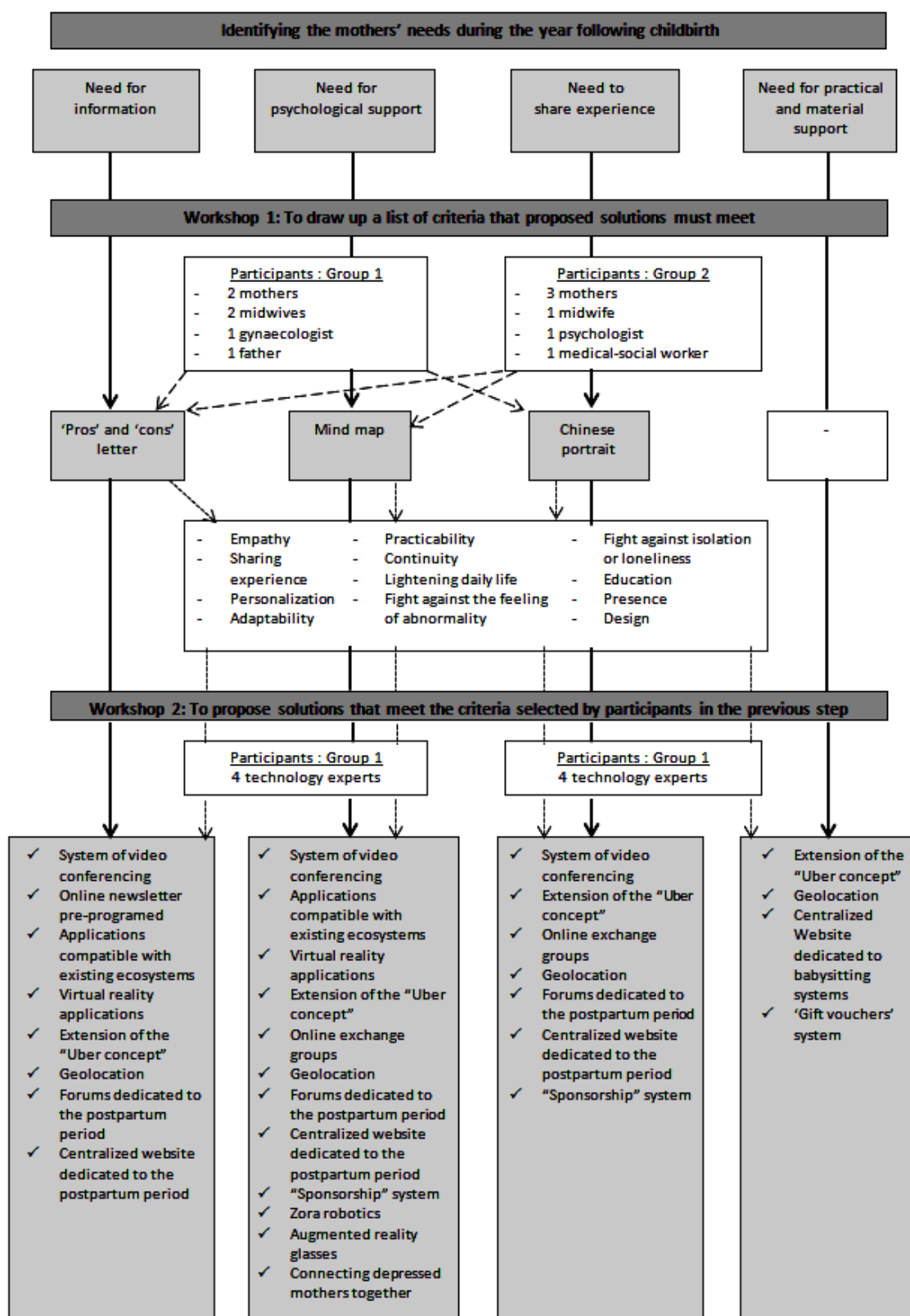
**Table 3.** List of criteria that proposed solution must meet.

| Criteria | Importance |
| --- | --- |
| **Empathy** | |
| Be accepted without judgement in distress | ●●●●●●●● (8) |
| Empathy, dramatization, lightness | ●●●●●●● (7) |
| Comfort into "my normality," "legitimacy of my requests" | ●●●●● (5) |
| No judgement | ● (1) |
| Restore confidence in myself | ● (1) |
| Be reassured | ● (1) |
| Be understood | ● (1) |
| **Sharing experience / fight against feelings of abnormality** | |
| Sharing experiences of mothers | ●●●●●● (6) |
| Comfort into "my normality," "legitimacy of my requests" | ●●●●● (5) |
| Counterpoint to the collective ideal | ●● (2) |
| Self-mockery | ● (1) |
| **Presence / fight against isolation or loneliness** | |
| Presence | ●●●● (4) |
| To anticipate needs and meet them | ●●●● (4) |
| Nonintrusive | ●● (2) |
| Be surrounded | ● (1) |
| The weakest people in the middle | ● (1) |
| <3 (= heart, love) | ● (1) |
| **Lightening daily life** | |
| Lightening daily life | ●●●●●● (6) |
| To let go | ●●●●●● (6) |
| Do not forget yourself | ●●●●● (5) |
| Loophole, wellness, serenity | ●●● (3) |
| Inspiring | ●● (2) |
| A change of scenery | ● (1) |
| **Personalization / adaptability** | |
| Costume made | ●●●●●●●●● (9) |
| Home visits | ●●●●● (5) |
| We interpret it as we want | ●●●● (4) |
| Do not forget the father: male perspective too | ●●● (3) |
| You adapt yourself depending on me | ● (1) |
| **Practicability** | |
| Available at all times | ●●●●●● (6) |
| Attractive and accessible | ●● (2) |
| Free | ● (1) |
| Timeliness of responses | ● (1) |
| Modern (online) and reliable | ● (1) |
| **Education** | |
| If needed | ●●●● (4) |
| Identify times when a solution is needed | ● (1) |

| Criteria | Importance |
|---|---|
| Identification of unexpressed needs | ● (1) |
| On demand | ● (1) |
| **Continuity** | |
| Contact from the beginning (since the beginning of pregnancy) | ●● (2) |
| **Design** | |
| Informal format, flexible | ●●●●●● (7) |
| With multiple entry points (eg, time route, keywords, experiences) | ●●●●● (5) |
| Quiet: "we can take the time" | ●●●● (4) |
| Language adapted at a social level | ●●● (3) |
| Comprehension and interpretation of the questions | ●● (2) |
| Scalable request | ●● (2) |
| Pedagogy decision support, enlightened information | ● (1) |
| Colored | ● (1) |

## Step 2: Propose Solutions to Meet Participants' Criteria

Several times during the second step of this study, the two work groups both underscored the importance of focusing not only on the technological side during the postnatal period but also on the human side.

> *To fight against isolation, we need someone, we need a presence; something more real than technological.*

> *Technology could help many new mothers ... For example, it would be interesting to have a tracking system to find services or information nearby where you live (eg, research by postal code).*

> *I do not see how we could assist daily life with technology. Technology will only provide information on how to turn to a supportive person; but will always go through a real person. It would be nice, to be able to sound the alarm ...*

Notwithstanding, many proposed solutions were debated during this step and are discussed as part of the results. These solutions are presented in Table 4.

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**Table 4.** Solutions discussed during the second workshop by the technology experts.

| Proposed solutions | Explanations of the solutions given by the experts |
|---|---|
| Videoconferencing system | "Women expressed a great need for information; thus, the goal of this solution would be to provide the most interactive and comprehensive responses. This approach would consist of filming experts speaking on a topic. This solution could provide access to tutorials, testimony, or to a 'call center' run by midwives (eg, videophone) and could also then meet the needs of shared experiences and psychological support. Indeed, midwives are able to say, thanks to their great experience with others mothers, if what a mother lives is normal or not." |
| Online newsletter preprogrammed | "Some newsletters in paper form that mothers can receive by post already exist. These newsletters provide information corresponding to child development. The experts suggested transforming these 'paper newsletters' into 'IT newsletters'. This concept would lead to a reduction in the cost of paper and provide the opportunity to create alerts corresponding with the baby's age. The goal of this solution is to anticipate mothers' questions." |
| Apps compatible with existing ecosystems (eg, ) | "These applications consist of integrating data from a sensor that could be programmed to respond to the needs of mothers. For example, sensors could be used to study the baby's sleep quality, the temperature of the baby's room or the walk of the mother. Warning messages may also be sent when a mother walks too much or too little. Information messages could also be transmitted directly to the mother to reassure her and to decrease the level of stress caused by the arrival of a child." |
| Virtual reality apps (eg, serious gaming) | "The experts suggested establishing some virtual scenarios to prepare mothers to learn how to become a mother (eg, deal virtually with life situations with a baby). Nevertheless, they felt that it was quite difficult to implement this solution because it would suggest an evaluation of mothers, and no one was qualified to do so. Mothers might feel judged or would compare themselves with other mothers." |
| Extension of the Uber concept | "Uber is an intermediation platform linking users and service providers. This platform allows a request to a specialist when needed. The experts in our study believed that such a platform could connect mothers with midwives, physiotherapists, osteopaths, housekeepers, babysitters, etc." |
| Online exchange groups (eg, Weightwatchers and Alcoholics Anonymous) | "Our previous study, evaluating the needs of mothers in the year following childbirth, showed that women are not really satisfied by forums or Facebook groups especially because there are a lot of French or Canadian mothers on these groups who live in a different environment with a different culture. Women were looking for mothers living in their area, who gave birth in the same hospital or who have the same doctor. Therefore, the experts came up with the idea of some online exchange groups where women could find mothers from their neighborhood. These online exchange groups would be created by the hospital or by a health professional to try to bring together mothers by region. With these systems, mothers would know that they are not alone." |
| Geolocation | "Finding people close to home was deemed very interesting. Indeed, on the Internet, mothers can find people from all over (from different cities or even different countries). Geolocation would provide the possibility of finding a professional near home or to organize meetings with mothers in one region."<br><br>"We lose a crazy amount of time trying to find the right people." (A technology expert who explained her experience as a mother.) |
| Forums dedicated to the postpartum period, supervised by professionals | "Our previous study showed that many mothers' forums already exist and are largely used by a lot of mothers, but they do not find them really reliable. These forums must be supervised by professionals if we want to make sure that the information given is of quality. Such geolocation-associated forums could better inform mothers with infants about meetings, which are often very poorly advertised." |

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| Proposed solutions | Explanations of the solutions given by the experts |
|---|---|
| Centralized website dedicated to the postpartum period | "Our experts imagined a website that could address most of the questions mothers ask themselves (eg, give them information they need such as details about places where they can go with their baby). Such a website could target both mothers and fathers, meet the need for information, and also help parents find the people or professionals they need. The experts imagined that professionals could advise this website to the mothers they care for. They saw this website as intermediary middle for carers or directly for mothers during the postpartum period, but not as a substitute for professionals." |
| "Sponsorship" system | "Every mother would have a 'godmother' assigned. The principle of this system would be to sponsor each young mother with a more experienced mother from the same city. The two mothers could chat online or meet (based on their desire/situation). Our experts suggested a non-profit association, which would be the first point of contact for every young mother who needs a referral or to talk with someone experienced." |
| Centralized website dedicated to babysitting systems | "Finding a babysitting solution induces stress for many mothers. To avoid having to phone each facility and to be registered on all waiting lists, the experts envisioned a website that mothers could visit to see a list of available spots at each day nursery." |
| Zora robotics | "Currently designed to support the elderly, such a robot could accompany mothers to fight loneliness and to provide them some psychological support." |
| Augmented reality glasses | "Relaxation programs through virtual reality or augmented reality allow the mother to go into states of 'total de-stress' (eg, by putting on glasses, the mother finds herself at the sea, mountains, or wherever she wants to go for 20 minutes a day). These glasses can be rented, and this system would help meet the need to escape." |
| "Gift vouchers" system | "Although the need for practical and material support was not explored, the idea of a 'gift voucher' system was outlined during the workshop. The experts thought about a system that already exists in Canada. This system invites family or friends of the parents to offer them some help with housework (eg, ironing, cooking, household chores). For example, a friend could offer two hours of ironing to the new mothers instead of a new cuddly toy." |
| Miscellaneous | The experts also spoke about a cradle that automatically rocks the baby (which already exists) or connecting together mothers, who are living with postnatal depression. |

## Discussion

### Principal Findings

The aim of this study was to find technological solutions that would meet the needs of mothers after childbirth. Parents and health professionals want solutions that provide empathy: mothers need people to understand that the postpartum period is a difficult period of life. Women also need solutions that help fight against feelings of abnormality, which many mothers feel: they want to know if other mothers experience similar situations. Fighting loneliness is essential for developing such solutions: many mothers feel alone during the postpartum period and want potential solutions to find resources to help fight this feeling. The ideal solution would help mothers in daily life: they want the solution to help them find some serenity to get through the postpartum period. Solutions should be personalized and adapted to different situations. They also want the solution to be educational and respond to the questions of the mothers. All of these criteria match the need for information, shared experiences, and psychological support already demonstrated [1-4,6,7]. Mothers also seem to need some continuity in their

contact with health professionals; they would like to address the same person from the beginning of pregnancy to the end of the postpartum period. This need for continuity has already been shown in several studies [23-26]. In practice, parents and professionals think that the solutions should be accessible to everyone and be available at all times. The participants in the first workshop also proposed that solutions also include fathers. It would be very interesting to do this work again with fathers, but doing so did not meet the objectives of the study.

In regard to these criteria, some technology experts tried to propose potential solutions for helping parents and health professionals. Some of the solutions proposed seem difficult to implement in real life; for example, the virtual reality app or companion robots. Nevertheless, some solutions could meet the needs of mothers during the postpartum period. There were many promising ideas during the second workshop, such as a forum dedicated to the postpartum period supervised by professionals, a system of videoconferencing, an online exchange group, a sponsorship system, or a centralized website dedicated to babysitting systems. The system of videoconferencing already showed some beneficial results in

cases of early discharge after childbirth. Indeed, a study [17] demonstrated that using videoconferencing can facilitate a meeting that makes it possible for new parents to be guided by the midwife in their transition into parenthood. In addition, this system was also appreciated by the midwives who were using it [27]. They judged this system easy to handle, useful for making assessments, valuable, and functional.

Some solutions could also be bundled together. Indeed, we can imagine a centralized website with many functions. Such a website could contain a forum dedicated to the postpartum period supervised by professionals. Health professionals could give interactive responses to mothers' questions through a system of videoconferencing. The website could provide the possibility of creating an online exchange group, whereby mothers or parents could meet each other. The exchange group could facilitate the possibility of a mother having a "godmother" with maternity experience, who could become a referent for her. The website could also link to a centralized website dedicated to babysitting networks to reduce the stress induced by the lack of places in day nurseries. An extension of the Uber concept could help mothers find the right people/professionals more easily. A website has already been tested to improve parenting satisfaction and self-efficacy during the postpartum period [15]. Nevertheless, no intervention effects were found: all the parents, having access to the website or not, improved their satisfaction and self-efficacy. The authors concluded that more research is needed in this field.

Another interesting idea is the geolocation system. Indeed, parents seem to be struggling to easily find the people they need. Experts spoke about a geolocation system to find a professional near home or to organize meetings with mothers in the same region. Such a system could also help parents find activities to do with the baby, service vouchers (ironing, housework, etc), institutions, or even shops for children. Some geolocation strategies are already being used for research and public health surveillance and management [28], even reducing urgent response times [29] in some regions. We can imagine using this method not only to meet the needs of the parents during the postpartum period but also in many other situations.

Finally, although the purpose of the workshop was to focus on the technological nature of the proposed solutions, the human component remains important not only for parents and health professionals but also for the technology experts. The transition to motherhood is a potentially vulnerable time for mothers' mental health [20,21,30,31]. Women have fears and anxieties around early motherhood and their changing role [5]. When mothers understand their babies and are able to respond to their baby's needs, they experience some feeling of security about their new role as mothers [32]. Mothers consider that the actual presence of professional care providers [5] and the family and friends' support [32,33] could help them feel more secure during

the postpartum period. Indeed, women are more likely to experience postnatal depression or anxiety if they feel they have low social support [34,35]. The postpartum period is therefore a difficult period of life, in which mothers (and fathers) have to be surrounded by support [7], and the human component cannot be ignored: a birth is above all a human experience. However, technology can help parents find reliable information, find the people they need (eg, professionals, godmothers, friends), and also bring them some comfort. For example, Danbjørg et al [36] developed an app for Parents Being Discharged Early Postnatally. They found that through the app, parents felt a sense of comfort, which is essential to start living parenthood positively. Additionally, another study [37] insists that technology is imperative for educating mothers (eg, credible electronic linkages, mobile phone technology, videos and access to provider and hospital websites). This access to information must be guided by care providers. By addressing the needs of mothers, women may be better able to experience parenthood with confidence because they would be better prepared and would *feel* better prepared.

## Strengths and Limitations

This study can potentially add to the knowledge that technological solutions may meet the needs of mothers during the postpartum period. This study explored some original co-creating methods that were drafted and exploited in collaboration with a group of experts for the co-created study design. The methods were therefore rigorous and strong. In addition, the participants came from all fields we wanted to represent within the focus groups.

However, our study also presented some potential biases. First, the sample was composed of voluntary participants, which can limit the extrapolation of the results to all mothers in Belgium. Second, having both parents and professionals together in the first workshop could represent a bias. Indeed, parents might not have felt comfortable raising certain issues or disclosing certain information while health care professionals were in the room. Nevertheless, none of the participants knew each other or even had met before and exchanges between parents and professionals were very relaxed during the whole workshop.

## Conclusions

Although the human and psychological components remain very important in the postpartum period, many interesting technological solutions can be used to address the needs of mothers. Technology could be a great ally for meeting the needs of mothers during the postpartum period. The technology could help to reliably inform parents, boost their security senses, and give them the tools to find the right people. Nevertheless, these technologies must be tested among mothers' cohorts in clinical trials.

## Authors' Contributions

JS, OB, PE, LV, AA, and JYR conceived the study and developed the hypotheses. JS, LV, AA, and MO conceived the workshop protocols. JS, LV, AA, and MO were responsible for data collection. JS was responsible for data management and data analyses. JS wrote the drafts of the article under the supervision of OB and PE. All authors have read, reviewed, and approved the final manuscript.

## Conflicts of Interest

None declared.

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## Abbreviations

**WeLL:** Wallonia e-health Living Lab

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<u>Original Paper</u>

# PatientVOICE: Development of a Preparatory, Pre-Chemotherapy Online Communication Tool for Older Patients With Cancer

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## Abstract

**Background:** Good communication around cancer treatment is essential in helping patients cope with their disease and related care, especially when this information is tailored to one's needs. Despite its importance, communication is often complex, in particular in older patients (aged 65 years or older). In addition to the age-related deterioration in information and memory processing older patients experience, communication is also complicated by their required yet often unmet role of being an active, participatory patient. Older patients rarely express their informational needs and their contributions to consultations are often limited. Therefore, older patients with cancer need to be prepared to participate more actively in their care and treatment.

**Objective:** The objective of this paper was to report the development of PatientVOICE, an online, preparatory tool with audio facility aimed to enhance the participation of older patients during educational nursing encounters preceding chemotherapy and to improve their information recall.

**Methods:** PatientVOICE was developed by applying the following 6 steps of the intervention mapping framework that involved both patients and nurses: (1) needs assessment, (2) specifying determinants and change objectives, (3) reviewing and selecting theoretical methods and practical strategies, (4) developing intervention components, (5) designing adoption and implementation, and (6) making an evaluation plan.

**Results:** A careful execution of these consecutive steps resulted in the ready-to-use preparatory website. PatientVOICE provides pre-visit information about chemotherapy (ie, medical information, side effects, and recommendations of dealing with side effects), information about the educational nursing visit preceding chemotherapy (ie, aim, structure, and recommendations for preparation), techniques to improve patients' communication skills using a question prompt sheet (QPS) and video-modeling examples showing "best practices", and the opportunity to upload and listen back to an audio recording of a patient's own nursing visit.

**Conclusions:** The development process resulted in PatientVOICE, a multi-component online intervention targeted to older patients with cancer. PatientVOICE contains information about the treatment as well as information about the role of the patient during treatment. Using different methods (QPS and audio facility), we hope to support these patients during their treatment. In the future, the utility and usability of this complex intervention will be evaluated in a group of older patients who receive or have received chemotherapy.

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## Introduction

More than 60% of all cancer patients are aged 65 years and above and it is expected that this number will increase due to the aging population [1]. Older patients with cancer are confronted with complex information about treatments, like chemotherapy, that impose high demands on their emotional and cognitive abilities. Communicating with their healthcare provider is even more challenging due to older patients' deterioration in cognitive (eg, memory, information processing), psychological (eg, resilience), physical (eg, hearing problems, multimorbidity), and social (eg, network, activities) functioning [2,3]. Indeed, during educational nursing encounters preceding chemotherapy, older patients only actively reproduce (recall) less than one fourth of the recommendations given on handling side effects [4].

Effective communication surrounding cancer treatment is essential as this can support patients in coping with their disease, treatment, and side effects [4-7]. This is especially true when the provided information is tailored to the patient's informational needs [8]. Providing tailored information not only requires advanced communication skills of caregivers, but also asks for more active, informed, and participatory patients [9-11]. To date, the conversational contribution of patients with cancer, and older patients in particular, is rather limited [12-15]. Older patients rarely express their informational needs or preferences [15,16], perceive several barriers to actively participate during the consultation, and lack the skills needed to obtain relevant information [17]. Despite having different needs with respect to information provision than younger patients [5,15,18,19], they equally value discussing realistic expectations and information about dealing with their treatment options and the corresponding side effects in daily life [6]. Older patients, therefore, not only need to be supported during, but also in preparation and/or after their communication with care providers about their treatment. As elderly do not form a homogenous population, attention is warranted for "what works for whom."

To this purpose, we restructured educational nursing encounters preceding chemotherapy and developed a preparatory paper brochure for older patients in the oncology departments of several Dutch hospitals [7]. The brochure "Talking about chemotherapy" (in Dutch: "In gesprek over chemotherapie") contained information about the nursing encounter's aim and topics and a question prompt sheet (QPS). The QPS was a list of statements that a patient could indicate which topics he or she would like to talk about during the encounter. In comparison with a control group, intervention group nurses spoke more about realistic expectations, reduced the amount of information in concordance with the patients' needs, and their patients asked more questions [7]. Patients' information recall, however, hardly increased. One possible explanation for this was preparation, the counseling itself was not yet sufficiently tailored to their

information needs, or there is a limit to what one can remember from a consultation [20].

The Internet is an important source of information and support for both cancer patients and their relatives [21], including older cancer patients [22]. Older people increasingly use the Internet, with more than half of the elderly aged between 65 and 75 years using it daily [23]. Internet or computer use even appears to be more predictive for using (online) tools than age [3,24,25]. A recent study found that older cancer patients evaluated Web-based health information tools to be very useful and that they were willing to use these kinds of tools [26]. A literature review revealed that online health information tools seem promising to facilitate immediate, intermediate, and long-term outcomes in older patients, including clinical outcomes such as blood pressure, hemoglobin, and cholesterol levels [27]. Aspects such as the burden and availability of (older) end-users and financial means must be taken into account when designing online tools together with patients (co-creation) [28]. Other challenges to consider are the funding of active technology companies and the time it takes to process the results of shorter development cycles.

This paper describes the structured development of PatientVOICE, an elaborated, online version of the paper brochure "Talking about chemotherapy" where older patients with cancer can prepare themselves on the educational nursing encounter preceding chemotherapy. PatientVOICE was built around effective facilities (QPS, audio recordings, video modeling, and preparatory information) known to enhance patient engagement and information recall, and to tailoring nursing information to personal circumstances and the information and emotional needs of the elderly. The results of the evaluation of PatientVOICE will be reported in another paper.

## Methods

### The Intervention Mapping Framework

The 6 steps of the intervention mapping framework were followed to systematically develop PatientVOICE [29] (Table 1). The intervention mapping framework integrates input from the "target group" (ie, older patients) with theoretical and empirical evidence and largely overlaps with the framework of the Medical Research Council for developing complex interventions (ie, interventions with several interacting components) [30]. Intervention mapping describes a process consisting of the following 6 consecutive steps: (1) assessing needs of the target group to identify the problem, (2) specifying determinants and change objectives, (3) reviewing and selecting theoretical methods and practical strategies, (4) developing intervention components, (5) designing an adoption and implementation plan, and (6) making an evaluation plan [29]. Several electronic health (eHealth) programs have been developed using the intervention mapping framework [31-33].

**Table 1.** The intervention mapping framework applied to the development of PatientVOICE.

| Step(s) | Description | Task(s) |
|---|---|---|
| 1 | Needs assessment | Assessing patients' needs regarding the nursing encounter preceding chemotherapy and preparing for chemotherapy |
| | | Evaluation of the brochure "Talking about chemotherapy" |
| 2 and 3 | Specifying determinants, objectives, theoretical methods, and practical strategies | Specifying determinants and change objectives |
| | | Reviewing scientific literature to identify practical strategies and techniques |
| 4 | Intervention development | Development of the intervention prototype PatientVOICE |
| | | Usability testing by patients with cancer and the elderly using a think-aloud procedure |
| | | Judgment of the website by software experts according to 20 heuristics relevant for older Web users |
| | | Adaptation of the prototype on the basis of usability tests |
| 5 | Adoption and implementation plan | Invitation of hospitals for participation and to contribute to the development of PatientVOICE |
| | | Creating a support base for the intervention in hospitals |
| 6 | Evaluation plan | Describing the study design, procedure, and methods for the evaluation of the intervention |

## Step 1: Needs Assessment

The first step in the intervention mapping framework is the needs assessment. Assessing patients' needs allows for the identification of important topics and preferences that should be integrated into the online tool PatientVOICE. For this needs assessment, we invited oncology nurses and patients treated with chemotherapy from 3 hospitals that consented to participate in this study.

Older patients (65 years or older) that recently had an educational nursing encounter preceding chemotherapy were invited by their oncology nurse for an interview to evaluate the "Talking about chemotherapy" brochure. A total of 10 patients participated, of which 3 (30%, 3/10) were female with a mean age of 76.6 years (range 67 to 83), and 7 (70%, 7/10) were men with a mean age of 72.3 years (range 66 to 90). Of the patients, 3 (30%, 3/10) were accompanied by a spouse.

The content of the brochure is summarized in Multimedia Appendix 1. As this brochure was used as the starting point of the online tool, it was important to identify its strengths and the components that could be improved. In addition, patients were asked about what they thought was important in the encounter preceding chemotherapy and in preparing for chemotherapy. In each hospital that was willing to participate, a coordinator was appointed that became part of the project team and facilitated the contact with the 10 oncology nurses that we interviewed to evaluate the brochure and to identify additional points for improvement. All of the nurses were female with a mean age of 50.0 years (range 37 to 62). The 10 nurses were informed about the study through a presentation by the researcher at their hospital and accepted the invitation for the interview.

## Steps 2 and 3: Specifying Determinants, Objectives, Theoretical Methods, and Practical Strategies

The aim of the second step was to specify determinants and objectives to determine what behaviors or factors could be influenced in order to reach the intended intervention goal. In

step 3, we reviewed the scientific literature to identify practical strategies that could be applied to the intervention. It was important that these strategies corresponded with the determinants and change objectives.

## Step 4: Intervention Development

In step 4, the components of the intervention were developed with input from the outcomes of the previous steps to inform the prototype of PatientVOICE. To evaluate and improve the prototype, usability tests were performed with 5 older patients with cancer and 3 older adults without cancer via a "think-aloud procedure". For this procedure, the participants performed practical tasks using the website while describing what they were doing and expressing what thoughts came to mind. The expressions were audio recorded. In addition, 2 software experts judged the website according to 20 heuristics relevant for older Web users [34].

## Step 5: Adoption and Implementation

The aim of step 5 was to enable and organize the adoption and implementation of the intervention. We approached 7 hospitals to participate, to contribute to the development of PatientVOICE, and to create a support base for the intervention. As indicated in step 1, oncology nurses were part of the project from the start and acted as coordinators in their respective hospitals.

## Step 6: Evaluation Plan

The final step of the intervention mapping framework consisted of a plan to evaluate the feasibility and user-friendliness of the intervention on feasibility. The evaluation plan describes the study design and methods used. Outcome measures that corresponded with the objectives of our intervention were specified.

# *Results*

## Step 1: Needs Assessment

### *Brochure Evaluation*

Of the evaluating patients, 7 (70%, 7/10) were familiar with the brochure, 3 (30%, 3/10) only read the brochure before the encounter, and 4 (40%, 4/10) also filled in the QPS. In addition, 2 (20%, 2/10) patients had not previously received the brochure and 1 (10%, 1/10) patient could not remember it precisely. Patients that did not complete the QPS gave the following reasons: one patient did not consider it useful because he already had the information from his wife and relatives, one patient had been treated previously with chemotherapy and was already familiar with it, and one patient answered that she would hear the information during the encounter.

However, most of the patients appreciated the brochure because it introduced the issues that were going to be addressed during the consultation. Patients considered it helpful in deciding what issues were important to them and found it supported them in asking questions. Although few patients wrote notes in the brochure, some wrote their questions in a notebook or made notes about the information provided by the healthcare provider, while others kept a diary. The nurses observed that most patients used the brochure and they considered the information clear. They also found the brochure to be a valuable preparation tool because it informed the patients about what to expect (ie, the aim and structure of the nursing encounter). Furthermore, some nurses indicated that their patients asked more questions and that the consultation was more focused when patients used the brochure, though other nurses had no experience with patients being hindered in asking questions in general. Some nurses found the statement in the QPS "What my companions can do to support me" difficult to discuss because they did not know how to advise patients in this matter and found it difficult to predict what kind of support a particular patient and his/her companions would need.

### *Chemotherapy Preparation Needs*

In general, many patients valued preparatory information about side effects, the practical consequences of those side effects, hygienic-related measures, as well as how to handle things at home. They also valued information about when and how to contact the hospital or nurse.

Patients mentioned that they would appreciate a picture of the outpatient treatment center where they will be treated to visualize the facility and set-up beforehand. Patients also preferred information about which oncology health professionals were going to be present when they were receiving care.

The overload of, and sometimes, contradictory information that patients received from different sources (eg, family and the Internet) upset some patients even though not all of the information was equally relevant to them. Therefore, it is important for patients to know what information applies to them and what information does not.

While they found the brochure useful, some patients said that one just cannot prepare for chemotherapy; it just happens to you and you have to cope with it. Other patients searched for additional information about the treatment and what to expect, for example, via the Internet or patient organizations. Often, patients' spouses and children looked for information on the Internet as well.

All patients said that they did not attend the nursing encounter on their own, rather were accompanied by a spouse or companion.

### *Suggestions for Information Improvement*

Many patients mentioned that they did not fully understand the medication list that was part of the treatment protocol or the list with additional medications to suppress side effects that was provided by the hospital. Patients preferred a clearer structure and overview of medications. Furthermore, half the patients wanted more information about how and when to use the medication. The nurses also agreed that the medication scheme should be made clearer. Some patients also indicated that they would like more specific information about the effects of the medication on their body.

### *Presentation of Information*

In general, patients expressed that information needs to be clearly, briefly, and orderly presented and difficult terminology has to be defined or avoided if possible.

### *Implications for the Online Tool*

The results of the interviews were used as input for the website. As the brochure was evaluated very positively, most information was transmitted with minor adaptations. Furthermore, the information on the website must be practical, succinct, and not disease specific. One topic that was brought forward was that it was important to state on the website that treatment is personalized, different for every patient, and that one shouldn't compare situations. As patients' companions are also involved in gathering information about chemotherapy, the website must be accessible for them as well.

## Step 2 and 3: Specifying Determinants, Change Objectives, Theoretical Methods, and Practical Strategies

The objectives of the intervention are (1) to enhance patient participation during educational nursing encounters preceding chemotherapy; and (2) to improve older patients' information recall. From the literature, it is known that the following techniques are especially effective in promoting participation during medical visits and patients' recall: (1) pre-counseling preparatory information, (2) QPSs, (3) video modeling, and (4) consultation audio recordings [11,35]. Therefore, these techniques were included in PatientVOICE.

### *Pre-Counseling Preparatory Information*

Preparing patients for upcoming consultations appears to have added value [12,36,37]. For instance, Albada and colleagues developed a tailored website that provides information regarding counselees' pre-visit needs (eg, the procedure of genetic counseling) and a QPS [31]. Results demonstrated that pre-visit (online) education about breast cancer genetic counseling improved counselees' information recall and knowledge. In

addition, the informational needs of prepared counselees were more addressed by the caregiver and counselees became more assertive by sharing their agenda, directing the communication, and checking for understanding [38].

To prepare patients for the nursing encounter and chemotherapy, PatientVOICE provides information about these topics. This information matches with patients' needs, as assessed in the needs assessment. Information on the website about the nursing encounter includes the aim and structure of the encounter, preparation of the encounter, taking a companion to the encounter, and expressing needs and concerns. Regarding chemotherapy, topics such as (the practical consequences of) side effects, hygienic related measures, handling things at home, (a picture of) the oncology outpatient clinic, and the healthcare providers that will be present were integrated.

### Question Prompt Sheet

A QPS consists of either a structured list of designed questions [7,39] or a blank sheet [38] on which patients can formulate their questions for their healthcare provider. Usually, patients receive a QPS before their consultation to read through and determine questions that they would like to ask. It is assumed that the use of a QPS increases the provision of personally relevant information, as patients acquire information that is tailored to their needs [40]. When the QPS is endorsed by the caregiver and introduced with clear instructions, the QPS enhances patient question asking and participation [41,42].

The QPS that was part of the brochure "Talking about chemotherapy" was used in PatientVOICE. It consists of 17 different statements about the treatment, emotions, sexuality, and coping with side effects and disease [7]. The QPS was adapted according to patients' and nurses' recommendations in the needs assessment and integrated in PatientVOICE.

### Video Modeling

Video modeling is a technique that demonstrates "best practices" to patients by preparing patients for procedures, providing information, and demonstrating coping strategies or self-care behaviors. Research shows that (online) video modeling can facilitate patient understanding, improve self-care, and increase patient centeredness [43,44]. In addition, Kinnane and

Thompson showed that the inclusion of a video to patient education surrounding chemotherapy improved information recall and the reporting of treatment-related symptoms [45]. In accordance with the self-management education theory of Lorig and Holman, the use of video examples appears to provide patients with the tools and (communication) skills to solve, handle, or act during certain situations [46].

In PatientVOICE, the video fragments that are used were developed for another intervention aiming to support communication between patients with malignant lymphoma in their communication with their healthcare provider [32]. The scripts were developed based on personal stories, needs, and the preferences of patients with cancer. Short video fragments about preparing for the consultation, expressing needs and concerns, and consultation audio-recordings were integrated.

### Consultation Audio Recordings

Providing patients with an audio recording of their own consultation can be effective in improving recall [47-50]. Consultation recordings can increase understanding and comprehension, reduce the anxiety related to forgetting or not hearing important information, and facilitate communication with family members [47]. Providing consultation recordings might even enhance patients' participation during subsequent oncology consultations [48].

An audio facility was built into PatientVOICE to upload audio files and to play the audio.

### Step 4: Program Development

Using the outcomes from steps 1 to 3 of the intervention mapping framework, a prototype of PatientVOICE was developed (Figure 1). PatientVOICE contains a section with information on the nursing encounter preceding chemotherapy, including the QPS and video fragments, a section with information about chemotherapy, and a section that consists of a secured personal page for patients that includes the QPS and audio facility (Table 2). These sections focus mainly on the pre-counseling preparatory information. To assure privacy, the personal page is only accessible with a personal, secured login code.

**Table 2.** Overview of the content and techniques of the PatientVOICE website.

| Section | Content | Technique |
|---|---|---|
| Welcome page | Aim and introduction of the website | N/A |
| Encounter preceding chemotherapy | Structure of the encounter | Pre-counseling preparatory information |
| | Preparation of the encounter | Pre-counseling preparatory information |
| | | Question prompt sheet[a] |
| | | Video modeling[b] |
| | Take someone to the encounter with you | Pre-counseling preparatory information |
| | Express your needs and concerns | Pre-counseling preparatory information |
| | | Video modeling[c] |
| | Audio recording | Pre-counseling preparatory information |
| | | Video modeling[d] |
| Chemotherapy | What is chemotherapy? | Pre-counseling preparatory information |
| | Oncology outpatient clinic | Pre-counseling preparatory information |
| | What providers are present at the day care setting? | Pre-counseling preparatory information |
| | Side effects | Pre-counseling preparatory information |
| | Practical measures at home | Pre-counseling preparatory information |
| | How do I tell it to… | Pre-counseling preparatory information |
| | Contacting the hospital | Pre-counseling preparatory information |
| | Help in making decisions | Pre-counseling preparatory information |
| | Useful websites | Pre-counseling preparatory information |
| Your personal page | Your consultation | Audio recording[e] |
| | Your notes | N/A |
| | Your questionnaire | Question prompt sheet[f] |

[a]A list of 15 statements that a patient can indicate which topics he or she would like to discuss during the encounter.

[b]A video fragment in which a patient and spouse can give advice on preparing for the encounter and asking questions.

[c]A video fragment in which a patient and spouse can express their concerns and what they discussed with their healthcare provider.

[d]A video fragment showing a patient talking about their experiences with recording encounters on audio.

[e]An audio file that can be uploaded to the patient's account. Patients have the option of listening back to their encounter.

[f]In your personal page, the question prompt sheet (QPS) can be saved.

The usability tests of the prototype indicated that participants and software experts were positive about the design and accessibility of the website, and they thought it was clear and complete. The information was understandable and plain. Some textual changes had to be made, the introduction of the QPS and the QPS itself were adapted (eg, the order of the words), and some extra options on the website were necessary to improve the navigation on the website (eg, the buttons should be bigger so that it is more clear that you can click on them). In addition, some adaptations had to be made to the layout and symbols.

The name of the website, PatientVOICE, had to be changed because patients did not understand that the name referred to chemotherapy or to the nursing encounter preceding chemotherapy; they preferred a Dutch title ('Chemowijzer').

Furthermore, participants navigated easily through the website. The more experience participants had with a computer or the Internet the better they were at navigating through the website. Some functionality needed to be changed, such as buttons to go to the top of the page and to return to a previous page in the QPS or to return to the website when a new page was opened. Participants with more experience were able to log in successfully, whereas participants with less experience could benefit from extra instructions about the login process. A suggestion was made to provide information about the login process by means of an instruction video, which was added.

The information about the audio recording should be somewhat clearer and more functionality was added to the audio player; having only "play" and "stop" buttons was not sufficient and functions for pausing, fast forward, and play back were added.

**Figure 1.** Screenshot of the homepage of PatientVOICE.
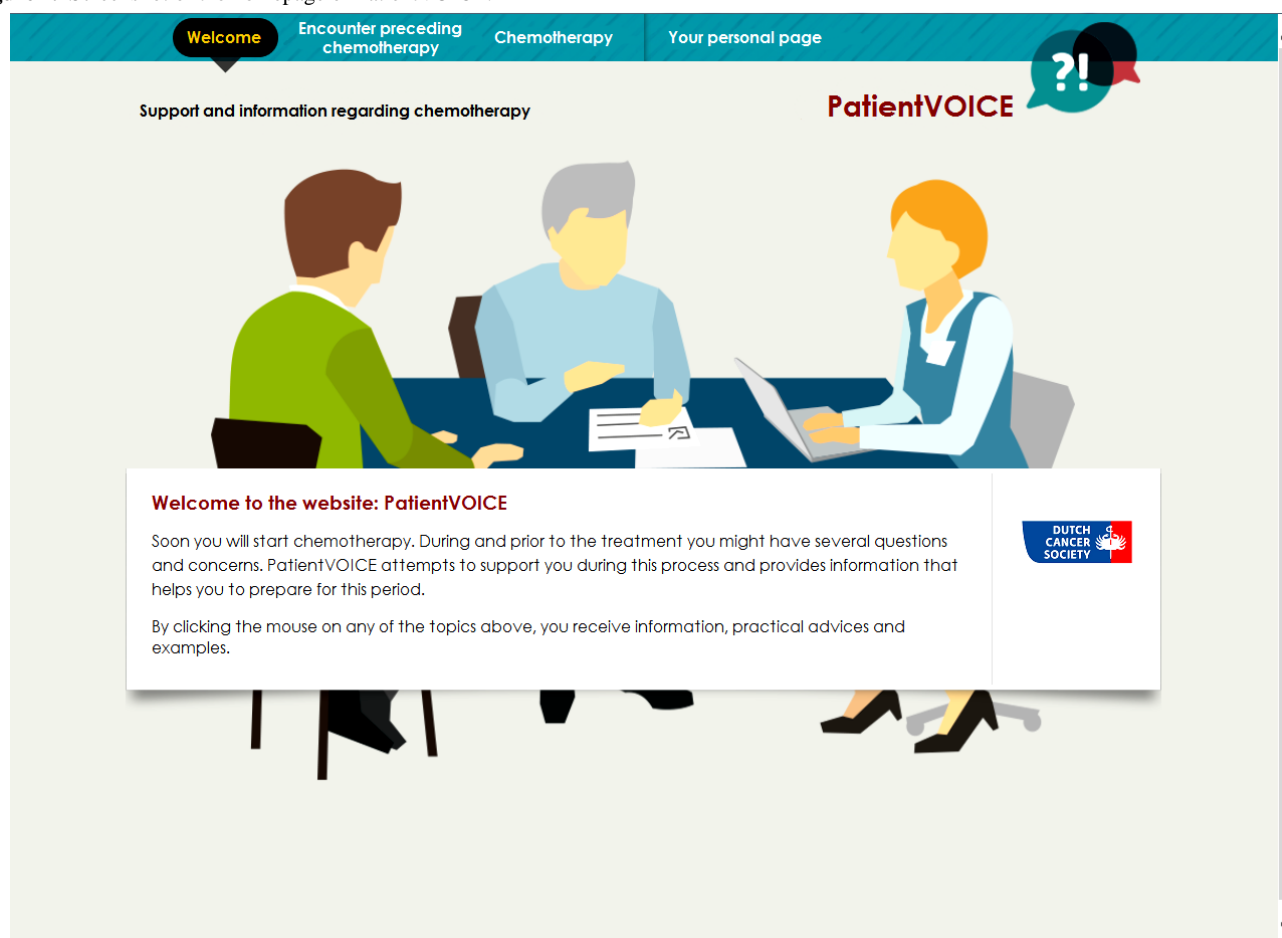


## Step 5: Adoption and Implementation

Healthcare providers (eg, nurses, assistants, team heads) of 4 hospitals were involved in the development of the intervention (eg, the needs assessment). After a kick-off meeting at the research institute, 2 meetings per hospital were held to discuss the content and logistics of the study and its implementation, as well as to create support for the intervention. These hospitals were very positive about the development of PatientVOICE and willing to implement the intervention.

## Step 6: Evaluation

A cross-sectional design will be used to evaluate the perceived usefulness and usability of PatientVOICE via an online questionnaire among older patients with cancer (65 years or older) who are receiving chemotherapy or have received chemotherapy in the preceding 5 years. The questionnaire will assess sociodemographics, type of cancer and chemotherapy, and the extent of their Internet and computer use. For the different sections of the website, patients will be asked whether they find the sections user-friendly, measured with the 10-item System Usability Scale [51] (ie, useful, easy to understand, helpful, reliable, reassuring, upsetting, confusing, timely, too elaborate, and complete [52]). Satisfaction with emotional support will be assessed using the Website Satisfaction Scale [53]. Regarding the QPS, patients will be asked to indicate whether it was useful, redundant, easy to complete, and whether it helped them to ask questions in the nursing encounter.

Statements are also formulated about whether the video fragments were useful, redundant, realistic, gave a good example of communicating with a nurse, touched the patient emotionally, and whether patients recognized themselves in the patient in the video fragments. Regarding the audio facility, patients will be asked about the usefulness, helpfulness, and value of an audio recording and whether it helped them to recall what awaits them.

## Discussion

### Principal Findings

This paper outlined the development of the online tool PatientVOICE. By using the intervention mapping framework, we aimed to make a useful and effective intervention for older patients with cancer scheduled for a nursing encounter preceding chemotherapy. As patients and healthcare providers were involved from an early stage and at several moments in the developmental process, we attempted to take patients' needs into account and to offer a user-friendly website for our target group. In our study, 8 older people performed the usability test. This number of assessors is sufficient to indicate 80% of the usability difficulties [54]. Since we combined patients' and nurses' input with empirical supported strategies to develop this intervention, we expect that the intervention not only matches with the needs of the target group, but that PatientVOICE also comprises the main factors on which to intervene, so that the intervention will be effective. In addition, we have engaged hospitals to create a support base for the intervention and expect

that implementation of the intervention will go as planned when PatientVOICE is available as a public accessible website after evaluation.

Following and completing the steps of the intervention mapping framework went without difficulty. Recruiting patients and elderly for the interviews and usability tests went as planned. Our study confirms that the framework is well applicable for developing eHealth interventions. The intervention mapping framework does not impose guidelines on how to involve patients. We decided to conduct interviews with patients and to follow the "think-aloud procedure", but other methods for patient involvement are available (eg, literature review on patients' needs, focus groups, using questionnaires to measure needs, and involving patients as a research partner) and might have led to other outcomes.

By using the intervention mapping framework we comply with the recommendations of several parties (eg, patients, politicians, clinicians, and research funds) to increase patient participation in healthcare-related research. It is important to empower laypersons (eg, patients) in research, which is mainly expert-driven, and to improve validity, feasibility and dissemination of the research or intervention. However, the effectiveness of patient participation in research is not yet demonstrated because of the heterogeneity in methodologies used and the reporting of studies [55].

After the evaluation of PatientVOICE, we will be able to conclude whether we developed a useful and user-friendly intervention. To gain insight into the effectiveness of PatientVOICE regarding improving patients' recall and participation in the nursing encounter, further research is needed. It has already been shown that implementation of the brochure "Talking about chemotherapy", which contains information about the nursing consultation and the QPS, was effective. It was found that nurses talked more about realistic expectations, the amount of information was reduced in concordance with patients' needs, and patients asked more questions during the encounters [7]. We expect that PatientVOICE will induce similar results since the brochure is the base of the website. Although patients' recall was hardly improved in the prior study, we assume that this intervention will lead to better recall of information because of the opportunity to listen back to the audio recording of the conversation [47-50].

## Strengths and Limitations

One of the strengths in developing PatientVOICE was that we used intervention mapping which provided a systematic, clear, and workable structure. However, this framework was not applied in the proposed linear way. Especially when developing eHealth interventions, which so often remain unused, the development process benefits from starting with the adoption and implementation step as early as possible. An investigation of expected implementation barriers and facilitators among all stakeholders (in terms of organizational, financial, motivational, privacy and skills issues) at an early stage could enhance the acceptability and use of the intervention in the future. The interviews with the patients and the nurses about their needs and experiences provided valuable input for the content of the intervention. However, there are also some limitations. The needs assessment aimed to assess the patients' needs regarding (preparing for) the consultation and to evaluate the brochure. Little attention was paid to patients' needs regarding an online tool, what they would expect from such a website, and whether they would appreciate this kind of tool. Our interviews with nurses did show that some of them expected great benefit from an online version of our previously developed brochure, especially given the added facilities like listening back to one's own audio recordings. Others advised us to continue to offer patients both options: the paper brochure as well as an online version. A recent study indicated that older cancer patients appreciated Web-based tools with information about cancer [26]. However, the latter study also indicated that within the group of older patients it is important to remain attentive to potential age-related problems such as cognitive and functional decline and navigation difficulties. Furthermore, nurses did not test the usability of the website, which might have indicated more points of improvement. Since nurses were not the target group of PatientVOICE, we did not ask their opinion.

## Conclusions

This article outlined the development of an online preparatory tool for patients scheduled for educational nursing encounters preceding chemotherapy, by following the consecutive steps of the intervention mapping framework. Patients (ie, the target group) and nurses were involved during several steps, as well as an examination of the theoretical literature to develop an effective and solid intervention that corresponds with patients' needs and intervenes on determinants to change behavior. The evaluation of the intervention will give insight into the utility and usability of the intervention.

## Conflicts of Interest

None declared.

## Multimedia Appendix 1

Content of the brochure "Talking about chemotherapy".

[PDF File (Adobe PDF File), 640KB - resprot_v6i5e85_app1.pdf ]

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## Abbreviations

**eHealth:** electronic health
**QPS:** question prompt sheet

Original Paper

# EpxMedTracking: Feasibility Evaluation of an SMS-Based Medication Adherence Tracking System in Community Practice

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## Abstract

**Background:** Medication adherence remains a difficult problem to both assess and improve in patients. It is a multifactorial problem that goes beyond the commonly cited reason of forgetfulness. To date, eHealth (also known as mHealth and telehealth) interventions to improve medication adherence have largely been successful in improving adherence. However, interventions to date have used time- and cost-intensive strategies or focused solely on medication reminding, leaving much room for improvement in using a modality as flexible as eHealth.

**Objective:** Our objective was to develop and implement a fully automated short message service (SMS)-based medication adherence system, EpxMedTracking, that reminds patients to take their medications, explores reasons for missed doses, and alerts providers to help address problems of medication adherence in real time.

**Methods:** EpxMedTracking is a fully automated bidirectional SMS-based messaging system with provider involvement that was developed and implemented through Epharmix, Inc. Researchers analyzed 11 weeks of de-identified data from patients cared for by multiple provider groups in routine community practice for feasibility and functionality. Patients included were those in the care of a provider purchasing the EpxMedTracking tool from Epharmix and were enrolled from a clinic by their providers. The primary outcomes assessed were the rate of engagement with the system, reasons for missing doses, and self-reported medication adherence.

**Results:** Of the 25 patients studied over the 11 weeks, 3 never responded and subsequently opted out or were deleted by their provider. No other patients opted out or were deleted during the study period. Across the 11 weeks of the study period, the overall weekly engagement rate was 85.9%. There were 109 total reported missed doses including "I forgot" at 33 events (30.3%), "I felt better" at 29 events (26.6%), "out of meds" at 20 events (18.4%), "I felt sick" at 19 events (17.4%), and "other" at 3 events (2.8%). We also noted an increase in self-reported medication adherence in patients using the EpxMedTracking system.

**Conclusions:** EpxMedTracking is an effective tool for tracking self-reported medication adherence over time. It uniquely identifies actionable reasons for missing doses for subsequent provider intervention in real time based on patient feedback. Patients enrolled on EpxMedTracking also self-report higher rates of medication adherence over time while on the system.

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## *Introduction*

### Overview

As medical innovation continues to give us powerful tools to treat and prevent disease, one major obstacle between patients and the benefits of treatment has been medication nonadherence. Nonadherence rates vary widely among different disease contexts and patient populations, but estimates of nonadherence typically range from 50% to 80% [1] with nonadherence notably elevated in asymptomatic [1] and chronic [2] conditions. This ultimately has a major impact on clinical outcomes as nonadherence is estimated to be a major factor in 125,000 deaths per year [3]. Medication nonadherence is also an important target for improvement in the context of increasing cost-containment pressures in the United States. For example, medication nonadherence has been estimated to cause approximately 10% of total hospital admissions and results in an estimated cost to the health care system of $100 to $289 billion annually [3].

Because by definition nonadherence is a problem that occurs outside of the clinic when patients are away from their providers, one strategy used to combat this problem in recent years has been eHealth. eHealth uses telecommunications and computer technology to enable provider-patient communication across geographic boundaries [4]. In particular, the growing ubiquity of telecommunication and mobile devices provides a novel route for provider-patient interaction at a distance and a powerful tool to reduce nonadherence. It is estimated that by 2017, 8 billion mobile phones with short message service (SMS) text messaging capability will be in use with especially high prevalence in certain medically vulnerable populations such as minorities and people in developing countries [5]. The use of basic SMS text messaging with such devices is an especially attractive option for eHealth intervention as it offers a familiar, nonintrusive, and easy-to-use tool for increasing medication adherence.

### Prior Work

The use of text messages and phone calls to improve medication adherence has been extensively studied over the past 15 years, and one recent meta-analysis found 11 articles using SMS- and phone call–based interventions showing a cumulative increase in medication adherence of 22% (risk ratio 1.22, 95% CI 1.09-1.36) [6]. Studies have also shown that SMS text-based medication reminders can result in significantly higher levels of medication adherence, fewer hospital admissions, and lower mortality rates [7,8].

One important concept that has emerged from this literature has been that technologies that facilitate 2-way communication with providers are significantly more successful than unidirectional interventions [9] or simple electronic reminder devices [10]. While it seems clear based on these studies that SMS messages and phone calls can improve medication adherence, there remains little evidence about how to best use this methodology. The vast promise of this methodology hinges on further work to better understand and refine eHealth techniques and establish evidence-based protocols.

### Theory

In terms of thinking about how an SMS-based system could be optimized to address medication nonadherence, it may be helpful to consider the problem in the context of the framework proposed in the systematic review by Yap et al [11] on the barriers to medication adherence in older adults, in which they organize the reasons for nonadherence that have been proven to date into 5 categories: patient factors, medication factors, physician factors, system-based factors, and other factors. Many of the factors they identified include situations and patient beliefs that could conceivably be identified and addressed by an SMS- or phone call–based system (see Textbox 1).

**Textbox 1.** Factors shown to affect medication adherence that could be identified or addressed by a short message service– or phone call–based eHealth intervention.

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Patient factors:

- Depression
- Poor memory
- Anxiety
- Sleep disturbances
- Poor physical function
- Nonadherence to follow-ups
- Problem drinking
- Beliefs about medication
- Lack of threatening view of illness
- Lack of perceived benefit of medications
- Knowledge of chronicity of illness
- Knowledge of consequences of illness
- Lack of knowledge about condition
- Lack of medication knowledge
- Misunderstanding of verbal instructions

Medication factors:

- Multiple medications
- Logistical barriers to medication filling
- Adverse drug reactions

Physician factors:

- Poor communication
- Lack of involvement of patients

System-based factors:

- Lack of follow-up
- Lack of medication review
- Lack of patient education

Other factors:

- At least one previous episode of nonadherence

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Given that Yap et al [11] identified 80 different factors shown to influence nonadherence, it seems clear that this problem is complex and multifactorial. While forgetfulness is often cited as a reason for medication nonadherence, Saberi et al [10] found that interventions relying solely on reminding HIV patients to take their antiretroviral therapy were largely not effective, leading them to speculate that the attributed forgetfulness was a simple excuse for more complex underlying reasons like stigma, depression, drug abuse, and lack of social support. Across all patient contexts, Brown et al [1] have also concluded that although most physicians believe nonadherence is due to forgetfulness or lack of access, it is often a deliberate choice by the patient.

In the design of any technology, it is critical that special attention is paid to end-user reactions to the technology. In this case both patients and providers are end-users. One theory known as the technology acceptance model has been shown to predict a substantial portion of the actual use of information technology in the health care setting [12]. As such, an effective eHealth intervention should pay special attention to key variables in the technology acceptance model such as perceived usefulness and perceived ease of use.

Because the reasons for nonadherence among individual patients and situations are nuanced and context-driven, designing an appropriate eHealth intervention provides a significant challenge. A successful intervention must be able to deconstruct and reorganize the complex reasons for nonadherence in a way

that is easily interpretable for providers. Furthermore, the use of bidirectional SMS or phone call messaging to improve medication adherence demands that patients and providers be willing to respond and engage with the system for long periods of time.

## Hypothesis

Recognizing the principles that have emerged from the literature, we set out to design a stand-alone automated intervention that would be more functional and cost effective than the current standard of care. The Epharmix Medication Tracking system, hereafter referred to as EpxMedTracking, is a medication adherence eHealth intervention that both reminds patients when they are supposed to take their medication and goes through a "differential diagnosis" of why that patient missed their dose and subsequently alerts their providers. In doing so, we hoped to give providers real-time insight into when a patient is feeling sick, out of meds, or may have mistaken beliefs about their medication regimen. By identifying patients who are not taking their medication because they feel sick or because the medication makes them feel sick, the system also has the capacity to detect adverse drug reactions as they occur. In this study, we aimed to evaluate the feasibility of the EpxMedTracking system as a tool to improve medication adherence in terms of its acceptability by patients and its ability to determine why patients are missing doses.

# Methods

## Study Design

### Data Collection

To assess the feasibility of using EpxMedTracking we analyzed de-identified aggregate data provided by Epharmix, an outside telehealth vendor that specializes in designing condition-specific, automated text messages that are optimized for both clinical utility and patient engagement. We piloted the system for 17.5 weeks and then made content changes based on feedback from current users and feedback from a focus group of other low socioeconomic status (SES) patients (specifically patients with HIV) and their case managers. This feedback was used to inform the design of the smart engagement module which included specific message wording and rotating greeting messages to improve patient engagement with the system. We specifically chose to solicit input from HIV patients and their case managers because this is a patient population where medication adherence is critical. As such we see it as an important population for future implementation of EpxMedTracking and studies to validate its efficacy. Following the implementation of those changes the official study period began.

### Participants

Because we used convenience sampling, we did not use specific eligibility criteria. Literacy was also not an eligibility criterion as all text message wording was scored at less than a 6th grade reading level as determined by the Flesch-Kincaid Grade Level scale. SMS literacy was a de facto eligibility criteria.

Patients included in both the pilot and study came from the commercial implementation of the system by several different provider groups that purchased the Epharmix service to improve the management of their patients. Thus we used convenience sampling of the data that we had access to, and recruitment to the study was handled by the providers themselves and not by the research team or Epharmix. Participants were therefore recruited remotely and offline from a clinic and were anonymous to the research team and Epharmix. Because this was a quality improvement project and not an institutional review board–approved trial, participants were not required to fill out informed consent and were briefed for recruitment at the discretion of their provider. Having multiple identities was not possible given the technical capacity of the Epharmix servers. Institutional affiliation with Washington University was not displayed to patients. Provider groups included in this study include two groups from St. Louis, Missouri, and one group from Georgia.

### Intervention

The intervention was developed as a collaboration between independent researchers and Epharmix, an independent company and owner of the software. Epharmix has sponsored a research center at Washington University School of Medicine to foster the design and development of eHealth interventions. We piloted the system for a period of 17.5 weeks (123 days) and 3324 total sessions. During the pilot period, we solicited feedback from patients enrolled in the system and found that many of them reported that interacting with the system felt like they were talking to a machine. Based on this feedback we added a smart engagement module, which includes encouraging messaging and phrasing that enables the service to take on the role of patient advocate and supporter. The smart engagement module also included rotating greeting messages (see Multimedia Appendix 1) to initiate text message interactions to add a degree of novelty for patients. The smart engagement module was included in the EpxMedTracking intervention for all patients using the system following the pilot period. Particular attention was also paid to designing messages that would be effective even for patients with low health literacy. In designing the smart engagement module, we also interviewed 5 low SES HIV patients not currently enrolled in the system and their case managers to solicit input on message wording and what they would want out of an SMS medication tracking system. We chose this particular demographic because we felt it would be a high-yield demographic for future use of the system and future studies to verify its efficacy using clinical outcome measures, such as tracking viral titers. The categories of nonadherence included "I forgot," "I felt sick," "out of meds," "I am no longer taking," "I felt better," and "other." These categories of nonadherence were designed in collaboration with two practicing physicians.

After the smart engagement module was added, we ended the pilot period and began the study period immediately with no washout period. For the pilot study, 26 patients were enrolled. Of those, 9 were deleted by their provider including 2 that opted out on their own before being deleted. Of those patients, 8 had scheduled stops (whereby the provider only prescribed EpxMedTracking for a certain period of time after which they discontinued use of the system). A total of 9 patients from the pilot continued on to the study of EpxMedTracking, and 16 new

patients were added after the pilot during the study period. Thus there were 25 total patients included in the study over a period of 11 weeks. The 9 patients studied in the official study period that had already been enrolled in the pilot were enrolled in the pilot for an average of 35.2 (SD 22.9) weeks.

Patients accessed the app by receiving an SMS message on their phone. Messages were free of charge to all patients and patients did not need to be a part of a special group to receive them. Providers accessed the platform via the Web portal [13] directly. A screenshot from the Web portal is depicted in Figure 1.

Epharmix monitors the message gateway status, and any major technical errors are accounted for when calculating the responses. In the case of the study, no major errors occurred. A patient who does not receive messages due to technology-based errors (poor cell reception, lack of SMS service, incorrect phone number entered into the system) would be displayed on the provider dashboard as unengaged, prompting provider follow-up to solve the technical problem. Epharmix receives delivery status reports for all messages sent to ensure their deliverability, and future iterations of EpxMedTracking will generate an internal alert at Epharmix for multiple undelivered messages to address these technical problems without provider involvement.

EpxMedTracking implemented a medication adherence assessment of patients that then engaged providers using a triaged report and alert system developed by Epharmix. Functionally, EpxMedTracking assessed patient medication adherence via question and then triaged for common possibilities of nonadherence. Based on responses, it then reported back to the provider actionable information to facilitate provider intervention and rapid return to an appropriate medication regimen. Provider workflow of EpxMedTracking is depicted in Figure 2. A more detailed workflow of the text messages is depicted in Figure 3.

The frequency of messages was determined by the provider based on the frequency of medication doses that patients were required to take. For this study, care providers were free to access the Epharmix platform as often as they saw fit and were free to offer assistance to patients with issues in whatever way they deemed appropriate. No prompts were used to remind either patients or providers to use the app. Epharmix staff trained and supported providers using the software. Providers introduced the Epharmix software to their patients and trained them to use it as they saw fit.

Figure 1. Web portal.
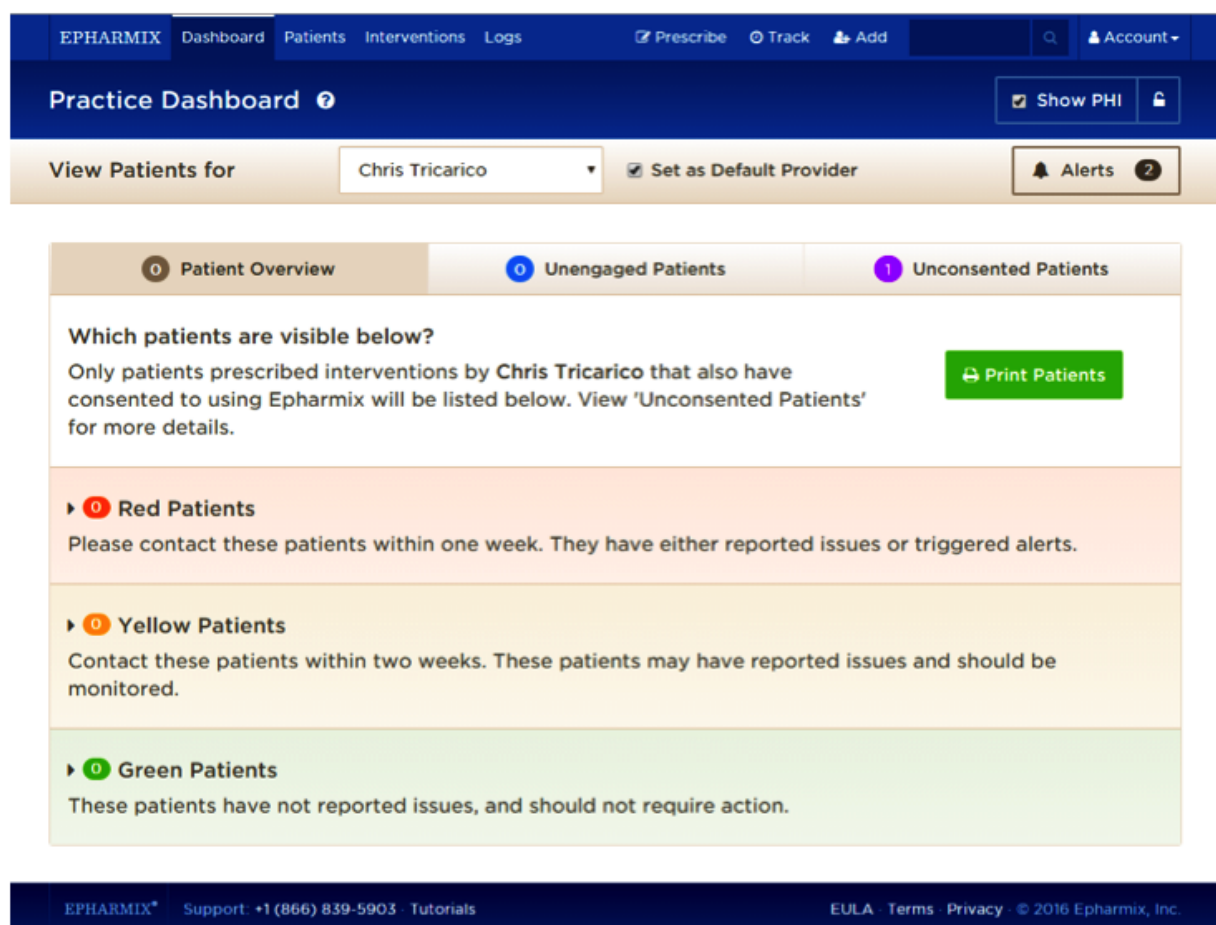
**Figure 2.** The workflow of messages and care managers used in EpxMedTracking. (A) Patients are initiated on EpxMedTracking with verbal consent to use. (B) EpxMedTracking assesses medication adherence and common issues. (C) A triage engine determines which patients can be aided in medication adherence (eg, running out of medication, a medication side effect) and care managers reach out to close the loop. Figure courtesy of Epharmix.
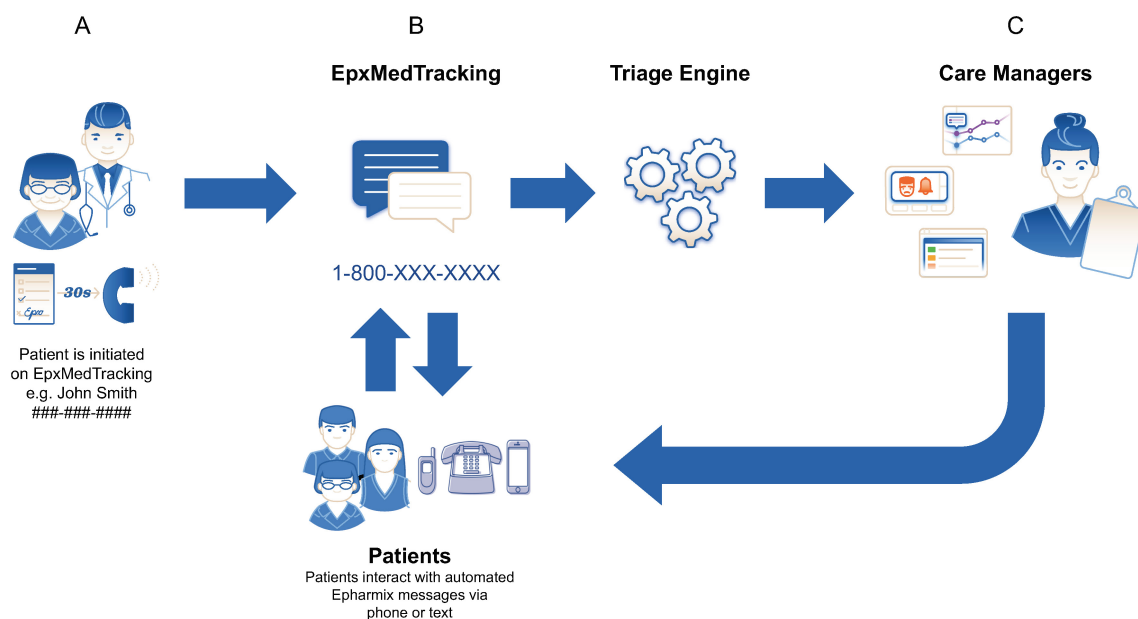


**Figure 3.** Text message workflow of the EpxMedTracking system.
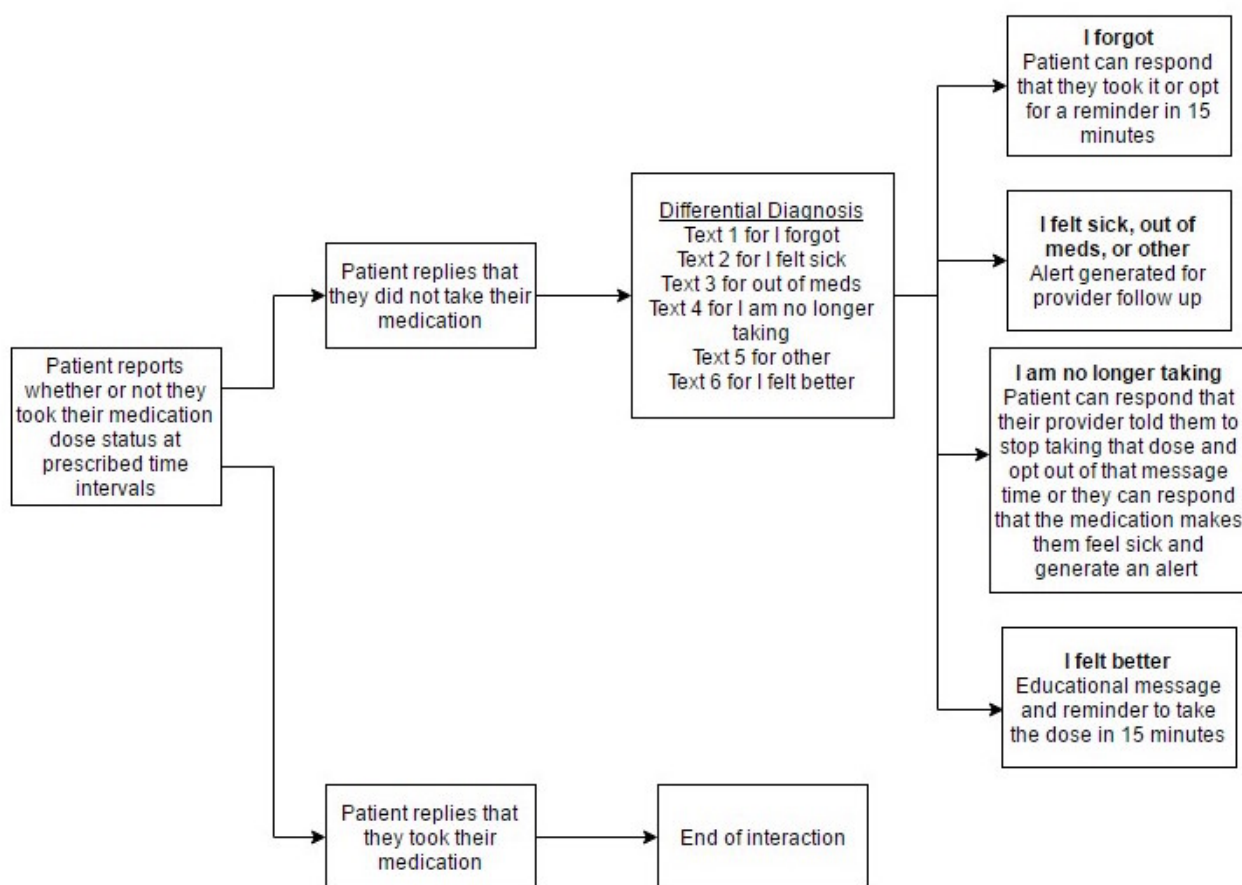
## Outcomes

Our primary outcome was patient engagement rate which was calculated as the number of unique patients who responded at least once divided by the number of unique patients with sessions scheduled in a given time frame (weeks or days). Secondary outcomes included the reported reasons for missing doses in the pilot and the study period and self-reported medication adherence in the study period. Self-reported medication adherence was calculated as the number of patients reporting that they took their medication on a given day divided by the number of total sessions in that day. Patients were considered nonadherent if they reported missing a dose or did not respond to the message. Patients were able to respond to a message and report adherence to a given dose of medication at any point between when they received the medication reminder text for the dose in question to the time in which they received their medication reminder text for their next dose. Normalized days 74 to 76 were excluded from the graph because they included data from fewer than 10 patients. Message engagement, reasons for missing, and medication adherence data were collected by querying the Epharmix server.

## Sample Size

We did not calculate a necessary sample size for this study. We used convenience sampling of all of the patient data generated to date from the EpxMedTracking system.

## Statistical Methods

Patients who were deleted by their provider, opted out of messages on their own, or had a scheduled stop in the delivery of messages were included in the calculations of engagement rate, missed doses, and self-reported adherence until the point at which they stopped receiving messages. Patients who did not respond to the app but continued to receive messages were included in all calculations.

## Ethics and Informed Consent

Because this was a service improvement project and postmarket evaluation of an existing system and not an institutional review board–approved trial, there were no informed consent procedures for enrollment into the study. The data analyzed was de-identified to protect patient privacy. Best practices in data protection and Health Insurance Portability and Accountability Act compliance were used by Epharmix in the use of communications with patients.

## Results

A total of 2065 sessions were analyzed from 25 different patients over the study period. Of the 25 patients, 3 never responded to the system. Of those 3 unresponsive patients, 2 patients were deleted and 1 patient opted out during the study period. The engagement rate normalized to weeks on the system was calculated (Figure 4). There were 198 unique patient-week combinations over the 11 weeks. Of those 198 patient-weeks, a patient was enrolled but did not respond at all in a given week 28 times for an overall weekly engagement rate of 85.9%. The engagement rate over the same time period normalized by day is presented in Figure 5. This overall engagement rate was higher than the overall weekly engagement rate observed in the pilot, which was 73.3% (51 patients enrolled but not responding out of 191 patient-weeks).

There were 109 reported missed doses (Figure 6). The causes for missed doses in order of frequency were "I forgot" at 33 events (30.3%), followed by "I felt better" at 29 events (26.6%), "out of meds" at 20 events (18.4%), "I felt sick" at 19 events (17.4%), and "other" at 3 events (2.8%). No patients responded with "I am no longer taking." An additional 5 missed doses occurred where the patient responded that the medication was not taken but they did not respond why. Such events are labeled in the chart as "Unknown." We also noted an overall increase in self-reported medication adherence in patients using the EpxMedTracking system during the study period (Figure 7).

**Figure 4.** Patient engagement rates to EpxMedTracking normalized by week during the study period.
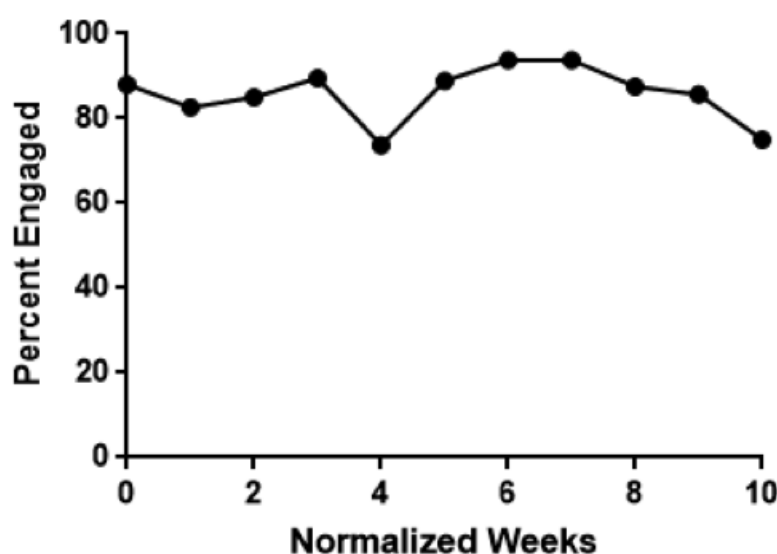
**Figure 5.** Patient engagement rate over time normalized by day.
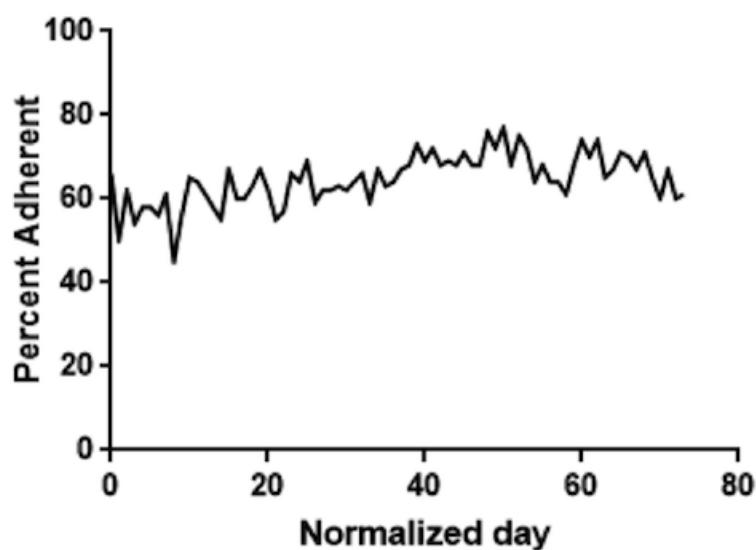


**Figure 6.** Reasons reported for missing medication doses in both the pilot and study period of EpxMedTracking.



Out of Meds (18.35%)
Felt Sick (17.43%)
Forgot (30.28%
Other (2.75%)
Felt Better (26.61)
Unknown (4.59%)

Total=100.0

**Figure 7.** Self-reported medication adherence of patients who responded to the EpxMedTracking system.
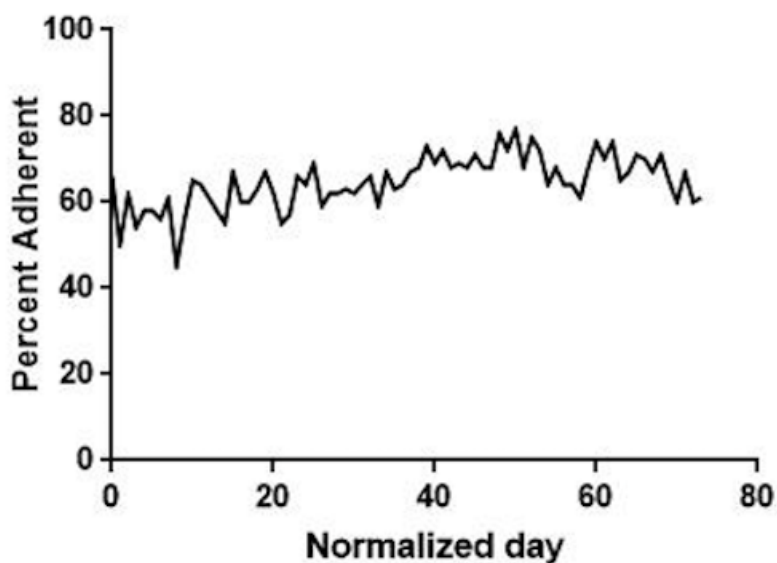
## Discussion

### Principal Findings

We set out to evaluate the feasibility of the EpxMedTracking system as a tool to improve medication adherence in terms of its acceptability by patients and its ability to determine why patients are missing doses. Our data suggest that the EpxMedTracking system is well received by patients as demonstrated by the high engagement rate of 85.9% (Figure 4) observed throughout the study period. This engagement rate remains high across the 11-week study period and never drops below 75%, indicating the EpxMedTracking intervention may be an effective tool for the longitudinal management of medication adherence in chronic conditions, which as mentioned previously are particularly susceptible to nonadherence [2].

A distinct strength of our system seems to be detecting when there is an actionable problem with a patient's regimen, as 62.4% of the missed doses were due to "out of meds," "felt better," or "felt sick" (Figure 6). Importantly, this indicates that the EpxMedTracking system can be used to direct provider attention to where it is both needed and most useful, thus making the system well suited to improve the efficiency of provider time and clinical outcomes in a wide range of disease states where nonadherence may be an issue.
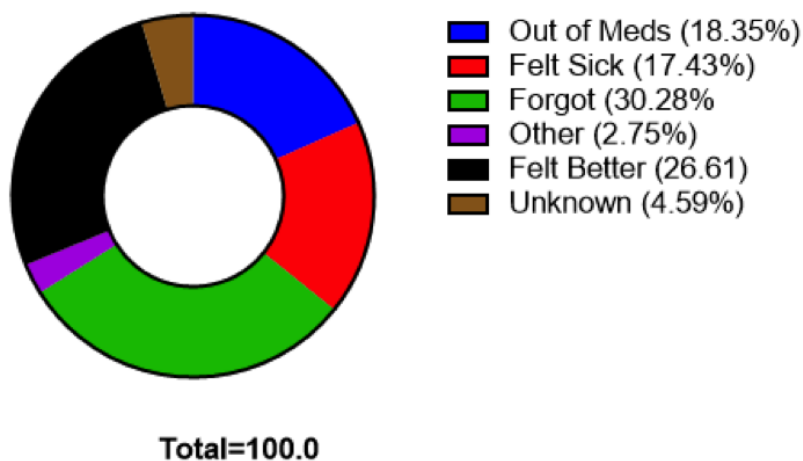
Improvements in self-reported adherence on the EpxMedTracking system indicate that enrollment in this system may also be able to change patient behavior over time (Figure 7). Future studies will look to expand on this possibility and see if system adoption corresponds to changes in relevant disease outcome measures such as viral titers in HIV patients.

### Comparison With Prior Work

In an analysis of phone call and SMS medication adherence interventions by Kashgary et al [6], many SMS- and phone call–based interventions to date have not been automated and required direct or manual messaging by a human provider [14,15]. This makes them useful for certain high-risk populations but prohibitively expensive and time-intensive in most clinical contexts. Of those that are automated, interventions often use only basic reminding [16] and thus only address the forgetfulness aspect of the complex and multidimensional problem of nonadherence, which only accounts for 30.3% of missed medication reasons in our sample. As such, the relatively low frequency of "I forgot" responses (30.3%) seems to support the theories of Saberi et al [10] and Brown et al [1] discussed above as they claim nonadherence is a complex, multidimensional problem that is not sufficiently explained by just forgetfulness.

While the technology and intervention described here are not novel, the nature of the intervention is novel. To date, the EpxMedTracking system is the first SMS-based intervention to both provide functional medication reminders and categorically identify problems leading to medication nonadherence, while simultaneously facilitating bidirectional patient-provider interaction. The categorical identification of patients who have actionable problems related to nonadherence allows the system to functionally identify and separate those

nonadherent patients who would benefit from provider attention from those who are merely forgetful. In theory this should lead to more targeted and effective provider intervention in the realm of medication adherence and improved patient outcomes in a way that would be impossible with other text message–based medication adherence systems. As such, our subsequent work will evaluate the effectiveness of the EpxMedTracking system in terms of patient outcomes.

Given the improvement in overall engagement noted during our iterative development of EpxMedTracking from the pilot, this study shows that it might be possible that patient behavior can be affected by variations in wording and messages. This importantly could indicate that 2 digital health interventions with largely the same substance may produce significantly different results if they use slight variations in messages and wording. As such, it may be difficult to accurately make broad claims about eHealth and digital health. In order to establish evidence-based protocols for optimizing eHealth in the future, it may be wise to evaluate all digital health and eHealth interventions narrowly and in terms of the specific wording they use. This is also relevant in the context of prior work as it may provide an explanation for any inconsistencies existing in the current literature.

Unlike many other eHealth interventions, the EpxMedTracking system has the added strengths of being highly accessible for even the most socioeconomically disadvantaged patients because the system is inexpensive to operate and all messages are free to patients. The messages are accessible by anyone with a landline or cell phone, and no smartphone is necessary. This stands as a significant advantage of the EpxMedTracking system and other SMS- or phone call–based systems over mobile device app-based systems. App-based systems are often more complex and require smartphones and Internet connectivity which may cause problems with elderly or socioeconomically disadvantaged populations [17]. Additionally, apps may be less prone to patient engagement because a user must continue to choose to use the app, whereas with SMS or phone calls, patients must actively opt out of receiving messages or continuously ignore incoming messages [17].

### Generalizability

Because our analysis includes data from multiple commercial accounts, our data thus necessarily includes multiple different providers and styles of practicing medicine. This indicates that the results detected in this study are not provider- or practice setting–specific and externally valid for other organizations. Given that our data come from use in routine clinical practice, there are no specially structured elements specific to this study that could have an effect on use, adoption, or outcomes outside of this study setting.

### Limitations

Although only 30.3% of participants reported missing doses because they forgot, it is important to realize that there are alternative explanations for this finding based on the limitations of the study. For example, it is possible that this finding could at least partially be explained by patients not wanting to confess that they forgot to take their medications to their provider,

instead perhaps opting to not respond or even deliberately choosing a false response. However, the fact that 30.3% of the time patients reported missing a dose because they forgot when there is no appreciable incentive for doing so suggests that patients engaging with EpxMedTracking probably respond as truthfully as they would in person.

It is also tempting to speculate that patients may feel less compelled to respond when they remember to take their medication and instead use the system for basic reminding and signaling to their provider when there is a problem with their regimen. Thus it is possible that the actual engagement rate could be higher than that observed in this study. In the future, we hope to explore these possibilities and better understand the patient experience using EpxMedTracking by administering anonymous surveys and comparing patient responses to medication refill data to validate the accuracy of the system and the honesty of patients using it.

While the results of this study show that enrollment in EpxMedTracking may be able to improve patient medication adherence over time (Figure 7), it is also possible that enrollment in telehealth interventions in general may be able to produce those kinds of changes. Because we obtained de-identified information, we also cannot comment on the patient demographics or disease states included in this study and the applicability of EpxMedTracking to different patient populations. Because patients come from both Missouri and Georgia, we do at least know that these findings are not community-specific. We also used convenience sampling for all of our analysis, and there was no control group and no washout period in between our pilot and the study period. Many of these limitations are inherent in a service improvement project with the currently available data, and we hope to address them in the future with more comprehensive trials.

## Conclusions

The evidence presented here shows that the EpxMedTracking system is a feasible tool that remains reliable over time and is useful for tracking self-reported medication adherence and identifying actionable problems with medication adherence in real time. Our data also raises the possibility that the wording and message algorithms of eHealth interventions might affect patient engagement and behavior, which would have important implications for the design of future eHealth interventions as well as the evaluation of the eHealth literature to date.

Despite a growing appreciation for the potential of eHealth in improving medication adherence, much work remains to be done before we realize its full potential. Further understanding in these areas has the ability to radically change our understanding of how patients and providers interact and shift the paradigm of how we monitor and treat medication nonadherence as well as countless other conditions.

## Conflicts of Interest

AS has a financial conflict of interest as a founder of Epharmix. All other authors have no conflicts of interest.

## Multimedia Appendix 1

Smart engagement module rotating greeting messages.

[PDF File (Adobe PDF File), 532KB - resprot_v6i5e87_app1.pdf ]

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## Abbreviations

**SES:** socioeconomic status
**SMS:** short message service

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Original Paper

# Development of a Web-Based Health Care Intervention for Patients With Heart Disease: Lessons Learned From a Participatory Design Study

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## Abstract

**Background:**   The use of telemedicine technologies in health care has increased substantially, together with a growing interest in participatory design methods when developing telemedicine approaches.

**Objective:**   We present lessons learned from a case study involving patients with heart disease and health care professionals in the development of a personalized Web-based health care intervention.

**Methods:**   We used a participatory design approach inspired by the method for feasibility studies in software development. We collected qualitative data using multiple methods in 3 workshops and analyzed the data using thematic analysis. Participants were 7 patients with diagnosis of heart disease, 2 nurses, 1 physician, 2 systems architects, 3 moderators, and 3 observers.

**Results:**   We present findings in 2 parts. (1) Outcomes of the participatory design process: users gave valuable feedback on ease of use of the platforms' tracking tools, platform design, terminology, and insights into patients' monitoring needs, information and communication technologies skills, and preferences for self-management tools. (2) Experiences from the participatory design process: patients and health care professionals contributed different perspectives, with the patients using an experience-based approach and the health care professionals using a more attitude-based approach.

**Conclusions:**   The essential lessons learned concern planning and organization of workshops, including the finding that patients engaged actively and willingly in a participatory design process, whereas it was more challenging to include and engage health care professionals.

## Introduction

Telemedicine is the use of information and communication technologies (ICT) to deliver health care at a distance [1]. During the last decades, use of telemedicine technologies in the health care sector has increased substantially, with the use of such technologies continuing to evolve. Such telemedicine approaches have the potential to improve patients' outcomes, offer remote access to health care, and reduce health care costs [1]. The benefits of telemedicine are widely described, including better communication between health care professionals and patients [2], improved quality of life for patients with heart failure [3], reduced hospitalization frequency and length [4], and increased patient empowerment [5,6]. However, it is important to cautiously assess the full impact of introducing telemedicine interventions [7], including the long-term effects and whether such interventions may have adverse effects in subsets of patients [8].

In parallel with this development in the health care sector, there is a growing interest in participatory design methods when developing telemedicine approaches to health care [9]. Participatory design entails the involvement of end users in the design and implementation of technology, with participatory design methods having been used for developing ICT-based services for different purposes and patient populations [10-12]. Ideally, participatory design should be initiated as early in the design phase as possible and in a setup that involves representatives of all major end user groups [13]. User involvement will increase the likelihood of creating technological solutions that meet the needs and preferences of end users in their specific social and organizational contexts [11,12]. In turn, this is likely to enhance efficacy and to ensure that the product makes a difference to patients and the health care system, while also increasing the likelihood of successful implementation in clinical practice [14].

### The ACQUIRE Project

Our study was carried out as part of the ACQUIRE (Advance the Quality of Life and Care of Patients with Heart Disease) project, aiming to contribute to the development and design of a Web-based health care intervention for patients with heart disease with an implantable cardioverter-defibrillator.

The overall objective of the ACQUIRE project is to evaluate the clinical efficacy and cost effectiveness of the health care intervention as an add-on to usual care as compared with usual care alone using a multicenter randomized controlled trial design. The health care intervention is based on a modular platform provided by an international information technology company. The platform is made available to end users as a Web app that supports both browsers on computers and mobile platforms, such as tablets. During the participatory design process, the health care intervention was extended with tools to support this specific study.

The health care intervention is expected to increase patient empowerment and to enable patients with heart disease and an implantable cardioverter-defibrillator to live a better life with their device and their disease. The intervention will encourage patients to become co-managers of their own disease and enable patients to routinely track their health status and symptoms of anxiety and depression, flag deteriorations early on, initiate interactions with the implantable cardioverter-defibrillator outpatient clinic, and give patients access to appropriate self-management advice and tools via a Web-based platform. The platform also serves as a tool to inform health care professionals in a timely manner about changes to patients' symptoms to allow early intervention, support shared decision making, and provide more tailored treatment.

### Aim

The aim of this paper is to present lessons learned from a Danish case study involving both patients with heart disease and health care professionals with respect to the development of a personalized Web-based health care intervention (the ACQUIRE project).

## Methods

### Design

The design basis for our participatory design study was the above-mentioned generic telemedicine platform that offered a variety of health tracking and self-management tools, of which we focused on patients' monitoring of health status (questionnaire), symptoms of anxiety and depression (questionnaire), and communication support. Furthermore, we included self-management tools in terms of online health information, debate forums, and diaries. We tested the platform on both tablet and computer interfaces.

The methodological approach was inspired by the method for feasibility studies in software development (MUST) [13,15]. MUST is a meta-method for participatory design, especially used for information technology projects. We used MUST as a conceptual framework, as the method describes 4 guiding strategies for action for the participatory process: (1) well-defined concepts to help understand and frame the intervention, (2) principles ensuring user involvement, first-hand experience with the technology, and anchoring, (3) techniques for data collection, and (4) organization of the participatory design process [13,15]. In our process, we used these strategies as guiding principles in the planning of workshops and application of workshop results.

### Workshops and Recruitment

To ensure first-hand experience with the platform (MUST guiding strategy 2), we organized a total of 3 workshops from December 2015 to January 2016. The duration of each workshop was 2 hours, with the following generic structure (MUST guiding strategy 4): (1) presenting the aim and procedure of the workshop, as well as participants' different roles during the workshop; (2) introducing a specific topic on the platform (eg, health status tracking and self-management tools); (3) testing the specific topic through hands-on exercises; (4) discussing the pros and cons of the specific topic, both in groups and in plenary; and (5) anchoring end users' first-hand experiences by documenting key learnings.

**Table 1.** Patients participating in the participatory design workshops.

| Sex | Age (years) | Duration of disease (years) | Experience with tablets and computers | Workshop 1 (tablet) | Workshop 2 (computer) | Workshop 3 |
|-----|-------------|-----------------------------|---------------------------------------|---------------------|-----------------------|------------|
| Male | 74 | Several | Some experience with computer | Yes | No | Yes |
| Female | 71 | 17 | Some experience with computer | Yes | No | Yes |
| Female | 46 | 16 | Experienced user of tablet and computer | Yes | No | Yes |
| Female | 66 | 1 | Experienced user of computer | No | Yes | Yes |
| Male | 76 | 6 | Experienced user of computer | No | Yes | Yes |
| Female | 57 | 1 | Experienced user of computer | No | Yes | Yes |
| Male | 66 | 11 | Experienced user of computer | No | Yes | Yes |

We aimed to include a diverse group of patients in terms of age, sex, and the duration that patients had lived with their heart disease. It was also essential that the participating patients had both communicative skills and sufficient motivation and capabilities to engage actively in the process together with health care professionals and systems architects. We included 7 patients with a diagnosis of heart disease: 3 men and 4 women. The patients' mean age was 65 years, and they had different levels of user experience with tablets and computers. Table 1 shows further details describing these patients.

We also intended to include physicians and nurses from the 5 participating hospitals to ensure ownership among the health care professionals who, in the end, would be working with the health care intervention. However, during the process, we had to give up on the idea of involving health care professionals in all workshops, as they were not able to take part due to time constraints. Thus, 2 nurses and 1 physician participated in the first workshop, all of whom were women and representing 2 hospitals.

In addition to patients and health care professionals, 2 systems architects, 3 moderators (researchers experienced in qualitative methods and participatory design), and 3 observers (a PhD student, a master's student, and a project nurse) were present during all workshops. The main responsibility of the moderators was to facilitate hands-on exercises and discussions, while the responsibility of observers was to make observational notes during hands-on exercises. The systems architects' main role was to present the concept and assist with technical issues (MUST guiding strategy 1). One moderator facilitated the overall procedure of the workshops. Textbox 1 presents the major content and attending participants in the 3 workshops.

**Textbox 1.** Overview of content and attending participants in the workshops.

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**Workshop 1: Tracking tools and related functions, tablet interface**

- Introduction to workshop and presentation of tracking tools (questionnaires assessing health status and symptoms of anxiety and depression)
- Hands-on exercises (in groups of 1 patient, 1 health care professional, 1 systems architect, 1 moderator, and 1 observer)
- Group discussions (groups of patients only and of health care professionals only)
- Plenary discussion

Participants: 3 patients, 2 nurses, 1 physician, 2 systems architects, 3 moderators, and 3 observers

**Workshop 2: Tracking tools and related functions, computer interface**

- Introduction to workshop and presentation of tracking tools (questionnaires assessing health status and symptoms of anxiety and depression)
- Hands-on exercises (in groups of 1 patient, 1 systems architect, and either 1 moderator or 1 observer, or both)
- Plenary discussion

Participants: 4 patients, 2 systems architects, 3 moderators, and 3 observers

**Workshop 3: Self-management tools**

- Introduction to workshop and presentation of self-management tools, including health information material on heart disease (text and video), a debate forum on Facebook for patients with heart disease, and an online letterbox for medical advice and support from health care professionals
- Hands-on exercises (in groups of 2 patients, 1 systems architect, and either 1 moderator or 1 observer, or both)
- Plenary discussion

Participants: 7 patients, 2 systems architects, 3 moderators, and 3 observers

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## Data Collection and Analysis

Prior to each workshop, we gave a detailed script to moderators, observers, and systems architects describing the various steps of the workshop and responsibilities of all stakeholders. The script also included a short semistructured interview guide for the hands-on exercises, as well as introductions to group and plenary discussions.

During the hands-on exercises, the observer made observational notes focusing on end users' main challenges during the exercises and their attitudes to the topic under discussion. Group and plenary discussions were audiorecorded and transcribed verbatim (MUST guiding strategy 3).

Following each workshop, we analyzed the themes of the observational notes and transcriptions of discussions. We coded the transcripts and observational notes according to the themes of the interview guide and then identified core themes, mapping end users' experiences and attitudes. The main results of each workshop were presented in work-in-progress reports addressed to the principal investigator (SSP) and systems architects who were deciding on the further development of the health care intervention.

## Formal Approvals and Ethical Considerations

The investigation conforms with the principles outlined in the Declaration of Helsinki [16]. A project nurse identified and contacted patients at the outpatient clinic of the Odense University Hospital to inform them orally and in writing about the participatory design process. Health care professionals were identified and contacted by the principal investigator (SSP).

The workshops were approved by the principal investigator, and all participants signed a consent form accepting participation, that discussions would be audiotaped, and that data would be published afterward.

We submitted the study protocol to the Regional Committees on Health Research Ethics for Southern Denmark, who indicated (email communication, October 19, 2015) that ethical committee approval is not required by Danish law on ethics related to health research (§ 14, 1). We also sought and obtained permission to proceed with the study from the Danish Data Protection Agency under the umbrella agreement of the University of Southern Denmark (2015-57-008).

## Results

Findings from the project fall into 2 parts. First, we focus on the outcomes of the participatory design process. This includes the actual contributions from end users—patients and health care professionals—to the development and customization of the generic telemedicine platform, as well as related work practices. Second, we describe the experiences gained from the process and reflect on the added value of conducting the participatory design research process from the researcher's perspective.

## Outcomes of the Participatory Design Process: Users' Input Into Customizing the Telemedicine Platform and Service

Based on the thematic analysis of users' input into the customization and refinement of the platform and related services, we categorized the findings into 6 major areas: (1) users' feedback on the ease of use of tracking tools and presentation of monitoring results, (2) users' feedback on platform design, (3) users' feedback on terminology, (4) insights into users' monitoring needs, (5) insights into patients' ICT skills and preferences, and (6) insights into patients' preferences for self-management tools.

### Users' Feedback on Ease of Use of Tracking Tools and Presentation of Monitoring Results

Although participants generally found that the tracking tools (questionnaires assessing health status and symptoms of anxiety and depression) were easy to use, they had several suggestions for refinement of the system's procedural flow. For instance, participants found it inappropriate that they could not correct their previous responses in the questionnaire and agreed that it should be possible to modify responses while completing the questionnaire. Similarly, they pointed out the inappropriateness of only being allowed to fill in their comments in questionnaire textboxes *before* giving a response, and accordingly agreed that it would be more suitable if the system allowed comment boxes to be filled in both *before* and *after* responding to a particular question. There was a general agreement on the relevance of including a visual indicator that would state how far they had come with completion of questionnaires (eg, question 5 out of 20).

### Users' Feedback on Platform Design

In terms of the presentation of questionnaire results, participants agreed on the necessity of including visual indicators supporting patients in the interpretation of graphs depicting their health status, symptoms of anxiety and depression, and accumulation of scores over time. One of the suggestions from the health care professionals was to add intuitive indicators, such as smiley faces on the y-axis, to make the interpretation of a rising or falling curve indisputable. Other design issues commented on by patients and health care professionals related to the number of topics presented on the welcome page (eg, display of completed questionnaires and future questionnaires to be filled in), which participants suggested should be reduced to create a better overview. Some patients argued that the font size used was too small considering the target group of elderly patients. Participants agreed that a built-in function in the system to enlarge font sizes would make the platform more accessible to (elderly) visually impaired patients.

### Users' Feedback on Terminology

Participants agreed that it was a core issue to use terminology uniformly throughout the platform. They stressed the importance of applying terms commonly used in the information material from the outpatient clinic rather than more technical terms, foreign words, or abbreviations (eg, participants preferred the use of "heart disease" to "congestive heart failure").

### Insights Into Users' Monitoring Needs

Patients expressed significant differences in their attitudes toward tracking their health status and symptoms of anxiety and depression. While none of the patients found it problematic to answer the health status questionnaire, some patients indicated that the anxiety and depression questionnaire was either irrelevant or that it "got too close" and thus was too confrontational. Moreover, patients' attitudes toward their monitoring needs differed substantially. Discussions during the workshops suggested that it was primarily patients with a new diagnosis, or patients whose health status had recently deteriorated, who were in favor of routine monitoring, as this contributed to an increased sense of security. Patients who had lived with the disease for many years had a more critical attitude toward the health status tracking tools and argued that there was a risk of inducing unnecessary concerns and focusing too much on disease.

### Insights Into Patients' Information and Communication Technologies Skills and Preferences

The lessons learned from the first and second workshops also related to patients' ICT skills. In workshop 1, patients tested the platform on tablets, while in workshop 2, they completed tests on computers. The fact that 2 out of 3 patients who participated in the first workshop hardly had any experience with tablets revealed that many of the taken-for-granted functionalities of the tablet interface were not evident to these elderly patients (eg, scrolling menus related to response options in questionnaires). One of the very basic lessons learned from this workshop was that, for the implementation of Web-based interventions to succeed, it is paramount that the system use a responsive design to support technology that is familiar to individual patients.

### Insights Into Patients' Preferences for Self-Management Tools

The focus of the third workshop was to generate ideas for self-management advice and tools to be added to the platform. In this workshop, patients tested the different types of tools presented in Textbox 1 on various platforms. Workshop discussions revealed patients' different attitudes to these self-management tools. Most of the patients favored having heart disease-related information easily accessible directly on the platform. Some of the patients already had experience with online debate forums and liked the idea of adding this tool to the platform, while, to other patients, online patient-to-patient contact did not seem like a relevant option. None of the patients had experience with receiving medical advice or support through an online letterbox and argued that they would prefer to contact their contact person at the outpatient clinic if they needed professional advice. Thus, a key finding from our workshops is that, given the heterogeneity of patients with heart disease and their different needs and preferences, it is important that not only the interface but also the content can be targeted to the individual patient.

### Value of Participatory Design in the Development of Telemedicine Services

As described in the methods section, our a priori strategy was to bring together patients, health care professionals, and systems architects in the same workshops to create mutual learning and understanding. We achieved this goal only in workshop 1, as no health care professionals participated in workshops 2 and 3. We found the combination of patients and health care professionals indeed appropriate and widely unproblematic. Prior to the workshop, we were concerned whether patients would be heard and therefore we structured group discussions for patients and health care professionals separately. However, all participants seemed aware of their responsibilities for everyone to be heard, both during group discussions and during plenary discussions. We found that the most distinct difference between patients and health care professionals was in their different ways of approaching the participatory process: patients actively engaged in the process and contributed with experience-based input, whereas health care professionals were more likely to observe and help patients and thus contribute with input of a more authoritarian and health care professional character. Furthermore, health care professionals' contributions referred to a large extent to how they figured the patients could handle the telemedicine platform and less to how they could integrate the platform in their own work practices in the outpatient clinic.

As mentioned above, in workshops 2 and 3, we only had patients and systems architects present. Because in workshop 1 we found the interaction between patients and health care professionals to be less dynamic than we had expected, the process regarding customization of the platform with only patients and systems architects present was just as fruitful.

Recruitment of health care professionals appeared to be a key challenge during the process of conducting workshops. Despite persistent efforts to adapt the planning of workshops to the health care professionals' work schedule (eg, conducting condensed workshops of no more than 2 hours, in different geographic areas, or at the end of a workday), we only partially succeeded in getting them involved; it remains unclear to us whether this was due to workload, lack of interest, or the way the participatory design process was introduced to them. We saw that the health care professionals who actually participated were engaged and showed genuine interest during the workshop. We might have more successfully involved health care professionals by conducting individual interviews; this would, on the other hand, have compromised mutual learning from the dynamics of the workshops.

We also learned that it is crucial to have systems architects present during the workshops, both because they contribute technical knowledge and because it is highly instructive for them to see their product being tested in practice, primarily in relation to the elderly patients and their challenges using the tablet interface.

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# Discussion

Our study aimed at understanding end users' priorities and critical processes in a participatory design process involving patients with heart failure and health care professionals in the customization of a Web-based health care intervention.

The definition of participatory design is broad and slightly ambiguous, although participatory design should *ideally* be initiated in the early phases of the design process [17], as mentioned in the introduction. In our study, we dealt with an existing platform, health status tracking, and self-management tools and, thus, our process is more likely to be a collaborative evaluation [17] or participatory customization process [2]. On the other hand, the MUST approach as a conceptual framework for participatory design comprises tailoring off-the-shelf, ready-made products for specific target groups [13]. Nevertheless, participatory design involves "more than having a voice;" it involves affecting the outcome by "having a say" [13]. When it comes to how our workshops actually helped shape the platform, it is more a question of "how" than of "what"—more of how to customize the usability of the specific platform than of deciding what it takes to empower and encourage patients. This customizing process around "how" is, according to this terminology, "having a say."

During the process, we faced several challenges; identification of the patient target group and challenges related to engaging health care professionals became core challenges. Regarding patients, representing the population's diversity was a challenge even though we aimed to include patients representing the population's heterogeneity in terms of age, sex, and the duration of their disease. Although this approach was methodologically appropriate, we only partly succeeded. Traditionally, some degree of homogeneity in the target group for participatory design is recommended [17]. On the other hand, the heterogeneity of our workshop participants clearly showed that both the intervention and the platform are not "one size fits all;" patients have different needs and preferences. Furthermore, the participatory design process contributed to identifying the target group that would benefit the most from the intervention, namely patients with a relatively recent diagnosis with some experience with tablets or computers.

We had expected health care professionals to engage fully in all 3 workshops, as the participating hospitals had agreed to test the platform. Nevertheless, engaging health care professionals appeared to be a challenge, and we had to adjust our expectations and the aim of including health care professionals in all workshops, and thus compromising the possibilities for mutual learning during the participatory design process [13]. But, because the few participating professionals seemed reluctant to test the platform themselves and contributed more attitude-based input, as opposed to patients' experience-based inputs, we did not see quite the level of interaction and dynamics between patients and professionals that we had expected. Some argue that a hospital setting is an obvious place for conducting participatory design, as both patients and health care professionals are ready at hand [13]. This is not a lesson learned from our study; despite the geographical proximity of health

care professionals, they might have multiple reasons for not participating.

A point of concern regarding telemedicine in general is the risk of introducing unwanted outcomes [8], and our workshops revealed that this could also be a risk of the ACQUIRE health care intervention. In particular, patients with many years of experience with heart disease mentioned the risk of the routine health status tracking inducing unnecessary concerns and focusing too much on disease; they expressed that they were less preoccupied with their heart disease and that they had moved on. This point of view was also reflected in patients' preferences regarding terminology. Other researchers found that patients prefer "heart problems" to "heart disease" [18], whereas our participants preferred "heart disease" to "congestive heart failure;" in both examples, patients preferred terms signaling fewer problems.

During the workshops, we observed that some patients were reluctant to respond to some of the questionnaire items, as these were of a more sensitive character and they "got too close." Despite guidance from the moderator, who emphasized that answering these questions was merely considered a simulation, some patients found it difficult to decouple the simulation from their actual situation. Triggering uncertainty regarding trust, sensitive information, and confidentiality may unintentionally influence the workshop outcomes. Hence, in line with the recommendations from Petrova et al [19], our workshops show the importance of ensuring that participants are aware that they are participating in the study to advance the development of a care intervention, and not to provide first-hand patient-specific data.

## Conclusion and Lessons Learned

Our customizing rather than participatory design process provided valuable knowledge of end users' views on a Web-based health care intervention. In addition, we learned some essential lessons concerning the planning and organization of workshops.

We found that end users involved in developing telemedicine interventions should reflect the specific target group that will finally use the intervention.

We also found that broad inclusion taking into account the heterogeneity of the patient group contributes multiple perspectives and nuances, especially regarding ease of use and interaction with health care professionals. Furthermore, through the process of conducting workshops, it became clearer for whom the intervention was most relevant. Including both patients and health care professionals revealed different perspectives, with patients using an experience-based approach and health care professionals using a more attitude-based approach. We also learned that patients engaged actively and willingly in the process, whereas it was more challenging than we had expected to include and engage health care professionals.

## Implications for Practice and Research

- Broad inclusion contributes multiple perspectives.
- Through the process of conducting workshops, it becomes clearer for whom an intervention is most relevant.

- Patients contribute with an experience-based approach.
- Professionals contribute with an attitude-based approach.
- Patients engage willingly in the participatory design process.
- It is challenging to engage health care professionals.

In conclusion, we recommend 2 important steps for this line of research. First, it is relevant to explore health care professionals'

values and preferences in relation to engaging in participatory design processes to improve their engagement. Second, future research should work with a larger and more representative sample to generate more generalizable knowledge in order to inform best practices.

## Conflicts of Interest

None declared.

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## Abbreviations

**ACQUIRE:** Advance the Quality of Life and Care of Patients with Heart Disease
**ICT:** information and communication technologies
**MUST:** method for feasibility studies in software development

Protocol

# Development of an Evidence-Informed Blog to Promote Healthy Eating Among Mothers: Use of the Intervention Mapping Protocol

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## Abstract

**Background:** Low adherence to dietary guidelines and a concurrent rise of obesity-related chronic diseases emphasize the need for effective interventions to promote healthy eating. There is growing recognition that behavior change interventions should draw on theories of behavior change. Online interventions grounded in theory lead to increased effectiveness for health behavior change; however, few theory-driven social media-based health promotion interventions have been described in the literature.

**Objective:** The objective of this study was to describe the application of the Intervention Mapping (IM) protocol to develop an evidence-informed blog to promote healthy eating among French-Canadian mothers of preschool and school-aged children.

**Methods:** The following six steps of the IM protocol were performed. In Step 1, a preliminary needs assessment included a literature search on theoretical domains predicting Vegetables and Fruits intakes and Milk and Alternatives intakes in adults (ie, knowledge, beliefs about capabilities, beliefs about consequences, intention/goals) and a qualitative study including focus groups to identify female Internet users' perceptions of their use of healthy eating blogs. In Step 2, two behavioral outcomes were selected (ie, increase daily intakes of Vegetables and Fruits and Milk and Alternatives of mothers to reach Canadian dietary recommendations) and subsequently divided into six performance objectives inspired by national and international dietary recommendations such as planning for healthy meals. A matrix of change objectives was then created by crossing performance objectives with theoretical domains predicting Vegetables and Fruits intakes and Milk and Alternatives intakes in adults. Step 3 consisted of selecting theory-based intervention methods (eg, modeling and goal setting) and translating them into practical applications for the context of a dietary intervention delivered through a blog. A 6-month intervention was developed in Step 4 in which we aimed to address one performance objective per month in weekly blog publications written by a registered dietitian. For Step 5, we sought to include engagement-promoting methods (eg, peer and counselor support) to promote mothers' use of the blog and adherence to the intervention. Finally in Step 6, a randomized controlled trial has been launched to evaluate the effects of the blog on dietary behaviors of French-Canadian mothers.

**Results:** The intervention study is expected to be completed in March 2018.

**Conclusions:** An intervention mapping protocol allowed for effective decision making in the development of a novel knowledge translation tool to increase adherence to dietary recommendations among mothers of preschool and school-aged children.

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## Introduction

### Low Adherence to Dietary Recommendations

Lifestyle modifications—including the consumption of a balanced diet—can reduce obesity and the risk of obesity-related chronic diseases despite minimal or no weight loss [1]. Many health agencies thus recommend adopting a healthy diet to prevent obesity-related chronic diseases [2-4]. As part of a healthy diet, Vegetables and Fruits as well as Milk and Alternatives food groups are components of the Canadian adaptation of the Healthy Eating Index [5], which measures conformity to Canada's Food Guide. Examples of Milk Alternatives included in Canada's Food Guide are buttermilk, cheese, fortified soy beverages, kefir, paneer, pudding/custard made with milk, yogurt, and yogurt drinks [6]. Higher intakes of vegetables and fruit [5], as well as dairy product consumption [7] have been associated with improved diet quality and reduction in the risk of cardiovascular-related clinical outcomes in adults in epidemiologic studies. Despite various healthy eating public health initiatives, fewer than 50% of Canadian adults and children reach daily recommended intakes for the Vegetables and Fruits and Milk and Alternatives food groups [8]. This gap between nutrition recommendations and population dietary habits emphasizes the need to develop effective knowledge translation strategies to help individuals improve their diets.

### Social Media Platforms as Knowledge Translation Tools to Promote Health Behavior Change

Social media represent an exciting strategy for health care professionals to improve knowledge translation to Internet users. Social media are Web-based platforms devoted to blogging, social networking, collaborative writing projects, and wikis [9]. Studies have shown potential effectiveness of social media interventions on health outcomes, such as a decrease in dietary fat consumption in adults [10,11]. According to a systematic review conducted by Webb et al [12], the effectiveness of Web-based interventions promoting health behavior change is enhanced by a more extensive use of theory and the incorporation of behavior change techniques. However, this review did not study interventions delivered through social media sites and currently few theory-informed social media based interventions in health promotion have been described in the literature [13,14].

Among the different types of social media, emerging evidence revealed that blogs are used by mothers notably for seeking information about child-feeding practices [15]. Blogs consist of Web-based personal journals with dated entries (posts) displayed in reverse chronological order [9]. The interactive communication between users and experts, such as registered dietitians (RDs), through blogs could improve knowledge translation in nutrition to support dietary behavior change efforts

[16]. While blogs could foster dietary behavior change among mothers through enhanced knowledge translation, they have never been studied in that context.

### Aim of this Study

The objective of this study was to describe the use of the Intervention Mapping (IM) protocol [17] to develop an evidence-informed blog written by an RD—used as a knowledge translation tool—to promote healthy eating among French-Canadian mothers of preschool and school-aged children.

## Methods

### Overview

The IM protocol [17] is a planning framework for developing evidence-based health programs through an ecological approach. IM protocol guides the selection of relevant theories to improve the likelihood of effectiveness in health behavior interventions [18].

This study followed six distinct steps inspired by IM protocol: (1) conducting a needs assessment through a literature search, and a preliminary focus group study, (2) specifying expected behavior outcomes and performance objectives for the intervention, (3) selecting theory-based intervention methods, (4) producing program components and materials, (5) planning for the adoption, and (6) the evaluation of the intervention blog (Figure 1).

### Step 1: Conducting a Needs Assessment

The aim of the first step of IM protocol was to assess the health problem and its impact on quality of life, the behavioral and environmental causes of the problem, and the determinants associated with these health-risk causes [17]. For this step, we performed a literature search of psychosocial determinants of Vegetables and Fruits and Milk and Alternatives intakes in adults, in January 2015, and conducted a preliminary focus group study [19], as described below.

#### Literature Search

According to a systematic review performed by Guillaumie et al [20], the most consistent psychosocial determinants predicting the consumption of Vegetables and Fruits in adults in cross-sectional and longitudinal studies were habit, intentions or goals, beliefs about consequences, and knowledge, with the addition of taste for vegetable consumption. In cross-sectional studies [21-24], the most consistent psychosocial determinants predicting the consumption of Milk and Alternatives were beliefs about consequences, beliefs about capabilities, and intentions or goals. We classified these psychosocial determinants according to the validated Theoretical Domains Framework [25]—an integrative framework of 12 theoretical domains derived from theories of behavior change [26].

**Figure 1.** Intervention mapping steps and tasks (adapted from Bartholomew et al).

| Step | Tasks |
|---|---|
| **Step 1**<br>**Needs Assessment** | • Conducting a literature search on psychosocial determinants of Vegetables and Fruits and Milk and Alternatives intakes in adults<br><br>• Conducting a preliminary focus group study to identify the salient beliefs and perceptions of female blog users regarding their intention to use blogs written by registered dietitians as knowledge translation tools to help them improve their dietary behaviors |
| **Step 2**<br>**Matrices** | • Building a logic model of change<br>• Identifying expected behavioral outcomes<br>• Specifying performance objectives<br>• Creating a matrix of change objectives |
| **Step 3**<br>**Theory-based intervention methods** | • Selecting theory-based intervention methods |
| **Step 4**<br>**Intervention Program** | • Consulting with social media users to determine preference for the design of the blog<br>• Creating the sequence of the intervention<br>• Designing the blog<br>• Writing blog posts and creating featured recipes |
| **Step 5**<br>**Adoption** | • Specifying engagement-promoting methods<br>• Specifying intervention characteristics linked to enhanced effectiveness in Web-based interventions |
| **Step 6**<br>**Evaluation Plan** | • Developing indicators and measures to assess the effect of the blog on dietary behaviors of mothers |
| **Implementation** | |

*Evaluation* (shown alongside the steps)

### Preliminary Focus Groups Study

Prior to measuring the impact of a healthy eating blog on health outcomes, user views and perceptions toward the use of such blogs to improve dietary habits should first be identified to guide the development of future interventions. Thus, as a second step of the needs assessment, we conducted a preliminary focus group study to identify the salient beliefs and perceptions of female blog users regarding their intention to use blogs written by RDs as knowledge translation tools to improve their dietary behaviors. Methodological details of this study are provided elsewhere [19]. In brief, 33 French-Canadian women with a

mean age of 44 years old completed the study that was conducted between April and June 2013. Data from this study showed that women preferred blogs that clearly identified the RD blogger (ie, name, picture, academic education, and professional expertise), that were visually attractive and well structured, that included recipes for putting dietary recommendations given by the RD blogger in practice, and that were updated with new information every week [19]. Women also preferred an RD blogger who supported their messages with references to published scientific papers or to other reliable sources [19].

## Step 2: Preparing Matrices of Change Objectives

The aim of the second step of IM protocol was to state expected outcomes for health-related and environmental conditions in a logic model of change, which represents pathways for intervention effects [17]. Then, a crucial step for IM was the creation of a matrix of change objectives by crossing performance objectives with theoretical domains of health behaviors and writing change objectives. Performance objectives enable an efficient transition from a behavior condition to a detailed description of its components and ensure the appropriateness of the intervention's behavioral outcomes. Change objectives specify what needs to be achieved in order to accomplish performance objectives.

### Building the Logic Model of Change

First, we developed a logic model of change (Figure 2) based on the results of the needs assessment described in Step 1. Working from right to left, the model starts with the goals for health and quality of life outcomes to be achieved by the intervention. Next, we specified performance objectives for obtaining behavioral outcomes. Performance objectives were then examined in light of the theoretical domains predicting the consumption of Vegetables and Fruits and Milk and Alternatives food groups in adults to generate change objectives. The assumption of this model is that changes in the selected theoretical domains will influence achievement of the performance objectives, which will enable accomplishment of the behavioral outcomes.

### Identifying Behavioral Outcomes

Behavioral outcomes should state, in terms of behaviors, what should be accomplished as a result of the health promotion program [17]. We formulated two behavioral outcomes for the intervention based on our previous needs assessment: (1) in the next 6 months, mothers will increase their consumption of Vegetables and Fruits to include seven servings per day, and

(2) in the next 6 months, mothers will increase their consumption of Milk and Alternatives to include two servings per day.

### Specifying Performance Objectives

We subdivided the behavioral outcomes into six performance objectives inspired by Health Canada Eat Well Campaign [27], health recommendations of the World Health Organization [28], as well as the perceived barriers of mothers to healthy eating, such as availability and costs of Vegetables and Fruits, and food skills confidence to prepare family meals [29-31]. In chronological order of appearance on the blog, performance objectives were (1) mothers have Vegetables and Fruits and/or Milk and Alternatives with every meal, (2) mothers plan adequately Vegetables and Fruits and Milk and Alternatives purchases and meal preparation, (3) mothers make healthy food choices at the grocery store, (4) mothers know economic food options to increase daily intake of Vegetables and Fruits and Milk Alternatives, (5) mothers increase the daily intake of Vegetables and Fruits and Milk and Alternatives of the family, and (6) mothers make healthy substitutions in recipes (Table 1).

### Creating a Matrix of Change Objectives

We then created a matrix of change objectives by crossing performance objectives with theoretical domains predicting Vegetables and Fruits intakes and Milk and Alternatives intakes in adults (Table 1).

## Step 3: Selecting Theory-Based Intervention Methods

The aim of the third step of IM protocol was to identify theory-based intervention methods to change the psychosocial determinants of health behaviors, while being sensitive to the target population and consistent with performance objectives [17]. For the selection of these methods, we used the Basic methods for behavior change from the IM taxonomy [33] and the behavior change techniques from the 93-item Behavior Change Technique Taxonomy v1 [34]. Theory-based methods for change are general techniques or processes that have been shown to enable change in one or more determinants of behavior and have their origins in behavioral and social science theories [17]. Behavior change techniques are defined as active components of interventions that aim to change health behaviors [34]. Behavior change techniques were grouped by the theoretical domains of the Theoretical Domains Framework [25], based on the structure proposed by Cane et al [35]. Two authors (A-AD and AL) independently chose theory-based methods that were applicable in the context of an online dietary intervention delivered through a blog [16,36].

**Figure 2.** Intervention logic model of change.
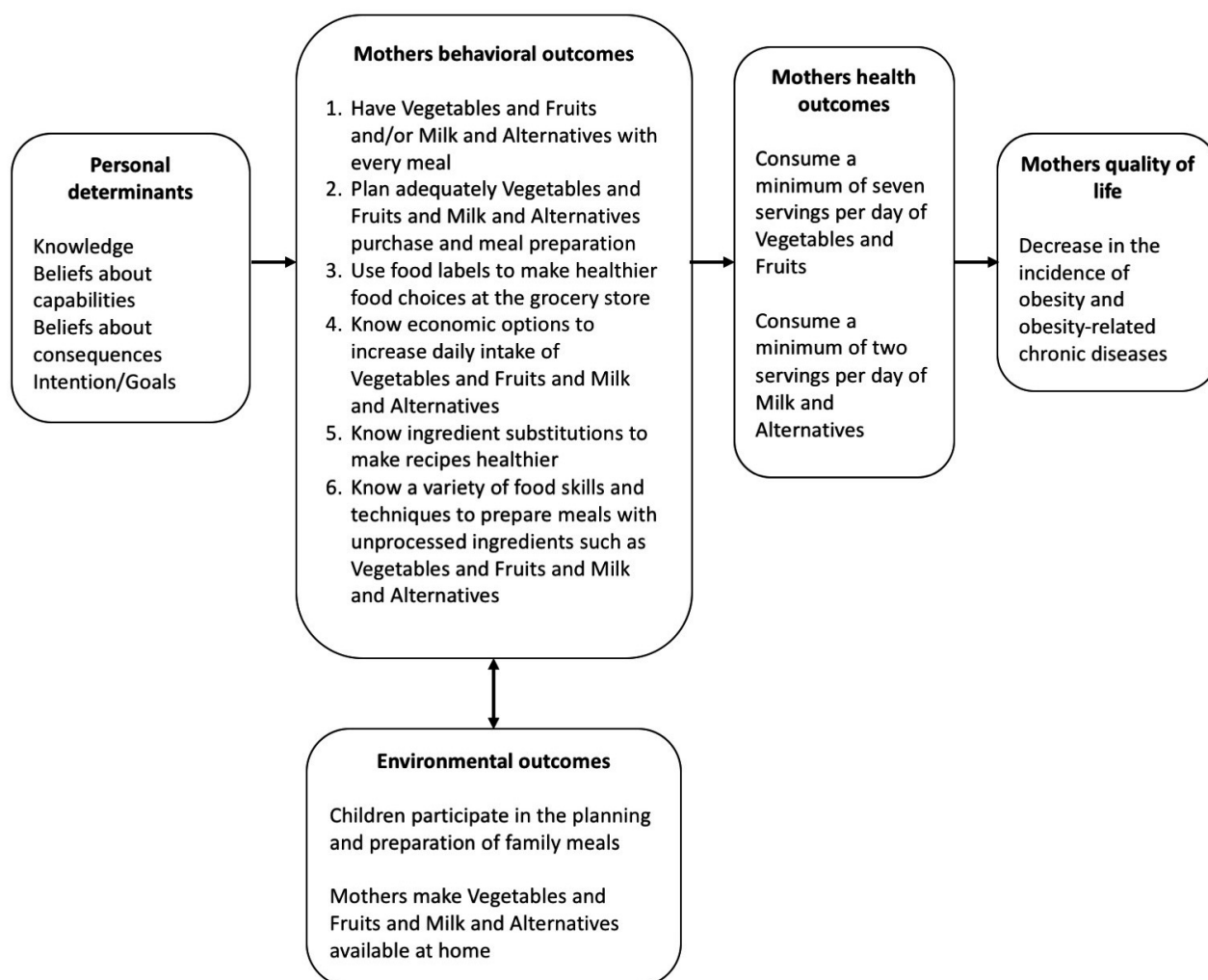


Then, theory-based methods were translated into practical applications to the blog ([Table 2](#)). Practical applications are defined as specific translation of theory-based methods for practical use in ways that fit the intervention population and the context in which the intervention will be conducted [17]. For example, "modeling" would be an effective technique to use in order to increase mothers' beliefs about capabilities (self-efficacy). For this task, we took into account theoretical parameters under which theory-based methods are shown to be effective [17]. For example, modeling can be a strong method only when certain parameters are met, for instance, when the participants identify with the model, when the model is reinforced for that particular behavior, and when they expect to be reinforced in a similar way [33]. One application for modeling in the blog was the demonstration by the RD blogger of real-life examples of how she used feasible skills (such as meal planning) to increase her consumption of Vegetables and Fruits and her consumption of Milk and Alternatives every day, and how changing these behaviors improved the quality of her eating habits. The final selection of theory-based methods and practical applications was performed by consensus between 2

authors (A-AD and AL). A third author (SD) was available to resolve conflicts when necessary.

Additionally, we selected techniques inspired by the core counseling skills of Motivational Interviewing (MI) [40]. This counseling approach aims to enhance behavior change through analysis and resolution of ambivalence, a normal process for change [40]. Previous studies have supported the effectiveness of MI for health promotion in individuals of different ages, genders, and ethnicities [41]. Previous interventions based on MI have increased the motivation and self-efficacy to eat Vegetables and Fruits [42]. In our study, the RD blogger sets a positive example for the experience of ambivalence by sharing her own experience in comparing her perceived benefits and her perceived costs or disadvantages to particular behavior change, such as to involve children in the preparation of weekly meals. Each blog post ended with an evocative open-ended question from the RD blogger to initiate change talk with the study participants in the comments' section of the blog. Each week, the RD blogger wrote empathic feedback messages based on these conversations as ways to address barriers to behavior change.

**Table 1.** Overview of performance and change objectives for mothers addressed in the intervention blog and classified by theoretical domains.

| Performance objectives | Theoretical domains | | | |
| --- | --- | --- | --- | --- |
| | Knowledge | Beliefs about consequences | Beliefs about capability | Goals |
| 1. Mothers have Vegetables and Fruits and/or Milk and Alternatives with every meal | Mothers define the concept of the Canadian Eat Well Plate [32]. | Mothers express the benefits of consuming Vegetables and Fruits and Milk and Alternatives at every meal. | Mothers express confidence to overcome barriers associated with consuming Vegetables and Fruits and Milk and Alternatives at every meal. | Mothers set the goal of consuming Vegetables and Fruits and Milk and Alternatives at every meal. |
| 2. Mothers plan adequately Vegetables and Fruits and Milk and Alternatives purchase and meal preparation | Mothers list tips to allow efficient planning of everyday meals. | Mothers express positive attitudes towards meal planning and meal preparation. | Mothers express confidence to overcome barriers associated with meal planning and meal preparation. | Mothers set the goal of using a written grocery list to buy all necessary food to prepare planned weekly meals. |
| 3. Mothers make healthy food choices at the grocery store | Mothers understand the nutrition information provided on Canadian food labels. | Mothers express the benefits of reading food labels to make healthier food choices. | Mothers express confidence to overcome barriers associated with efficient use of food labels while purchasing food. | Mothers set the goal of selecting healthier foods at the grocery store based on food labels. |
| 4. Mothers know economic options to increase daily intake of Vegetables and Fruits and Milk and Alternatives | Mothers list economic substitutions to fresh Vegetables and Fruits. | Mothers express the benefits of cooking meals at home with unprocessed ingredients such as Vegetables and Fruits and Milk and Alternatives food groups. | Mothers express confidence to overcome barriers associated with food purchases and home cooking. | Mothers set the goal of cooking a weekly meal with seasonal Vegetables and Fruits. Mothers set the goal of cooking restaurant-inspired dishes or takeout favorites at home. |
| 5. Mothers increase daily intake of Vegetables and Fruits and Milk and Alternatives of the family | Mothers list tasks that can be performed by children in the kitchen. | Mothers express positive attitudes towards involving children in the planning and preparation of meals. | Mothers express confidence to overcome barriers associated with involving children in the kitchen. | Mothers set the goal of making lunches for oneself and children based on the Canadian Eat Well Plate. Mothers set the goal of involving children in the planning and preparation of a weekly meal. |
| 6. Mothers make healthy substitutions in recipes | Mothers list a variety of techniques to cook Vegetables and Fruits. Mothers identify ingredient substitutions to make recipes healthier. | Mothers express the benefits of varying the techniques to cook Vegetables and Fruits, and using ingredients substitutions. | Mothers express confidence to overcome barriers associated with ingredients substitutions. | Mothers set the goal of cooking Vegetables and Fruits with a cooking technique that preserves the nutritional values of food (eg, steaming). Mothers set the goal of adjusting a recipe to make it healthier. |

## Step 4: Producing Program Components and Materials

The fourth step of IM protocol involved creating intervention themes, scope, and content sequence by consulting with the intended intervention users to determine preference for intervention program design [17]. We were guided by the results of our preliminary focus group study [19] for creating the sequence and the design of the blog as well as writing blog posts and creating featured recipes. An overview of the blog intervention timeline and components is presented in Multimedia Appendix 1.

### Creating the Sequence of the Intervention

A 6-month intervention was then developed during which we will address one performance objective per month in weekly blog publications written by an RD. A total of 26 weekly posts will be published. Each weekly post will target alternately one behavioral outcome (increase Vegetables and Fruits intake or increase Milk and Alternatives intake). In a typical month, posts published in the first and third weeks will target the theoretical domains knowledge and beliefs about consequences. The posts published in the second and fourth weeks of each month will target the theoretical domain beliefs about capabilities. We will address the theoretical domain goals (intention) in every post using the theory-based methods prompting goal setting and reviewing of behavioral goals. Multimedia Appendix 1 provides more details on the components and sequence of blog posts throughout the intervention.

**Table 2.** Overview of selected theory-based methods clustered by theoretical domains, parameters for use, and examples of practical applications to the blog[a,b,c].

| Theoretical domains | Theory-based methods | Parameters for use | Examples of practical applications to the blog |
|---|---|---|---|
| Knowledge | Information about health consequences | Messages need to be relevant and not too discrepant from the beliefs of the individual; can be stimulated by surprise and repetition; will include arguments. | The use of the intervention blog itself allowed us to transfer relevant nutritional knowledge, eg, about the health benefits of consuming recommended daily servings of Vegetables and Fruits and Milk and Alternatives food groups. |
| | Feedback on behavior | Feedback needs to be individual, follow the behavior in time, and be specific. | The RD blogger provided positive feedback on participants' behavior through comments function of the blog. |
| Beliefs about consequences (attitude) | Emotional consequences | Present messages as individual and undeniable and compare them with absolute and normative standards. | The RD blogger provided knowledge about the advantages of consuming Vegetables and Fruits and Milk and Alternatives food groups every day and shared real-life examples on how changing these behaviors improved the quality of her eating habits. |
| | Information about social and environmental consequences | May include awareness about serving as a role model for others. | The RD blogger provided knowledge about the advantages of efficient planning meals, such as reducing meal preparation time and food expenses, and improving the diet quality of their child. |
| Beliefs about capabilities (self-efficacy, perceived behavioral control) | Verbal persuasion to boost self-efficacy | Credible source. | Through an empathic and positive writing style, the RD blogger told study participants that they could all perform the weekly goals and ascertained that all could increase their daily intakes of Vegetables and Fruits and Milk and Alternatives food groups. |
| Goals (intention) | Goal-setting (behavior) | Commitment to the goal; goals that are difficult but available within the individual's skill level. | At the end of each post, the RD blogger encouraged study participants to take up a challenge, such as involving children in meal preparation in the upcoming week. |
| | Review of behavior goal(s) | Raising awareness must be quickly followed by increase in problem-solving ability and self-efficacy. | At the beginning of every blog post, the RD blogger prompted the study participants to comment on their experience of the previous week's challenge with an open-ended question. |
| Social influences (social support, social norms) | Modeling or demonstrating the behavior | Attention, remembrance, self-efficacy and skills, reinforcement of model, identification with model, coping model instead of mastery model. | The RD blogger provided real-life realistic examples of how she overcomes barriers to increase her daily servings of Vegetables and Fruits and Milk and Alternatives. Each post contained a step-by-step recipe featuring Vegetables and Fruits and Milk and Alternatives food groups. Recipes were described textually and with step-by-step pictures. |
| Skills | Graded tasks | The final behavior can be reduced to easier but increasingly difficult sub-behaviors. | As the intervention moved forward, the sequence of the blog provided an overview of more general aspects of healthy eating (eg, the Canadian Eat Well Plate [32]) to more complex skills (eg, reading food labels). |

[a]Theory-based methods were selected from the Basic Methods for Behavior Change from the IM taxonomy [33] and the behavior change techniques from the Behavior Change Technique Taxonomy v1 [34], grouped by the theoretical domains of the Theoretical Domains Framework [25], based on the structure proposed by Cane et al [35].

[b]We judged it appropriate to use behavior change techniques associated with the construct of skills, as the acquisition of real skills is complementary to improvement in self-efficacy for behavior change [34,37]. Given the important social aspect of blogs [38,39], modeling, a behavior change technique associated with the construct of social Influences, was also used.

[c]Parameters for use were drawn from the IM taxonomy [33].

## Designing the Blog

The intervention blog was developed on the self-hosted blogging platform, WordPress [43]. We worked in collaboration with the Web designer at the Office of the Executive Vice Rector, Development, at Laval University to respect the preferences of female social media users according to our preliminary focus group study [19]. Blog features included a home page composed of a colorful header (graphic and text identifier at the top of every page) and a clear identification of the RD blogger (name, professional picture, expertise and professional credentials); an archiving system of blog posts by date and keywords to facilitate navigation; blog posts divided by subtitles and paragraphs to facilitate reading; internal and external links to references to peer-reviewed scientific papers or other reputable online resources (eg, government websites); and a comments section for interactive communication between the RD blogger and the study participants. The blog also included a Recipe page (recipes published on the blog and categorized by types of meals) and a Resource page providing supplementary healthy eating tools (eg, Health Canada Eat Well Plate [32]). Multimedia Appendix 2 provides screenshots of the intervention blog.

### Writing Blog Posts and Creating Featured Recipes

One author (A-AD, RD blogger) wrote each post with careful attention to providing positive messages on healthy eating that were adapted to the realities of mothers of preschool and school-aged children. Posts were then reviewed by 3 authors (AL, SL, and SD) to produce a final version.

In line with the results of the preliminary focus group study [19], we included a step-by-step recipe featuring Vegetables and Fruits and/or Milk and Alternatives food groups in every post. Two authors (A-AD, AL) and their families pretested all the recipes. Recipes were described textually and with step-by-step pictures.

## Step 5: Planning Program Adoption

The aim of the fifth step of IM protocol was to plan for the adoption of the intervention. Considerations from blog adoption began as early as the needs assessment, as suggested by Bartholomew et al [17]. The specified intervention adoption outcome was that mothers in the intervention group choose to adopt the intervention as indicated by study compliance, participation, and attrition rates. In order to perform adoption outcome, mothers will have to achieve the following performance objectives: (1) complete more than 70% of study questionnaires, (2) attend over 90% of in-person appointments (compliance rate), (3) assess a minimum of 75% of the blog posts (participation rate), and (4) complete the 6-month intervention and follow-up assessment at 12 months, for a study attrition rate below 25%.

Practical applications were planned in order to stimulate mothers to use the blog. Prior to the beginning of the intervention, 2 authors (A-AD and AL) will provide instructions on how to navigate the blog website and how to post comments to all recruited mothers in order to facilitate their use of the blog throughout the study. Mothers who do not log in to the blog for 2 consecutive weeks will be reminded of the blog by email. As low actual reach, decline usage of online tools, and high attrition rates are common difficulties in Web-based interventions [44], we included engagement-promoting methods identified in previous Web-based lifestyle promotion interventions to promote mothers' adoption of the blog and adherence to the intervention, as described below.

### Specifying Engagement-Promoting Methods

Brouwer et al [45] found that key exposing-promoting methods that could increase the participants' exposure to Web-based healthy lifestyle promotion interventions (eg, more average logins and longer visits on the website) were peer and counselor support, email or phone contacts and updates, and regular updates of the website. In addition, data from our preliminary study showed that women preferred RD bloggers to whom they could relate, as opposed to an unrealistic expert [19]. Recent research suggests that users of narrative health blogs identified more with the bloggers and were more likely to feel they were socially interacting with them compared with users of non-narrative blogs providing expert advice [46]. Consequently, we wrote blog posts and responses to participants' comments in a narrative approach. By sharing personal experiences involving food, the RD blogger provided a model for mothers to aspire to.

### Specifying Intervention Characteristics Linked to Enhanced Effectiveness

In addition to engagement-promoting methods, we developed the intervention with special attention to characteristics enhancing effectiveness in Web-based behavior change studies. Webb et al [12] showed that intervention characteristics associated with larger effect size on health-related behaviors in Web-based interventions included more extensive use of theory; incorporating multiple behavior change techniques (eg, modeling, goal setting, and provision of feedback on performance); and using additional methods of communicating with participants, such as providing access to an adviser to request advice. Kohl et al [47] found consistent evidence of effectiveness for tailored feedback, use of theory, interactivity, goal setting, and potentially social support for dietary behaviors. Accordingly, we applied multiple theory-based methods in the experimental blog, as described previously in IM Step 3. In addition to the comments function of the blog, where communication and support between the RD blogger and study participants will be promoted, the research coordinator (AL) will be available by phone or email throughout the study to support mothers with any issues related to the use of the blog website.

## Step 6: Planning for Evaluation

The aim of the sixth step of IM protocol was to plan for an effect evaluation of the intervention, which involves determining whether behavior outcomes change as a result of the intervention [17]. For this task, a randomized controlled trial will measure the effects of the developed intervention blog on dietary behaviors of mothers (Clinical Trial Protocol ID: NCT03156803).

The main objective of the study will be to evaluate the effects of the intervention blog on daily intakes of Vegetables and Fruits and daily intakes of Milk and Alternatives of mothers. As

secondary objectives, we will (1) explore the effects of the intervention blog on the dietary habits of mothers' children, including mean usual food group and nutrient intakes, (2) explore the association between mothers' child-feeding practices and change in children dietary habits, (3) explore association between intervention blog usage and change in mothers' dietary habits, and (4) evaluate mothers' acceptability of the intervention blog.

### Trial Overview

A total of 110 mothers aged 18 years old or over are being recruited in the Quebec City area of Quebec, using the following strategies: advertisement to a list of people that had indicated their interest to participate in our research institute clinical studies and to email lists of Laval University employers and students; flyers in community centers targeting families, schools, and daycares; and advertisements on Facebook. Mothers will be eligible if they have Internet access, have at least one child aged between 2 and 12 years, are primarily responsible for food purchases and preparation in the household, and consume fewer than the recommended daily serving of Vegetables and Fruits and/or of Milk and Alternatives food groups in Canada's Food Guide (ie, less than seven servings per day of Vegetables and Fruits (560 g), and/or less than two servings per day of Milk and Alternatives). We sought participants with suboptimal dietary eating habits, and mothers were selected as the target population as they are active blog users [48] and have an important influence on the diet quality of their children [49].

**Figure 3.** Description of the study and measurements performed at baseline, 3 months, 6 months, and 6 months after the end of the intervention blog exposure.
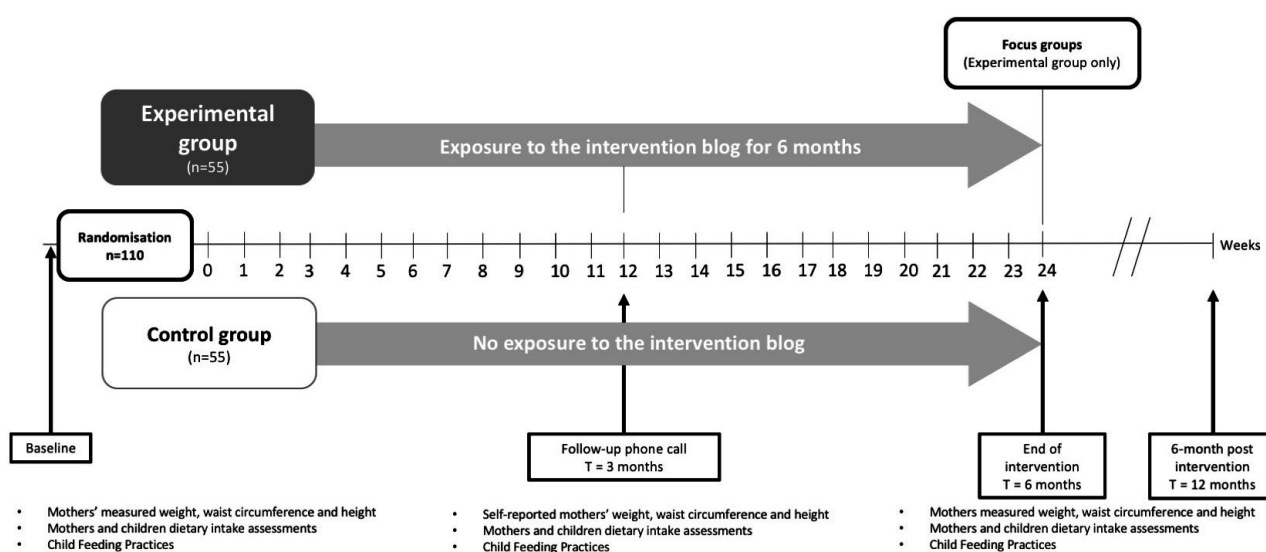


Eligible mothers will be randomized to the experimental group, which will include access to the blog over a 6-month period, or to a control group with a delayed exposure to the blog (Figure 3). All study participants will complete outcome assessments at baseline, 3 months, 6 months, and 6 months after the end of the intervention (T=12 months). Once baseline testing and the randomization are performed, mothers in the experimental group will receive an email including a unique identification code and a password to log in to the intervention blog and for the research team to collect log data over the intervention. In addition to login information, this email will invite mothers to consult the first published post on the blog through a Web link. Once a week for 26 weeks, mothers will receive by email an alert advertising that a new post has been published. New posts will be dated and displayed in reverse chronological order on the blog home page, making new entries easily traceable. Additionally, posts will be archived by themes, and a user "search terms" feature will be available for mothers to consult previous posts or comments throughout the 6-month intervention. These features have been identified by female social media users in our preliminary focus group study as being useful and likely to increase their use of the blog [19].

The control group will be a delayed control condition. During the 6-month intervention period, mothers in the control group will not be allowed to access the blog. They will not be contacted by the RD blogger but will meet the research coordinator (AL) at our research institute for baseline, 3-month, 6-month, and 12-month outcomes assessment. After the 12-month follow-up, mothers in the control group will be granted access to the blog's archives containing the RD bloggers' posts and comments to the posts' authors by fellow study participants. Interactions with the RD blogger or study participants through the comments function of the blog will not be possible for mothers in the control group.

### Outcome Measures

Outcome measures for effect evaluation were selected after reviewing the intervention logistic model (Figure 2) with emphasis on the evaluation of mothers' behavior change.

#### Dietary Variables

The primary outcomes of the study are mothers' daily servings of Vegetables and Fruits and Milk and Alternatives food groups, which will be assessed by three automated, self-administered, Web-based 24-hour dietary recalls completed by mothers at each assessment time, for two unannounced weekdays and one weekend day selected at random. Multiple administrations of 24-hour dietary recall in prospective studies that aim to determine change between points of time in mean usual intakes

of groups are supported by national recommendations [50]. Recent evidence has shown that, for all food groups but the most rarely consumed, two to four dietary recalls were superior to use of Food Frequency Questionnaire data to estimate usual intake [51], and that obtaining 3 nonconsecutive days of 24-hour dietary recalls per month over a period of 6 months was adequate to estimate energy and macronutrient intakes [52]. The Web-based automated 24-hour dietary recall that will be used in this study was developed in French [53] based on the US Department of Agriculture Automated Multi-Pass Method [54] and validated among French-Canadian adults [55]. In addition to data on food groups servings [6], a list of foods and beverages selected by mothers, and macronutrients and micronutrients intakes will be obtained from The Nutrition Data System for Research (software version 4.03, Food and Nutrient Database 31) [56] and the Canadian Nutrition File (version 2015) [57] in order to assess whether changes in mothers' daily servings of Vegetables and Fruits and Milk and Alternatives food groups will be accompanied by other dietary changes.

Mothers will complete one 24-hour dietary recall administered by an RD with the Automated Multi-Pass Method [54] for their oldest eligible child (aged between 2 and 12 years old) at each assessment time. We have chosen to administer one 24-hour dietary recall at each time point to assess children's diet as a secondary outcome so as to not overburden mothers with questionnaires and also because the National Cancer Institute's latest recommendations [50] support the single administration of 24-hour dietary recall to assess change in mean usual intake of a food group between two points in time. The collection of food data by a 24-hour dietary recall has been considered as an appropriate approach with children in previous studies and national nutrition surveys [5,58,59].

### Mothers' Child-Feeding Practices

We will assess mothers' child-feeding perceptions, attitudes, and practices, and mothers' relationships to children's developing food acceptance patterns, the control of food intakes, and obesity with the Child Feeding Questionnaire [60] at each assessment time. The Child Feeding Questionnaire is a validated, self-reported 31-item questionnaire that was designed for use with parents of preschool and school-aged children [60]. Maternal child-feeding practices, such as the extent to which mothers control how much, when, and what their child eats, have been shown to impact their child's development of food-intake controls [61].

### Blog Usage

In line with our adoption plan of the blog (Step 5), we will explore the associations between the dose of the intervention that mothers in the intervention group received, using blog usage data, and change in their dietary habits. Over the 6-month intervention, we will monitor total number of logins, blog posts viewed, submission of comments, and the most frequently accessed links and blog pages viewed using the Web analytics service Google Analytics [62] and the Web analytics plug-in Slimstat Analytics [63].

### Acceptability of Blog

We will explore mothers' acceptability of the blog using focus groups at the end of the 6-month intervention blog exposure. A trained female research coordinator (AL) will use a semistructured interview guided on Patton's recommendations [64]. A standardized open-ended interview questionnaire will be developed according to three constructs of the Technology Acceptance Model [65]: mothers' perceptions on utility and ease of use of the blog, and mothers' attitude (advantages/disadvantages) regarding its use to improve their dietary behaviors.

### Recruitment Procedure

We will perform a three-phase intervention study to reduce the delay between recruitment and the actual start of the intervention. We will conduct each experimental phase subsequently to allow the RD blogger to be entirely dedicated to each virtual social community. In each phase, the nutrition information and recipes in the blog will be identical, with the exception of the interaction in the comments' section, which will be shaped by the participation in each phase. The three experimental phases will be conducted in different periods of the year (ie, winter through summer; autumn through spring; and spring through autumn), and possible seasonal variations in Vegetables and Fruits food group intakes will be tested for in our statistical model. This study was approved by the Laval University Research Ethics Committee (project n°2014-257 A-5 / 12-07-2016)

### Sample Size

Sample size calculations were based on a previous study investigating the effect of a dietary intervention on fiber, vegetables, fruits, and fat intake in free-living adults [66]. It was estimated that a sample size of 82 mothers would allow the detection of a 28% difference in vegetable intakes at 12 months, with a standard deviation of 2.05 in servings of vegetables, a power of 0.95 and a two-sided .05 significance level. Based on attrition rates varying between 10% and 37% in Web-based dietary behavior change interventions [67], we anticipate an attrition rate of 25% and therefore plan to recruit a total of 110 mothers.

## Results

The intervention study is expected to be completed in March 2018.

## Discussion

### Principal Considerations

This study describes the use of the IM protocol to develop an evidence-informed blog to promote healthy eating among French-Canadian mothers of preschool and school-aged children. This study will provide valuable guidance for future researchers, health agencies, and health care professionals who are interested in using this systematic approach to develop a blog as a novel knowledge translation strategy to promote health behavior change.

IM protocol allowed for effective decision making at each step of the planning, implementation, and evaluation of the intervention blog. IM protocol enabled a systematic application of evidence from empirical studies, theories of behavior change, and preliminary research data. Well-designed and effective health promotion interventions should draw on theories of behavior and behavior change to advance an understanding for mechanisms of change [68]. A systematic process is thus a valuable guide to identify determinants of behavioral causes related to the targeted health problem and to select the most appropriate theory-based methods to address the identified determinants to achieve behavior change [17]. In this study, combining performance objectives with selected determinants to create matrices for change was a crucial step of the IM protocol to determine which evidence-based knowledge should be disseminated through the blog.

There is emerging research on adaptation of behavioral interventions for social media delivery [36], and on which behavior change techniques could be applied in digital contexts (eg, goal setting, barrier identification/problem solving, prompt review of behavior goals) [16]; however, these results do not explain how behavior change techniques should be translated into practice applications in online settings (ie, when, where, and in what format they will be effective). Webb et al [12] identified behavior change techniques associated with larger effect sizes in Web-based health interventions. In particular, interventions providing stress management or general communication skills had the largest effects on behavior. Web-based interventions were also more effective when more behavior change techniques were included [12], suggesting that the combination of behavior change techniques may be more effective than using one or two techniques in isolation. The results from a meta-analysis [69] on re-analyzed data from Webb et al [12] supported this hypothesis to some extent. The combination of barrier identification/problem solving with providing rewards for behavior change yielded a synergic effect on behavior change [69]. Future research should focus on practical application methods and evaluate which combinations of theory-based methods would increase effect sizes in social media delivered behavior change interventions.

To the best of our knowledge, this is the first publication to describe the development of a social media based intervention study using the IM protocol. Previous studies have documented successful use of IM protocol to guide the development of Web-based computer-tailored interventions for health behavior change, such as promoting regular physical activity [70,71] and healthy eating [72]. However, a health intervention delivered through a blog differs from computer-tailored interventions in the use of computer technology and the level of implication from researchers. Computer-tailoring consists of adapting health materials to one specific person through a computerized process based on prior individual assessments [73]. The development of computer-tailored interventions is a time-consuming process, but it requires minimal efforts to carry out once the creation and implementation of the intervention are executed [70]. Blogs, on the other hand, require constant attention to write personalized messages based on users' comments. Although more time-consuming, this interaction between the blogger and users allow for individualized exchanges and empathic feedback to promote behavior change. As an advantage, blogs may be operated on low-cost Web platforms that are intuitive to navigate and that require minimum programming competencies for the research team.

Blogs are increasingly used by health professionals such as RDs to share information, promote healthy behaviors, and educate and interact with the population and colleagues [74]; however, there is limited empirical evidence on how to design, evaluate, and implement blog-delivered behavioral change interventions. This study therefore has the potential to have a significant reach in the field of social media in dietetic practice by providing the first evidence on the systematic development of an evidence-informed blog written by an RD to promote adherence to dietary recommendations. Blogs facilitate lengthier content-rich conversations whose development can be traced back to the blog [75], unlike other social media tools such as Facebook, which focuses more on relationships, or Twitter, which shares short messages mostly as real-time status updates on timely issues. These conversations can offer social support to blog users [39,76] and include evidence-informed health information, expert opinions, and patient experiences [77]. Additionally, female social media users believe that such blogs make the interaction with an RD more accessible, allow the gain of credible nutrition knowledge and nutritionally balanced recipes, and allow reading of other readers' comments and links to them [19].

## Conclusions

In conclusion, this is the first study to rigorously describe the use of the IM protocol for the development of an evidence-informed blog to promote healthy eating. IM protocol allowed for effective decision making to produce a novel knowledge translation tool that could be used by health care professionals, such as RDs, to increase adherence to dietary recommendations. A randomized controlled trial is planned to evaluate the effect of the blog on dietary habits and behaviors among French-Canadian mothers of preschool and school-aged children.

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## Authors' Contributions

SD, AL, SL, JR, and VP designed the study, and A-AD conducted the literature search for the needs assessment. A-AD and AL formulated matrices of change objectives, selected theory-based intervention methods, and developed the sequence of the intervention. A-AD wrote the manuscript, and SD had primary responsibility for the final content. All of the authors critically reviewed the manuscript and approved its final version.

## Conflicts of Interest

None declared.

## Multimedia Appendix 1

Overview of the blog intervention timeline and components.

[PDF File (Adobe PDF File), 28KB - resprot_v6i5e92_app1.pdf ]

## Multimedia Appendix 2

Screenshots of the intervention blog.

[PDF File (Adobe PDF File), 6MB - resprot_v6i5e92_app2.pdf ]

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## Abbreviations

**IM:** intervention mapping
**MI:** Motivational Interviewing
**RD:** registered dietitian

Original Paper

# Using Beta-Version mHealth Technology for Team-Based Care Management to Support Stroke Prevention: An Assessment of Utility and Challenges

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## Abstract

**Background:** Beta versions of health information technology tools are needed in service delivery models with health care and community partnerships to confirm the key components and to assess the performance of the tools and their impact on users. We developed a care management technology (CMT) for use by community health workers (CHWs) and care managers (CMs) working collaboratively to improve risk factor control among recent stroke survivors. The CMT was expected to enhance the efficiency and effectiveness of the CHW-CM team.

**Objective:** The primary objective was to describe the Secondary Stroke Prevention by Uniting Community and Chronic Care Model Teams Early to End Disparities (SUCCEED) CMT and investigate CM and CHW perceptions of the CMT's usefulness and challenges for team-based care management.

**Methods:** We conducted qualitative interviews with all users of the beta-version SUCCEED CMT, namely two CMs and three CHWs. They were asked to demonstrate and describe their perceptions of the CMT's ease of use and usefulness for completing predefined key care management activities. They were also probed about their general perceptions of the CMT's information quality, ease of use, usefulness, and impact on CM and CHW roles. Interview transcripts were coded using a priori codes. Coded excerpts were grouped into broader themes and then related in a conceptual model of how the CMT facilitated care management. We also conducted a survey with 14 patients to obtain their perspective on CHW tablet use during CHW-patient interactions.

**Results:** Care managers and community health workers expressed that the CMT helped them keep track of patient interactions and plan their work. It guided CMs in developing and sharing care plans with CHWs. For CHWs, the CMT enabled electronic collection of clinical assessment data, provided decision support, and provided remote access to patients' risk factor values. Long loading times and downtimes due to outages were the most significant challenges encountered. Additional issues included extensive use of free-text responses and manual data transfer from the electronic medical record. Despite these challenges, patients overall did not perceive the tablet as interfering with CHW-patient interactions.

**Conclusions:** Our findings suggest useful functionalities of CMTs supporting health care and community partners in collaborative chronic care management. However, usability issues need to be addressed during the development process. The SUCCEED CMT is an initial step toward the development of effective health information technology tools to support collaborative, team-based models of care and will need to be modified as the evidence base grows. Future research should assess the CMT's effects on team performance.

## Introduction

Health information technology (HIT) has the potential to facilitate the delivery of collaborative, team-based approaches to chronic illness care [1]. Although such chronic care models—which often involve health care and community partnerships—can lead to improvements in patient care and health outcomes [2], implementation requires streamlined information processing, communication, and management. Bauer et al [3] described HIT capabilities that may increase the effectiveness and efficiency of chronic care delivery. These include HIT tools that enable users to create care plans that can be shared among members of the care team, provide clinical decision support, incorporate treatment algorithms, monitor patients' progress, alert providers of patients in need, and track patient visits and outreach efforts. Despite the promise of HIT to support team-based models of chronic disease care, a systematic review by Dorr et al [4] found that the most common intended users of HIT tools tend to be physicians. HIT tools for use by health care and community partners to support improved care coordination for chronic conditions have been understudied. Investigations of HIT in service delivery models with health care and community partnerships are needed to build the evidence base of how technology-enabled models of team care can improve team performance and reduce costs. To begin, beta versions of the tools need to be developed to confirm the key components and assess the performance of the tools and their impact on users.

A research team consisting of clinicians, implementation scientists, systems engineering and human factors specialists, and end users—care managers (CMs) and community health workers (CHWs)—worked with a software company to develop a care management technology (CMT) for an intervention that uses a team of care providers to collaboratively improve risk factor control among stroke survivors. This technology-facilitated intervention—called Secondary Stroke Prevention by Uniting Community and Chronic Care Model Teams Early to End Disparities (SUCCEED)—is being tested for its impact on secondary stroke prevention and cost-effectiveness analysis in a randomized controlled trial with a multiethnic, underresourced population in Los Angeles County, California [5]. The fundamental purpose of the CMT in the SUCCEED program was to facilitate more effective and efficient care management and care coordination among care team members and to facilitate encounters with patients. This paper presents results from our investigation of perceptions of care team members regarding the usefulness and challenges of the CMT for recurrent stroke prevention care management. We also discuss our experience designing, developing, and implementing the CMT and implications for researchers interested in conducting research studies using CMTs. We intended for the SUCCEED CMT to serve as an initial step toward the development of HIT tools to facilitate effective and efficient collaborative, team-based models of chronic illness care.

### SUCCEED Program Description

Recent stroke survivors enrolled in the SUCCEED program received care for 1 year from a care team consisting of a CM, who was either a nurse practitioner or physician assistant, and a CHW. The goal of the care team was to improve patients' control of stroke risk factors (ie, blood pressure, cholesterol, diabetes, diet, physical activity, smoking, alcohol, and illicit drug use) and to assess for and address complications including social isolation and depression. The team provided participants with self-management tools, including blood pressure cuffs, blood pressure logs, and risk factor goal cards. CMs, physically located in the health care system, introduced patients to self-management skills, prescribed and adjusted medications, and encouraged medication adherence. Meanwhile, in the community, CHWs reinforced self-management skills, served as liaisons between the patient and the health care system, assessed for and assisted in reducing social isolation, and educated patients about stroke risk, especially those related to lifestyle. CMs and CHWs worked collaboratively to address patients' fluctuating needs, develop and maintain care plans, communicate about patients' progress, and address barriers as they arose. A physician (vascular neurologist or cardiologist) supervised the CMs and CHWs.

**Figure 1.** SUCCEED program protocol.
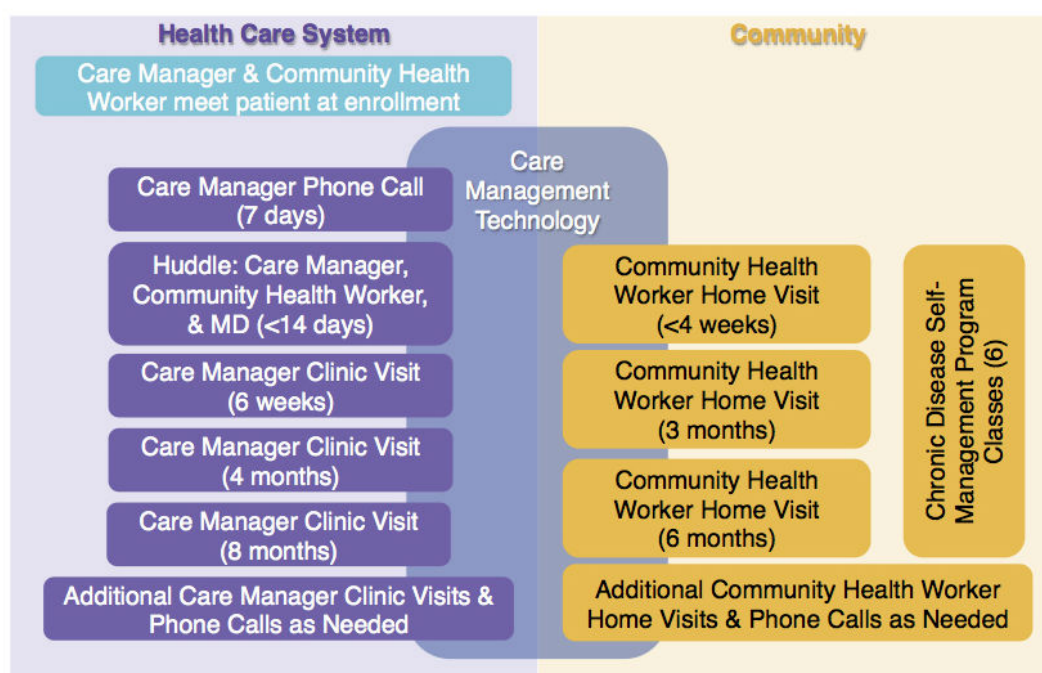


The SUCCEED program protocol (Figure 1) began when a patient was randomized into the program arm and was met by the CM and CHW in the hospital or at an outpatient clinic. The CM followed up with the patient via telephone 1 week after enrollment. During the following week, the CM, CHW, and physician reviewed the patient's status and jointly developed a care plan. During the course of the year, the patient received clinic visits and home visits by the CM and CHW, respectively. Between visits, patients received phone calls from both the CM and CHW. The patient was also encouraged to attend Chronic Disease Self-Management Program (CDSMP) workshops led by the CHW in community venues [6]. The minimum set of interactions with the patient consisted of three clinic visits and three home visits. Additional interactions took place as needed, particularly for patients with complex care needs.

## SUCCEED Care Team Recruitment and Training

Physicians trained CMs to follow evidence-based protocols and to teach self-management skills and educate patients. CHW training was two-phased. A pool of potential CHWs was recruited through community networks to undertake a 4.5-day training to become certified as CDSMP facilitators. A Master Trainer who had been certified by the Stanford University Program and was affiliated with a local community agency (Watts Labor Community Action Committee) led the training. From the pool of graduates of our CDSMP facilitator training, we recruited individuals to undertake an additional 80 hours of training. The SUCCEED research team collaborated with the Los Angeles Health care Workforce Development Program/Worker Education and Resource Center to develop the curriculum for this 80-hour training on topics specific to SUCCEED, including stroke and vascular risk factors. From the graduates of this longer training, CHWs were hired for the SUCCEED study.

## Design of Care Management Technology for SUCCEED

The CMT was expected to make achieving the target health outcome of decreased stroke risk both more effective and efficient, such that the SUCCEED program could be feasible in other public safety-net settings where resources are highly constrained yet stroke risk factor control is low. SUCCEED researchers worked with a software company to develop the CMT for use by CMs and CHWs, using an existing open-source mobile platform the company developed. The CMT consisted of a CM app containing 22 forms, a CHW app containing 24 forms, and 5 Web-based reports. CMs and CHWs accessed the apps using Android tablets. The CMT was not part of the health system's electronic medical record (EMR); any information from the EMR that was needed in the CMT had to be manually entered. The CMT was not interfaced with the EMR since the health system was in the process of implementing an EMR during the time that the CMT was being developed.

When the CMT development process began, the SUCCEED program had hired two CMs and two CHWs. All four participated in the development process by developing the content and structure of the forms and reports, testing the forms and reports in the CMT after the software company developed them, and joining regular phone calls with company representatives and SUCCEED researchers. The CMT development process spanned 2 years. The four CMs and CHWs who participated in the development process received in-person training from company representatives. Other CMs and CHWs who were hired later learned how to use the CMT on the job, with assistance from the previously hired and trained CMs/CHWs. All CMs and CHWs received CMT user guides.

The forms contained in the CM and CHW apps were designed to facilitate patient–CM, patient–CHW, and CM–CHW

interactions during each step in the SUCCEED program protocol (Figure 2). The basic structure of the apps and how forms were used in each step is shown in Table 1. For example, CHWs used the CMT during home visits to access forms that guided them in administering depression, self-management, and lifestyle habit assessments. CMs used the CMT to capture patient health information that would then be accessible to CHWs via the CHW app.

In addition to the forms accessed via the apps, CMs and CHWs could access several reports via the platform's website (Table 2). These Web-based reports were not part of the existing platform but had to be developed specifically for the SUCCEED program. CMs and CHWs could use the reports to view patient-specific care management information, including blood pressure control status, lab results, notes, previous form submissions, completed encounters with patients, and task lists.

## Methods

We conducted qualitative interviews from April to June 2015 with CMs and CHWs in the SUCCEED program.

### Participants

We interviewed all users of the CMT in the SUCCEED program at the time the interviews were conducted, namely two CMs and three CHWs. All were female, one was between 18 and 24 years old, two were between 25 and 34 years old, one was between 35 and 44 years old, one was between 45 and 54 years old, all had at least a high school diploma, and three were Latino. One CM and no CHWs had experience in stroke prevention care management prior to working in the SUCCEED program. Participants had been using the CMT between 9 and 14 months, with an average of 12 months. Both CMs and two of the CHWs participated in CMT development activities. Many of these participant characteristics, most notably, gender, are aligned with the demographic and professional profile of CHWs [7].

### Procedure

We developed the semistructured interview guide based on the Technology Acceptance Model [8] and input from SUCCEED project leaders and the software company's project manager. The interview consisted of two parts. The first part involved asking CMs and CHWs to demonstrate how they used the CMT to perform predefined key care management activities (Figure 1). Following each demonstration, they were asked to describe their perception of the CMT's ease of use and usefulness for completing the activity. The second part of the interview probed CM and CHW perceptions of the development process (if applicable), technical support, and the CMT's information quality, ease of use, usefulness, and impact on CM and CHW roles. Sample interview questions can be found in Multimedia Appendix 1. Interviews were conducted individually (by the first 2 authors), took place in a private room, and lasted an average of 4 hours (range 1-5 hours).

**Figure 2.** How CMs and CHWs use CMT forms (shown in italics) in the context of the SUCCEED program protocol.
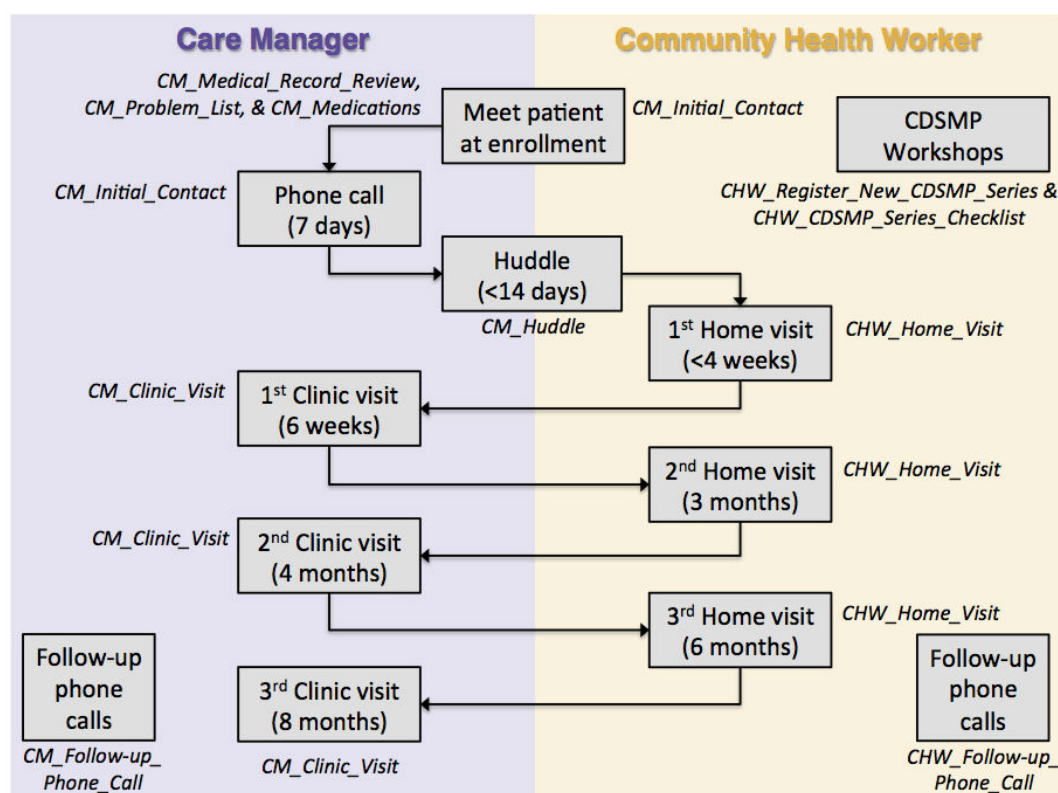
**Table 1.** Structure of CM and CHW applications.

| App | Form name | Description |
|---|---|---|
| CM | CM_Initial_Contact | Used during the first interaction with a patient after they are enrolled in the program. Used to review contact information, discuss home blood pressure monitoring, and schedule the first CM phone call. |
| | CM_Medical_Record_Review | Used to capture baseline blood pressure, body mass index, and key lab results. CMs manually populate this form using data from the hospital's EMR. |
| | CM_Problem_List | Used to capture a patient's latest blood pressure, body mass index, and key lab results. CMs manually populate this form using data from the hospital's EMR. The form is also used to develop a care plan. CMs indicate a patient's status (at goal, not at goal, not relevant) for each risk factor and can add free-form notes that are visible only to them. |
| | CM_Medications | A collection of forms, organized by risk factor, that are used to capture medications prescribed to a patient. CMs manually populate these forms using data from the hospital's EMR. |
| | CM_First_Phone_Call | Used during the first CM phone call to capture current health status, blood pressure, medication adherence, smoking status, and transportation barriers and to schedule the first clinic visit. |
| | CM_Huddle | Used during care team huddles to guide discussion about a patient. The form pulls the care plan from the Problem List and allows the team to make revisions. |
| | CM_Clinic_Visit | Used to guide clinic visits. The form pulls the care plan from the Problem List and allows CMs to make revisions. The end of the form generates a clinic visit summary that CMs can copy and paste into the hospital's EMR. |
| | CM_Follow-Up_Phone_Call | Used to document additional CM phone calls. Tasks can also be created in this form. |
| | CM_Edit_Patient_Schedule | Used to skip the next interaction that is being suggested in the Patient List report. |
| CHW | CHW_Home_Visit | A collection of forms used to guide home visits. Each form addresses a different topic: stroke literacy, blood pressure, cholesterol, diabetes, antithrombotic use, smoking cessation, depression, diet, physical activity, alcohol and illicit drug use, transportation, communication preferences, and access to care. Forms are organized into 6 sections: assessment, information provision, self-management and adherence, adjustment of medications, clinical support, and resource provision for the patient. Tasks can be created in any of the forms. |
| | CHW_Review_of_Key_Patient_Data | Used to view the care plan, baseline and latest values for various stroke risk factors, latest medications, which home visit forms have been completed, and a patient's contact information. |
| | CHW_Follow-up_Phone_Call | Used to document additional phone calls by the CHW. Tasks can also be created in this form. |
| | CHW_Register_New_CDSMP_Series | Used to register a new CDSMP workshop series, which consists of 6 weekly sessions. The form captures details such as session dates and meeting location. |
| | CHW_CDSMP_Series_Checklist | Used during each of the 6 CDSMP sessions to document patient attendance and self-management goals. |
| CM and CHW | CC_Edit/Update_Patient_Info | Used to update a patient's home address, preferred language, phone number, family contact information, and primary care physician information. |
| | CC_Add__Appointment | Used to capture a patient's appointments with health care providers outside of the SUCCEED care team. |
| | CC_View/Update_Appointments | Used to view a list of appointments with health care providers outside of the SUCCEED care team, update the appointment details, or close a completed appointment. |
| | CC_Create_New_Task | Used to create a new task. Tasks can be assigned to another care team member. |
| | CC_Task_List by_Panel_ | Used to view a list of all CM–CHW care team tasks for all patients. The list cannot be filtered by person responsible for completing the tasks (CM or CHW). A task can be revised or closed once it has been completed. |
| | CC_Task_List_by_Patient | Used to view a list of all CM–CHW care team tasks for a specific patient. The list cannot be filtered by person responsible for completing the tasks (CM or CHW). A task can be revised or closed once it has been completed. |

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**Table 2.** Description of Web-based reports.

| Report name | Description |
| --- | --- |
| Patient List | Displays a list of all patients and key data such as date of patient enrollment in program, next suggested interaction per the SUCCEED program protocol, and blood pressure control status. |
| Patient Information | Displays select data about a patient, including contact information, primary care physician information, lab results, and notes. |
| Form Submissions | Displays a list of all forms that have been submitted for a specific patient. Forms on the list can be opened to view a readable version. |
| Interactions with Patients | Displays, at the patient level, the minimum set of interactions with patients and their target completion dates per the SUCCEED program protocol. When an interaction has been completed, the report shows the date of completion and the name of the care team member who completed it. The report displays an alert when an interaction is overdue. Additionally, it provides a snapshot of risk factor control status. |
| Care Management Tasks | Displays a list of all CM–CHW care team tasks for all patients. The list can be filtered by person responsible for completing the tasks (CM or CHW) and by patient. A task can be revised or closed once it has been completed. |

## Data Analysis

Interviews were audio recorded and transcribed verbatim, resulting in 500 pages of transcripts. Dedoose version 7.1.3 (SocioCultural Research Consultants) was used to manage and code the data. Two members of the research team (the first 2 authors) developed an initial coding scheme that included a priori codes derived largely from literature on the impact of HIT on workflow, unintended consequences of HIT, technology acceptance, and care coordination models [9-13]. Three coders (including the first author) then coded 60 pages of transcripts independently. Coding discrepancies were discussed with the second author until consensus was reached. New codes were added and code definitions were adjusted for clarity. The same individuals independently coded the remaining pages of transcripts (each page was coded by 2 individuals) and met regularly with the second author to discuss and resolve any coding discrepancies. The coded excerpts were grouped into broader themes and then related in a conceptual model of how the CMT facilitated care management activities. These interpretations were shared with the larger research team for final review.

## Patient Survey

We conducted a patient survey in order to obtain the perspective of patients regarding CHWs' use of tablets during home visits. After patients completed the SUCCEED exit interview, they were given an informational flyer that invited them to participate in a new research study. Interested patients consented to being called by a research assistant who explained that the research study entailed a one-time survey. Patients were eligible to participate in the survey if they received at least two home visits from a SUCCEED CHW. If patients were eligible, they met in person with the research assistant who administered the survey in English or Spanish. All patients provided written informed consent. The survey consisted of 16 Likert-type questions. Examples are, "To what extent do you agree or disagree that the tablet computer helped the CHW explain your condition and how to care for it?" and "To what extent do you agree or disagree that the CHW's use of a tablet computer made home visits feel less personal?" At the end of the survey, patients were asked if they wanted to comment on the CHW's use of a tablet during home visits. Responses were recorded verbatim. The

Institutional Review Boards at the University of California, Los Angeles, University of Southern California, and Rancho Los Amigos National Rehabilitation Center approved the patient survey procedures. Patients who completed the survey received a US $20 gift card.

## Results

CMs and CHWs described their perceptions on the usefulness and challenges of the CMT's intended functions (summarized in Table 3). In addition, they discussed broader usability issues of the beta-version CMT that disrupted their use of the tool. Patient responses to the survey of CHW tablet use are described.

### Care Management Technology Usefulness and Challenges

Overall, CMs and CHWs expressed that the CMT was useful in helping them to perform key aspects of stroke prevention care management (Figure 3). Statements by CMs and CHWs indicated that the CMT helped them keep track of their interactions with patients and plan their work accordingly to ensure that patients received the minimum set of interactions per the SUCCEED program protocol. CMs thought the CMT was helpful for developing care plans and sharing these plans with CHWs in the field. CHWs reported that the CMT enabled electronic data collection of clinical assessments and provided decision support when performing patient education and self-management training. According to CHWs, the CMT was helpful for tracking patients' stroke risk factor values and accessing these values and other important patient-specific care management information remotely during home visits. Finally, CMs and CHWs explained how the CMT had necessary features in place for facilitating task management and coordination—namely, documenting work by creating personal tasks and tasks for other team members, tracking tasks, viewing task lists—but cited usability problems as a barrier to use.

CMs and CHWs experienced several challenges when using the CMT. The number of clicks and screen changes needed to create, update, or close tasks deterred CMs and CHWs from using the CMT for task management. Additional issues resulted from limitations of the platform, including the inability to link to educational materials outside the platform or to generate graphics of risk factor values over time. Finally, issues with the

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design of the CMT's content—extensive use of free-text responses, lengthy forms, and especially the manual transfer of data from the EMR to the CMT—severely hindered CM and CHW efficiency.

## Care Management Technology Usability Issues

The main challenge to using the CMT was long loading times, as evidenced by the numerous statements from both the CMs and CHWs expressing their frustration. The slow response times created an unpleasant user experience. As one CHW stated, "[The CMT] is so painfully slow." It hindered CM and CHW productivity because they could not move freely and keep their attention focused on the task at hand; they reported performing other tasks while waiting for the CMT to finish loading. The consequence was that some participants bypassed the CMT entirely for certain care management activities, developing their own ways of accomplishing the work with greater efficiency. CMT reliability was another barrier that was reported. It was not uncommon for the CMT to be down for an unspecified period of time and without warning. CM workflow was significantly affected, especially if it happened during clinical huddles or clinic visits. One CM said that the CMT's reliability issues made her feel "anxious and vulnerable" during clinical encounters. For this reason, she reported printing CMT form submissions as a backup.

**Table 3.** CM and CHW perceptions on the usefulness and challenges of the CMT's intended functions.

| Intended CMT functionality | Usefulness | Challenges |
|---|---|---|
| Facilitate implementation of the SUCCEED program protocol | Provided list of patient interactions, suggested completion dates, and provided actual completion dates | Decreased efficiency by increasing amount of steps needed to extract certain types of information |
| | Allowed CMs to view completed and pending CHW interactions (and vice versa) | Did not always have accurate or complete information of patient interactions |
| | Provided dates that helped with prioritizing patients with upcoming graduations in order to meet minimum required patient interactions | Did not allow CMs and CHWs to add additional patient interactions beyond minimum set nor change order in which they wanted interactions to occur/be displayed |
| Guide development of care plans | Enabled CMs to indicate whether each risk factor was controlled | Did not specify who could add and view free response notes, causing confusion among CMs and CHWs about how to use free response notes |
| | Enabled CMs to display care plans during huddles and make any necessary adjustments in real time | |
| | Reminded CMs and CHWs what risk factors to focus on during clinic and home visits, respectively | |
| Facilitate task management and coordination | Enabled CMs and CHWs to create personal tasks and tasks for other team members, track tasks, and view task lists | Required undue effort to create task |
| | | Did not allow CMs and CHWs to filter tasks by person responsible when viewing task list using app |
| Facilitate clinical assessments and provide decision support | Eliminated paper forms and manual documentation during home visits | Contained lengthy forms that made form navigation difficult |
| | Guided CHW-patient conversations and tailored forms in real time | Created additional steps in workflow because it did not directly link to educational materials |
| | Prompted CHWs to take specific actions to address patients' unique needs | Made extensive use of fields requiring free-text responses |
| Track risk factor control goals | Capable of tracking patients' risk factor values | Did not display or provide easy access to all of patients' risk factor values collected over time |
| | Displayed patients' baseline and most recent risk factor values | Could not generate useful visualizations to display for patients |
| Provide access to patient health information | Enabled CHWs to immediately access patient health information during home visits | Required CMs to manually transfer data between CMT and EMR, which was time consuming, subject to errors, and difficult to keep current |
| | | Contained incomplete information for CHWs during home visits when CMs had not completed data entry |

**Figure 3.** A conceptual model showing CM and CHW perceptions of how the CMT facilitated care management activities involving interactions between three key players: patients and CMs, patients and CHWs, and CMs and CHWs.
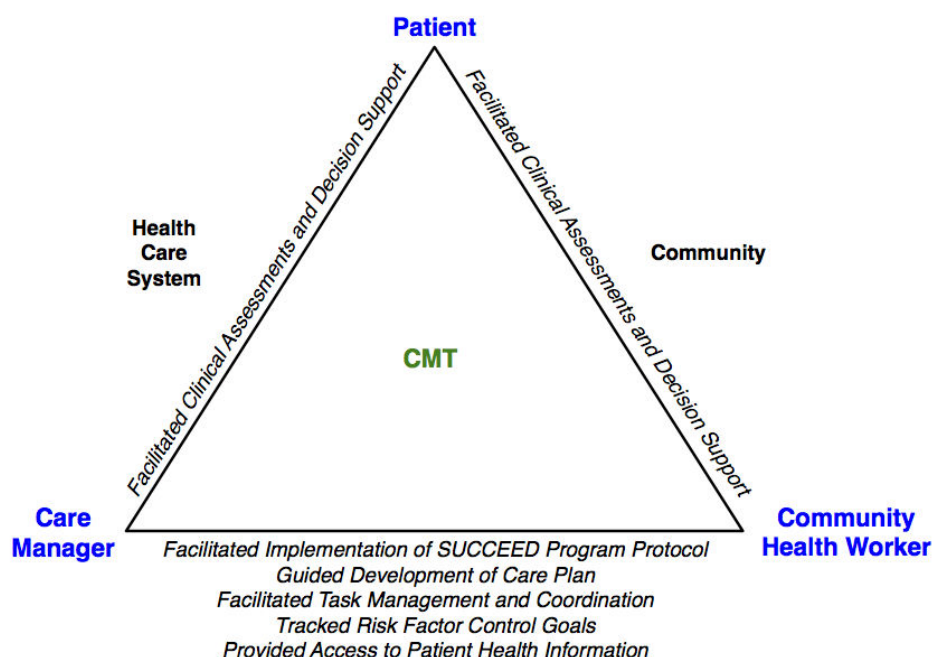


## Patient Perspective of Community Health Workers' Tablet Use

Out of 25 who were approached and consented to being contacted by the research assistant, 14 patients completed the survey. Patient characteristics and responses to each item in the survey are shown in Multimedia Appendix 1. The average age of survey respondents was 54 years, 71% (10/14) were male, and 64% (9/14) were Latino. Overall, patients viewed favorably CHWs' use of a tablet during home visits. For example, all patients agreed or strongly agreed that the tablet helped the CHW explain their condition and how to care for it. All patients agreed or strongly agreed that they were comfortable talking to the CHW about their health when she used the tablet, and only one patient agreed that the CHW's use of a tablet made home visits feel less personal. Furthermore, several patients described specific ways in which the tablet computer enhanced the CHW-patient interaction during home visits: ability to view patients' prescribed medications and lab values, guide which questions to ask patients, reduce paper-based documentation, and print patient handouts.

## Discussion

### Principal Findings

The overall assessment by CMs and CHWs was that the CMT was useful in terms of its intended functions of facilitating implementation of the SUCCEED program protocol, guiding development of care plans, facilitating clinical assessments and providing decision support, tracking risk factor control goals, and providing access to patient health information. On the other hand, CMs and CHWs encountered usability problems that made it difficult to use the tool as it was intended for task management and coordination. In addition, problems with the

CMT's performance had a substantially negative effect on the user experience.

The CMT functionalities that CMs and CHWs in this study found to be useful are aligned with some of the ways it was proposed in a systematic review that HIT could support effective collaborative care [3]. These included providing data about patient interactions and highlighting interactions that have not occurred, making the care plan visible and allowing it to be shared across care team members, enabling care team members to document clinical data, making clinical data accessible to all members of the care team (not just clinicians), and providing decision support. Providing alerts for patients who are not improving has also been suggested as an HIT capability for supporting collaborative care models, but this was not mentioned as a potentially useful CMT functionality by CMs and CHWs in our study. Given the promise of using electronic provider alerts to effectively improve blood pressure control [14], the next iteration of the CMT design could include alerts for when patients' risk factor values are not at goal and future research could examine CM/CHW acceptance and impact of these alerts.

Like CMs and CHWs in our study, there is consensus among experts that important HIT components for supporting team-based models of chronic illness care include the ability to conduct clinical assessments and surveys, display a patient's progress in terms of the long-term treatment plan, and provide graphs of outcomes over time to show patients [15]. Unlike our findings, experts have also identified as important the ability to present a history of treatment. Perhaps the CMs in our study did not mention this as a desirable CMT feature because the information was available in the EMR, which was used alongside the CMT when needed. Nonetheless, it may be helpful if health care and community partners alike can easily determine what everyone in the care team is currently doing and has

previously done [16], which is information that may not necessarily be available in the EMR.

## Lessons Learned

We summarize the key lessons that we learned from designing, developing, and implementing a CMT in the SUCCEED program. Our experience may help other researchers who are also considering customizing an existing platform for use in studies of how CMTs enhance team-based care for chronic disease management.

### Lessons 1: Ask Vendor Key Questions

Prior experience indicates that it is best to ask potential vendors to walk through how their product would be used to accomplish predefined scenarios [17]. However, when scenarios cannot be demonstrated because no existing platforms have the desired functionality, as was the case for the SUCCEED program, we determined critical questions to ask during the vetting process. We asked potential vendors whether they could develop additional features to meet the needs of the program, and we incorporated that scope of work into the contract. If we could do this process over, we would negotiate and agree on what would happen if the development of these new features negatively affected the system. Are the vendor's efforts to fix these potential problems included in the cost of the system? How soon after problems are discovered will the vendor look into them to figure out a solution? The contract would then specify, as the National Learning Consortium has recommended [17], the conditions under which a breach of contract has occurred.

### Lessons 2: Carefully Select Essential Data That Should Go Into Care Management Technology

We also learned that it is vital for the data entered into the CMT to complement rather than duplicate data that are already available in the health system's EMR. A systematic review found that mobile technologies are most commonly used by CHWs to collect health data [18]. However, SUCCEED CHWs needed to be able to both collect and retrieve data while in the field. There was no guidance in the literature about the necessary data elements to include in the CMT for CHW retrieval. We had intended for CMs to use the CMT to document and share with CHWs only key pieces of data needed for CHW work. However, we lost sight of this vision in the midst of the long process of customizing the platform. Consequently, some CM data collection forms ended up requiring that CMs enter information from the EMR that was not essential. This adversely affected their efficiency given that they had to manually transfer the data. Until CMTs and EMRs are compatible, which we predict will eventually happen, careful selection of which essential data should go into the CMT will help to reduce duplication.

### Lessons 3: Engage More Experienced End Users in the Design Process

We learned that it is important to engage more experienced users in the design process to think critically about the necessary CMT components, and for project leaders to make a distinction between must-have versus nice-to-have components. Indeed,

the user-centered design literature recommends involving users with high levels of competence and experience [19]. However, because the SUCCEED program was a new model of care, the end users who were actively involved in designing the workflows and the CMT did not have experience with the type of care management and care coordination that would be required. Instead, these CMs and CHWs, working with the project's scientific and clinical leaders, designed both the workflows and the CMT based on a projection of what would be needed. The lack of experience of the end users—a consequence of this being a new approach to care—partially contributed to building a system that was more complicated than necessary. Because platforms may have a limited amount of processing power, design teams should err on the side of caution and focus on developing the must-haves first. Then, if the CMT is performing as expected, teams can work on the nice-to-haves, as time and resources permit.

### Lessons 4: Apply a Structured, Iterative Approach When Improving the Care Management Technology

After implementation, CMs and CHWs reported to the vendor performance issues they encountered when using the CMT. Generally, the vendor would plan a fix and often but not always communicate with the end users when the fix had been implemented. In addition, there was not a closed loop, systematic tracking mechanism to determine the effects of the fix for end users, including both intended and unintended effects. We need to apply a structured, iterative approach when improving the CMT to assess whether the changes actually produced the desired results. The plan-do-check-act cycle could serve as a model [20]. When an issue is reported and the vendor plans and communicates the timing of implementing a fix, the vendor, end users, and project leaders would all agree on tracking data and a process for assessing the impact of the fix. The vendor would plan further improvements if the feedback indicated that they were necessary. Ideally, such performance issues would be addressed during the development phase instead of after the CMT has been implemented.

## Limitations

This study was limited to a small sample of CMT users, some of whom also helped design the SUCCEED CMT. Thus, the interviewed participants may not necessarily represent the larger user population. However, the sample size is consistent with findings from user-experience research indicating that 5 users can detect most problems [21]. Additionally, we believe that participants' experience with using the CMT prior to this study enabled them to readily assess the CMT's usefulness. A second limitation was that the CMT evaluated in this study was designed specifically for stroke prevention. The findings about useful CMT components may therefore not be generalizable to CMTs for other chronic conditions. Nonetheless, care management and care coordination for people with multiple health and social needs, such as the patients in the SUCCEED program, share similar elements [8], suggesting that our findings of perceived useful components may also be useful to care teams beyond stroke prevention. A third limitation is that the CMT evaluation involved a product in its beta stage of development. There were no guidelines regarding the range of CMT

functionalities needed for collaborative, team-based models of care. The development team erred on the comprehensive side and hence may have caused more usability issues than a mature product would present.

## Conclusions

The CMT used in the SUCCEED program is an initial step toward the development of effective HIT tools to support collaborative, team-based models of care. The CMs and CHWs we interviewed generally perceived the CMT as useful for stroke prevention care management. Our findings suggest useful functionalities of CMTs supporting health care and community partners. These functionalities include enabling users to collect clinical assessment data from patients, access patient information, develop a care plan, track implementation of the program protocol, track risk factor control goals, manage and coordinate care tasks, and receive decision support during patient interactions. Efforts to implement CMTs, however, will be futile unless usability issues are properly addressed during the development process. The CMT will need to be modified as the evidence base grows. Future research should go beyond user perceptions of the CMT's usefulness by assessing the CMT's effect on team performance. If the SUCCEED intervention is shown, once the trial is completed, to improve stroke risk factor control, we anticipate disseminating this model of care broadly and encouraging uptake in safety-net health care settings that are implementing team-based models of chronic illness care.

## Conflicts of Interest

None declared.

## Multimedia Appendix 1

CM and CHW interview questions, patient characteristics, and patient survey results.

[PDF File (Adobe PDF File), 236KB - resprot_v6i5e94_app1.pdf ]

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## Abbreviations

**CDSMP:** Chronic Disease Self-Management Program
**CHW:** community health worker
**CM:** care manager
**CMT:** care management technology
**EMR:** electronic medical record
**HIT:** health information technology
**SUCCEED:** Secondary Stroke Prevention by Uniting Community and Chronic Care Model Teams Early to End Disparities

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<u>Original Paper</u>

# Development of a Modular Research Platform to Create Medical Observational Studies for Mobile Devices

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## Abstract

**Background:** Observational studies have proven to be a valuable resource in medical research, especially when performed on a large scale. Recently, mobile device-based observational studies have been discovered by an increasing number of researchers as a promising new source of information. However, the development and deployment of app-based studies is not trivial and requires profound programming skills.

**Objective:** The aim of this project was to develop a modular online research platform that allows researchers to create medical studies for mobile devices without extensive programming skills.

**Methods:** The platform approach for a modular research platform consists of three major components. A Web-based platform forms the researchers' main workplace. This platform communicates via a shared database with a platform independent mobile app. Furthermore, a separate Web-based login platform for physicians and other health care professionals is outlined and completes the concept.

**Results:** A prototype of the research platform has been developed and is currently in beta testing. Simple questionnaire studies can be created within minutes and published for testing purposes. Screenshots of an example study are provided, and the general working principle is displayed.

**Conclusions:** In this project, we have created a basis for a novel research platform. The necessity and implications of a modular approach were displayed and an outline for future development given. International researchers are invited and encouraged to participate in this ongoing project

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**KEYWORDS**

mHealth; telemedicine; mobile health; app-based study; research platform

## Introduction

In recent years, mobile devices, such as smartphones and tablet computers, have become an important data acquisition tool in observational studies. Only in the last two decades have researchers noted a shift from traditional paper-based surveys to Web-based questionnaires [1-3]. The rapid spread of mobile phones and other devices, as well as the increasing functional abilities of those devices, has led to yet another shift in technologies that we are currently experiencing. An increasing

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number of medical professionals from various disciplines, for example, dermatology [4], psychology [5], gynecology [6], and pulmonology [7], are conducting studies based on mobile apps. While some reasons may be individually motivated, a number of advantages drive this development. In particular, "[t]hese research apps enhance widespread participation by removing geographical barriers to participation, provide novel ways to motivate healthy behaviors, facilitate high-frequency assessments, and enable more objective data collection" [8] by collecting the data in a domestic setting.

Piwek et al [9] have analyzed what prevents mobile phones from being the standard research tool for psychologists and conclude that "[s]martphones may only become an asset […] when development software that is both easy to use and secure becomes freely available." In conclusion, the authors identified three reasons that limit the extensive growth and further use of mobile devices for research studies: (1) programming barriers, (2) consenting issues, and (3) concerns regarding privacy and data security.

The project presented in this paper depicts a Web-based platform solution aimed at solving these limiting factors with a clear focus on programming barriers and data security. The platform allows the creation of study apps without programming skills.

## Methods

The concept of our modular research platform focuses mainly on usability and an easy-to-use approach. A Web-based user interface to build studies (StudyBuilder) and to analyze ongoing studies (StudyAnalyzer) forms the key component of the platform. All created studies are stored in a database and become available via the study app (ResearchApp: ParticipantView). More complex studies, which exceed simple questionnaires to be answered by a participant, require the option to enter specific medical information by a medical professional. This feature is realized by a third essential component provided for doctors and other medical professionals (DoctorsView). Figure 1 gives a schematic overview of the general concept followed in this work without the DoctorsView.

In order to allow a flexible study design, a thorough analysis of essential components and required functions was necessary. Apple ResearchKit breaks down every observational app study into an introduction, an eligibility check, an informed consent, questionnaires, and surveys. Participant profiles, as well as sections with general information and progress of the study, are often included but not essential. Figure 2 depicts this concept [10-12].

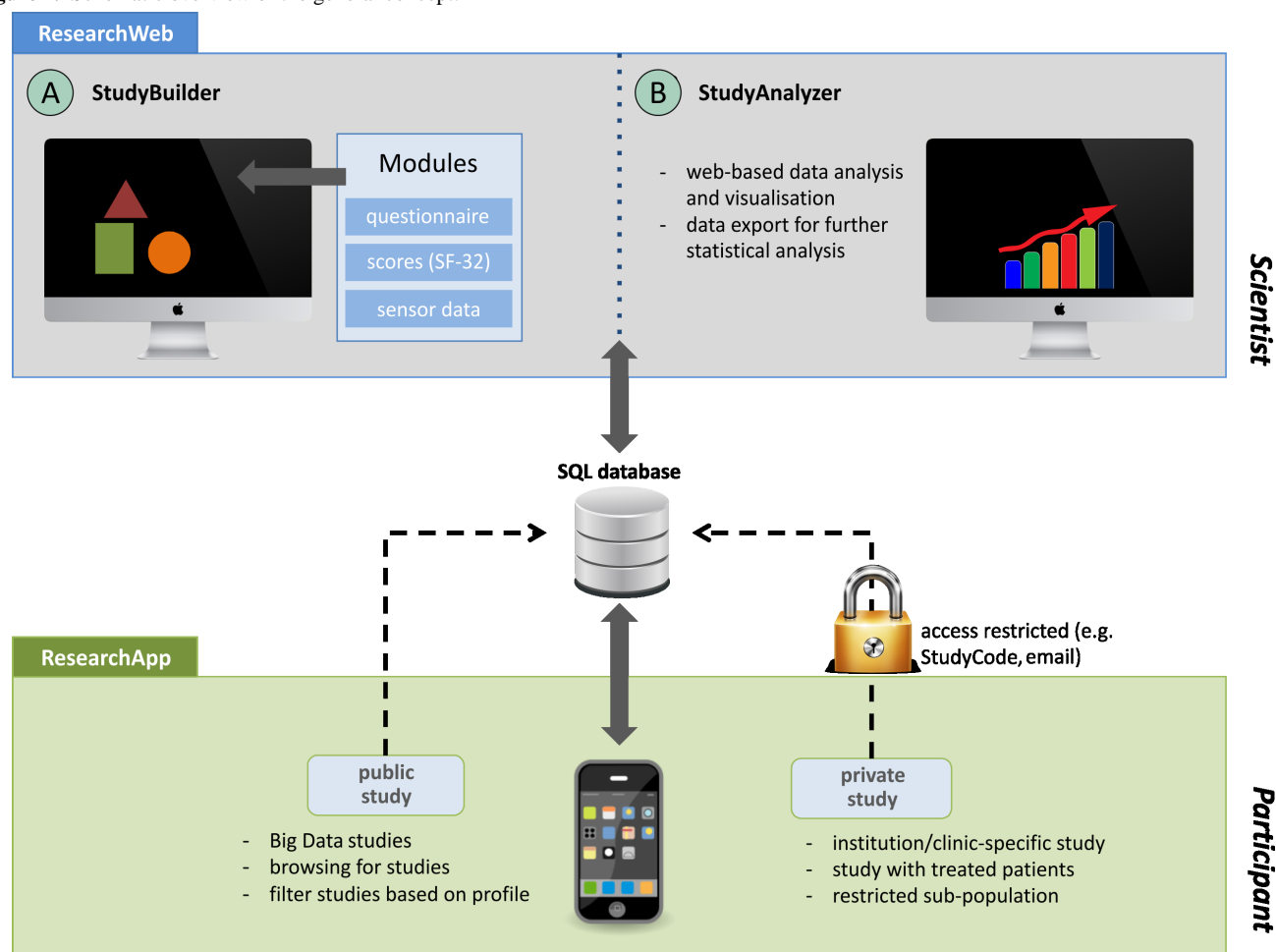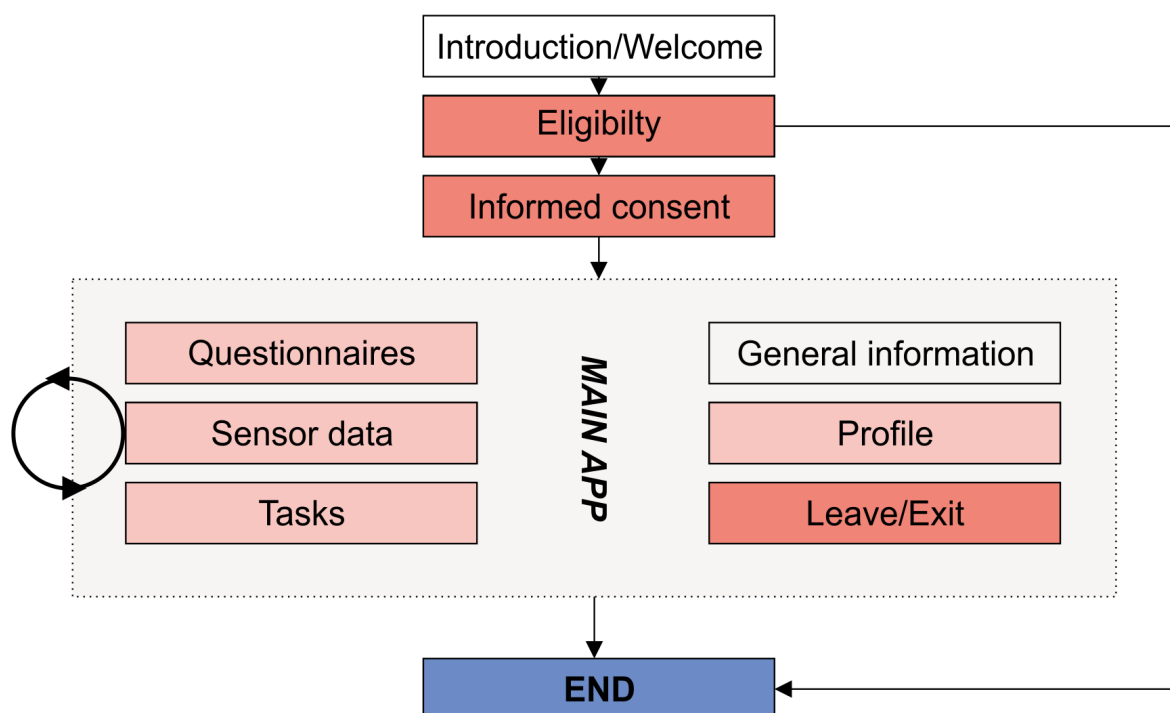**Figure 1.** Schematic overview of the general concept.

**Figure 2.** General concept of app-based observational studies. Red colored modules are mandatory.



## Module: Questionnaire

We further considered how app-based questionnaires are conducted and which functionality is needed. The required components can be broken down into different question types, transitions, and intervals. Question types can be open questions, multiple-choice questions, scale questions, and many more various kinds. In our terminology, transitions describe the flow within a study and intervals allow any sort of timing. All aspects are defined in more detail below.

Primarily, the concept of *modules* was introduced to manage studies. Each study consists of at least one or multiple modules (ie, questionnaires). Possible other modules are tasks, sensor data, reminders, and tips. In the current version of the research platform, only questionnaires are available and all further discussion in this work is limited to questionnaires. Every questionnaire consists of one or multiple questions. Each question is considered to be an *element* of the module.

Elements within a module and modules within a study are by default sequentially connected. When the last element of the last module is completed, the study is completed.

*Transitions* allow one to customize the flow of a study. A transition defines what is supposed to happen next, given external or internal conditions. A transition can define (1) a jump to a specific element (eg, question), (2) a jump to another module, (3) repetition of the same module, or (4) termination of the study.

The internal or external conditions can be determined simply by the outcome of one element (eg, answer to question 3 is yes), any numeric outcome (eg, age >30), a combination of numeric outcomes (eg, Comparative Pain Scale value 5 + continuous hours with this pain) or the overall outcome represented in a

key figure out of multiple answers (eg, sum(), max(), avg(), min()). This idea also allows researchers to use established scores (eg, Short Form-36, Wells-Score, $CHA_2 DS_2$-VASc) to trigger transitions and influence the study flow.

In many studies, a timed execution of a module is desired. This may be regularly (eg, every 4 weeks) or with respect to a condition (eg, 6 weeks after surgery). The concept of *intervals* was introduced to (1) allow a timed execution of modules and (2) store answers and outcome of a module with respect to an interval.

By default, the study starts with the first module and ends with the last. The user can determine further starting modules that will also be triggered when the study begins, independent of any other events. This initiates a separate module flow.

## Module: Introduction, Eligibility Check, and Consent

Torous et al and Hwang et al [13,14] discussed the complexity of app-based eligibility checks and an informed consent. In summary, it can be stated that this issue is highly dependent on responsible ethics committees and applicable law in the country or region of the research institution. Again, the focus of our work is to provide tools within the research platform that facilitate principal investigators of a study adapting predefined solutions for their individual purposes. As concluded by Eysenbach et al [15], every medical study—app-based observational studies are no exception—require an eligibility check and an informed consent in order for participants to enroll. This project distinguishes between two main options: (1) a fully app-based information, eligibility check, and informed consent and (2) a paper-based enrollment by a doctor. The StudyBuilder provides an eligibility module that checks the inclusion criteria for the study and an informed consent module that allows a customized app-based consenting. A separate module is

provided allowing a doctor to inform participants about a study and using the app only for support. This module is available only for closed, non-public studies. Different study types are as follows.

## Technical Architecture

The prerequisite for the concept presented in this paper is a centralized database structure. Data security and privacy are often mentioned as a disadvantage of mobile studies and reasons for researchers and participants to refrain from app-based studies [16,17].

Piwek et al [9] mention that data security is certainly not one of the strong sides of most medical professionals and thus requires the involvement of cost-intensive information technology specialists or computer science departments. A centralized data structure and shared research platform for numerous projects and research groups, as proposed in this work, eliminates the necessity to develop individual solutions regarding data security.

A structured query language database has been created that is stored on a webserver located in an independent German medical research foundation. Comprehensive German and European Union data protection law regulates the general conditions. High-end encryption algorithms have been implemented on the secure server, incremental backups are transferred to secure locations regularly, and all communications have been secured using secure sockets layer protocols. Most importantly, the established security level is continuously maintained and enhanced to meet new requirements and regulations.

## Customization, Language Support, and Study Publication

All studies can be customized and managed using the StudyBuilder. Customizing allows setting a study logo, colors, and institutional logos of the sponsor or research foundation. Currently English, French, Spanish, and German are the supported languages of the research platform. All studies may be created with single- or multilanguage support.

The StudyBuilder controls publication, pausing, and termination of studies. Each study may run in a predefined timeframe but may also be paused or terminated at any point by a (senior-) scientist. Studies may be published publicly or privately. Private studies are accessible only with an access code (StudyCode). This feature enables researchers to create studies for a predefined group of participants, for example, treated patients or within a specific institution. Public studies are available worldwide and may be accessed via the study browser in the participant app.

## User Concept, Profile, and Information

Research is never a one-man show. Representing the complexity of research institutions in a Web-based research platform is challenging. We propose a solution with defined user roles for the Web-based research platform (Figure 3). Every user is assigned to an organization. Users may sign up to the research platform themselves or may be invited by email. The email contains a sign-up link. After completing the registration process, the user is either auto-verified, -approved, and -assigned by an institutional email address or they may request a new organization or enter an existing organization. A user may incorporate different roles in different studies.

**Figure 3.** User concept for the Web-based part of the research platform (StudyBuilder and StudyAnalyzer).

| Level | Description |
| --- | --- |
| **Super-Admin** | is product owner and manages organizations |
| **Orga-Admin** | manages user access and all other general matters of the organization |
| **Senior-Scientist** | can publish studies |
| **Junior-Scientist** | can create studies, but cannot publish or terminate studies manually |
| **Assistant** | can answer user questions and view the study structure and configuration, but cannot edit existing or create new studies |
| **Supervisor / Facilitator** | can access study data and complete participant modules (assigned to doctors or nurses) |
| **Read-only** | can see everything, but cannot create / change anything |

**Figure 4.** Screenshots of the current beta version of the a) StudyBuilder and b) StudyAnalyzer.
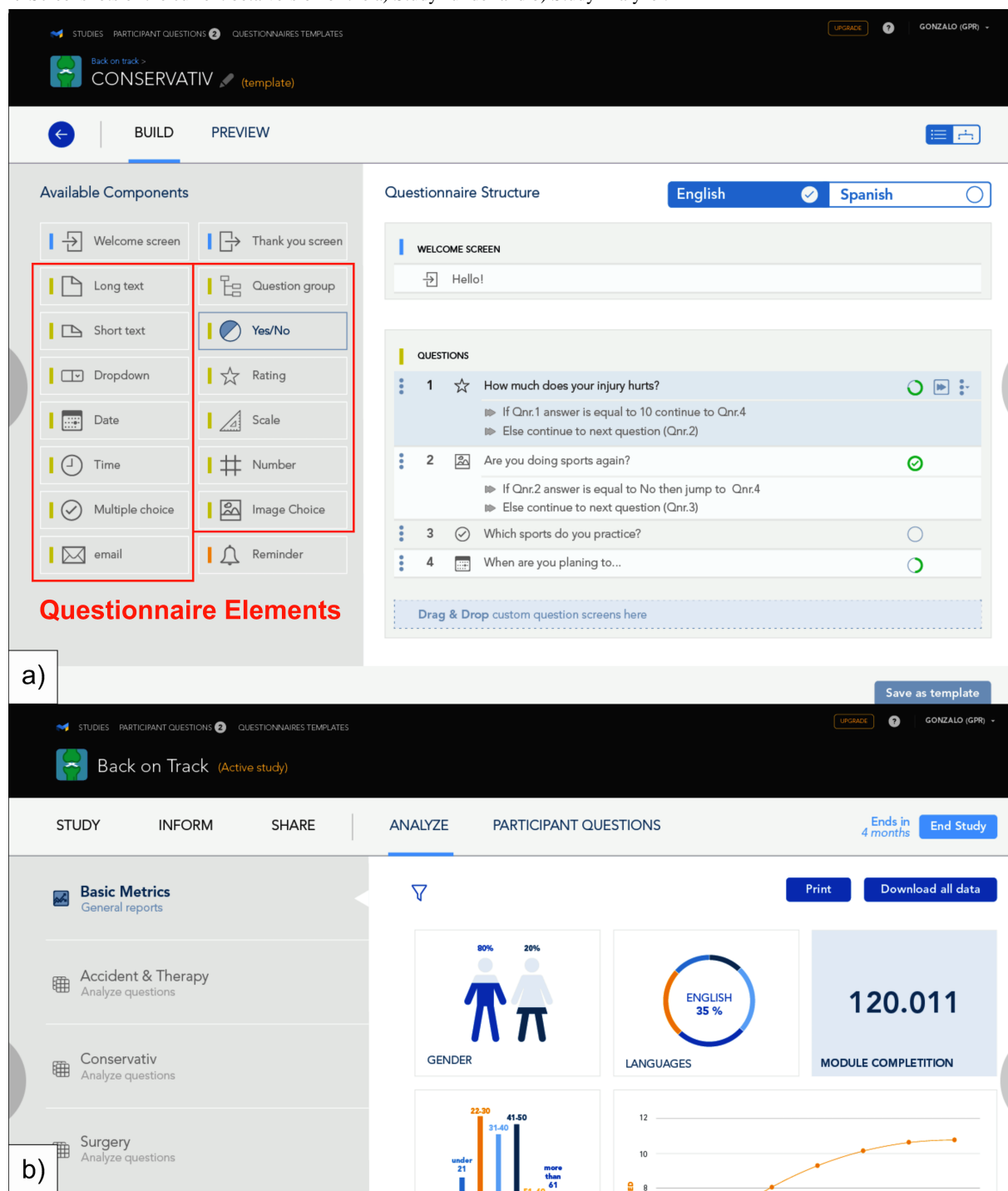


## Results

In January 2017, a beta version of the proposed research platform was completed and made available for a chosen group of testers. Figure 4 shows screenshots of the StudyBuilder and StoryAnalyzer. The StudyBuilder features multilanguage support and allows the composition of studies out of 13 prebuilt question types. In the current version, the StudyAnalyzer delivers basic demographic data on each study. A full dataset can be downloaded for further processing and statistics.

Several steps of the ParticipantView of an example study are displayed in Figure 5. Each participant has to register to the research platform with basic demographic information. Then, every user can join one or multiple studies.

Within the first 12 months of this 24-month long project, we successfully developed a running prototype of a novel research platform to simplify app-based medical studies. The prototype consists of a strong database structure—a Web-based platform that can be used to easily create simple studies within minutes. Furthermore, it is possible to publish those studies for use in a study app. Studies can by multilingual and support complex user hierarchies.

**Figure 5.** ParticipantView of an exemplary study created with the research platform.
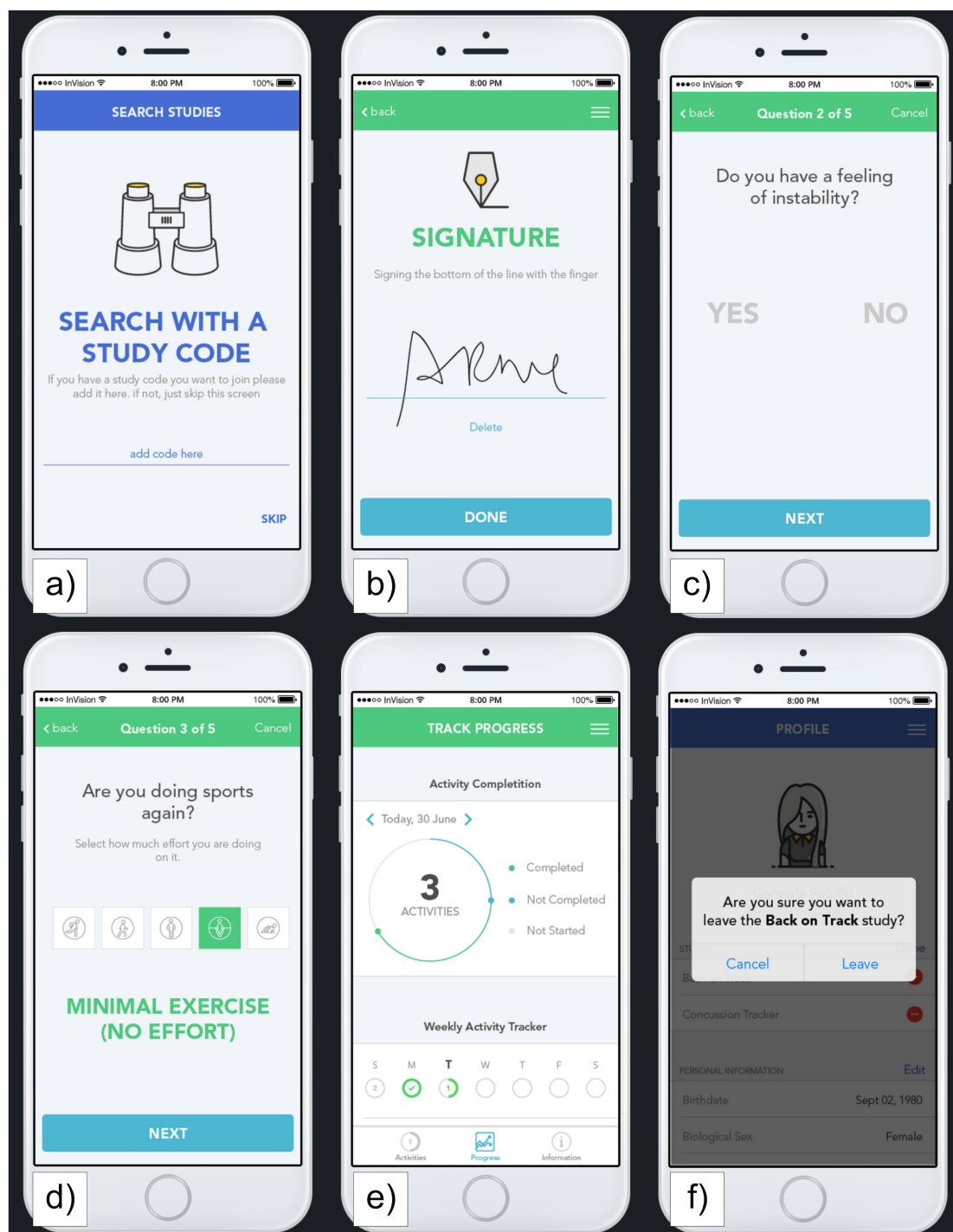


## Discussion

### Principal Considerations

This work presents a novel research app development platform that allows the creation of mobile research apps without the need for programming skills.

In recent years, we have seen an increasing number of medical studies supported or entirely based on mobile apps. So far, little is known about the impact and merit of this technology, but first results are promising when this method is used adequately [8]. Specifically the psychology [18,19] and epidemiology [20]

fields, but also every other medical discipline, are hoping to benefit from this technology and gain new insights regarding prevalence, diagnosis, and treatment of diseases [11,21].

Early studies, however, have identified challenges to this new technique, mainly programming and other technical issues [10,22]. In our opinion, it is neither cost-efficient nor time-efficient to develop individual apps for each study. The research platform we present lowers costs and improves quality as well as data safety. Apart from that, synergy effects in acquisition of participants are possible. A platform with possibly hundreds or thousands of studies might attract participants to

join multiple studies or to take note of other studies and recommend those to family and friends.

The modular platform is itself built out of modules. Further functionality is planned and will be added throughout the entire first development period of 24 months.

## Comparison With Prior Work

In March 2015, Apple, Inc. announced the launch of ResearchKit, an open-source framework aimed at revolutionizing medical research studies. Until today, Apple is the only major software company providing such a framework [9]. During the initial presentation and announcement, the framework was described as a simple and easy-to-use tool for medical specialists. First studies [4,9,10,12,21] mutually agree that Apple has missed this goal of simplicity. Significant Object C or Swift programming skills are necessary to achieve a fully functional app.

Apart from that, ResearchKit supports only iOS devices. However, the majority of all mobile devices sold and being distributed is based on an Android system (Open Handset Alliance) [23]. This disadvantage has been recognized and addressed by two independent project groups. One of those being ResearchStack [24], which is maintained by Cornell Tech's Small Data Lab and Open mHealth. A different solution called ResearchDroid [25] is commercially available and provided by Applied Informatics Inc.

ResearchStack is a fully functional software development kit and user experience framework aimed at developing research apps for Android devices. The framework is comparable to ResearchKit and aims at speeding up the transfer process for existing ResearchKit apps. This is achieved by "offer[ing] enough shared functionality and a common framework and naming scheme" [24].

ResearchDroid is "an Android library developed for automating survey forms and information consent building process" [25]. The library is very similar to the initial version of ResearchKit but allows the creation of Android instead of iOS apps.

ResearchKit, ResearchStack, and ResearchDroid have in common that all projects provide software libraries, frameworks, and development tools that require extensive programming skills to create apps. Appbakery (TrialX) [22,26], on the contrary, is the solution most similar to our work. The main goal of Appbakery as well as our approach is to enable researchers to create apps without programming skills. By using and integrating ResearchKit and ResearchDroid, Appbakery is capable of creating powerful and native iOS and Android apps. According to the company's website, the product features HealthKit support, GoogleFit support, sensor support, and a data storage solution compliant with the Health Insurance Portability and Accountability Act, as well as simple surveys and prebuilt consent modules. A monthly fee is charged for this commercial solution. Figure 6 compares these different solutions.

To the best of our knowledge, other examples of comparable work exist only for computer-based software. Notable ones are PsychoPy [27] or LabView (National Instruments) for technical measurement systems. Both examples enable users to create individual software solutions with a graphical user interface engine and without programming skills.

**Figure 6.** Comparison of currently available study building frameworks and platforms with the solution presented in this work.

| | MoRe (this project) | Appbakery | ResearchKit | ResearchStack | ResearchDroid |
|---|---|---|---|---|---|
| *License* | open source | commercial | open source | open source | commercial |
| *Supported platforms* | platform independent | iOS/Android | iOS | Android | Android |
| *Programming skills* | none (DIY platform) | none (DIY platform) | Swift/Object C | JSON/HTML (ResearchKit AppCore reusable) | JSON/HTML |
| *Release date* | Jan 2017 (Beta) | Nov 2016 | Apr 2015 | Oct 2015 | Nov 2015 |
| *Owner* | University of Freiburg - Medical Center | TrialX Inc. | Apple Inc. | Cornell Tech and Open mHealth | Applied Informatics Inc. |
| *App-per-study* | universal app for all studies | individual apps | individual apps | individual apps | individual apps |

## Limitations

A limitation of this work is that mainly only technical problems are addressed and potentially resolved. Social implications of a centralized research platform are yet unknown. Currently, critics argue that this technology has the possibility of security breaches. Furthermore, a vast percentage of the population is very sensitive and cautious about sharing personal health data via mobile devices. However, in our opinion this platform could also be a chance to build trust in this technology. With time and success, skepticism might vanish.

Another limitation is that not every study design can be created with the StudyBuilder. Although numerous options and possibilities have been taken into account, it is technically impossible to be prepared for every possible research scenario.

## Conclusions

This ongoing project attempts to solve many issues regarding mobile phone research. According to the United Kingdom's National Health Service, development costs currently range from £1000 to £30,000 depending on the extent and functionality of a study app [11,28,29]. It seems necessary to concentrate resources for the development of a uniform and secure platform rather than supporting individual developments.

Furthermore, computer scientists, clinical doctors, psychologists, and many other professions are asked to work together for an all-embracing solution. The ultimate goal has to be a patient-oriented solution that is cost-effective, meets researchers' needs, and helps gather important medical data for a broad variety of diseases.

The first 12 months of the project were used to develop a first fully functional version of the proposed research platform that allows the creation of simple survey-based studies. Sensor support, HealthKit and GoogleFit connectivity, automated trial registration, and extended backend functionalities will be added in the second project phase. Our institution has agreed to cover maintenance and support subsequent to the initial development phase of 24 months. Possible contributors and additional funding for further development are currently being identified. The vital source code will be available online under the Creative Commons license.

Scientists or companies willing to contribute to this project are welcome to contact the authors.

## Acknowledgments

## Conflicts of Interest

None declared.

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Protocol

# Knowledge, Attitude, Behavior, and Practices Regarding HIV, Viral Hepatitis, and Sexually Transmitted Infections Among Migrants From Sub-Saharan Africa Living in Germany: A Multicenter Survey Protocol

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## Abstract

**Background:** Migration has an impact on the epidemiology of viral hepatitis B and C (HEP) and HIV in Germany; migrants from sub-Saharan Africa (MisSA) in Germany are disproportionally affected by HIV. In the last 10 years, a total of 10%-15% of all newly diagnosed HIV cases were among MisSA; 20%-30% of them acquired HIV in Germany. Prevalence of HEP among MisSA in Germany is unknown, but Western Africa, from where most MisSA in Germany originate, reports the highest prevalence of hepatitis B worldwide. There is limited information on knowledge, attitudes, behaviors, and practices (KABP) regarding HIV, HEP, and sexually transmitted infections (STIs), as MisSA are not reached with surveys targeting the general population.

**Objective:** Our objective was to determine the HIV, HEP, and STI information and prevention needs of MisSA in Germany.

**Methods:** We conducted a multicenter, cross-sectional, KABP survey regarding HIV, HEP, and STIs among MisSA living in Germany using convenience sampling. The study design was developed as a community-based participatory health research (CBPHR) project; HIV/STI-prevention specialists, key persons from MisSA communities, and HIV/STI researchers were involved in all steps of the research process. Trained peer researchers recruited participants in six study cities. Potential modes of survey administration were interview or self-completion, and the questionnaire was available in English, French, and German. Questions on knowledge about HIV, HEP, and STIs were presented as true statements; participants were asked if they had known the information before. Focus groups with MisSA were conducted to interpret results. Data collection took place from October 2014 to November 2016.

**Results:** Recruitment by peer researchers concluded with 3040 eligible participants. Data collection was completed in November 2016. We are currently analyzing the quantitative data and qualitative data from focus groups. We are conducting working group meetings to discuss the results in the respective study cities and to evaluate the application of participatory health research in epidemiological studies. First results are expected by the end of 2017.

**Conclusions:** Working with peer researchers to collect data allowed accessibility to a diverse sample of MisSA and, particularly, allowed us to reach vulnerable subgroups, such as MisSA without legal status. The ability to access hard-to-reach groups is one of the big advantages of CBPHR. The active inclusion of the persons under study in the design of the study resulted in higher acceptance and ownership of the research project in the target community; this ultimately lead to better quality of collected data. Furthermore, the participation of MisSA in the development of study design and data collection assures a better understanding of the interests, needs, and living conditions of this group.

## Introduction

### HIV, Sexually Transmitted Infections, and Hepatitis B and C Among Migrants From Sub-Saharan Africa Residing in Germany

Research shows the impact of migration on the epidemiology of hepatitis B and C (HEP) and HIV in Western Europe [1,2].

### HIV

Worldwide, an estimated 36.7 million people (range 34.0-39.8 million) were living with HIV at the end of 2015 and 2.1 million people (range 1.8-2.4 million) acquired HIV in 2015. Sub-Saharan Africa is the region mostly affected by HIV, with 25.6 million people (range 23.1-28.5 million) living with HIV in 2015 [3]. In addition, sub-Saharan Africa accounts for two-thirds of new HIV infections worldwide [3].

In Europe, migrants accounted for 40% of newly reported HIV diagnoses and most of these cases were among migrants from sub-Saharan Africa (MisSA) [4]. A total of 12 countries reported to the European Centre for Disease Prevention and Control (ECDC) that the majority of HIV cases with heterosexual transmission originated from high-prevalence countries [4].

In Germany, men who have sex with men are most affected by the HIV epidemic [5,6]. However, heterosexual contacts (HET) have always been the second-most common mode of transmission and have been increasing since 2012 [7]. Between 9% (2012) and 14% (2014) of all new HIV diagnoses in Germany were among persons originating from sub-Saharan Africa. Since 2013, there has been an increase in diagnosed HIV cases, particularly among female MisSA [6-8]. A total of 75% of all newly diagnosed HET cases were people from countries of origin other than Germany; between 40%-50% annually are MisSA [7].

There is no accurate estimate on the number of MisSA living in Germany because population statistics include neither MisSA with German nationality nor those without legal status. The estimated number of MisSA with sub-Saharan nationality was approximately 200,000 in 2013 [9]. Even though this number might underestimate the number of MisSA, it highlights that in comparison to other migrant groups, this population is small and disproportionately affected by HIV. At the beginning of the HIV epidemic in Germany, epidemiologists generally assumed that MisSA acquire their HIV infection in their country of origin. However, current surveillance data has shown that the proportion of HIV infections acquired in Germany varied from 15%-28% in 2009-2014 [10]. This proportion might be underestimated: a UK study showed that the estimated proportion of MisSA who acquired infection within the United Kingdom—based on CD4 cell counts—was three times higher than the figures resulting from clinicians' reports [11].

MisSA with HIV infection are often late presenters [12-14], potentially due to barriers to HIV testing, prevention, counseling, or health care in general [15]. Therefore, the proportion of undiagnosed MisSA might be higher than in other subpopulations affected by HIV [13].

### Hepatitis B and C

The estimated prevalence of chronic hepatitis B is 240 million and is highest in sub-Saharan Africa and East Asia, where between 5% and 10% of the adult population is chronically infected with hepatitis B. The reported prevalence of chronic hepatitis B in Western sub-Saharan Africa, from where most MisSA in Germany originate, is up to 14% [16].

In Europe, hepatitis B often occurs in migrants from highly endemic countries. In 2011, 53% of the reported hepatitis B cases from 18 European countries were imported [3,17]. Recent studies show that migrants in Germany show higher sero-prevalence of hepatitis B (2.1%-3.6%) than the German general population (0.3%) [18,19]. However, these studies did not include sufficient samples of MisSA.

Globally, the prevalence of chronic hepatitis C in 2016 is between 130 and 150 million persons [20]. The estimated prevalence of hepatitis C infections in sub-Saharan countries is 3% [16,21,22]. In Europe, only 17 countries reported data on country of birth or importation status for newly diagnosed hepatitis C cases to the ECDC. Of these 12,111 cases, 8.3% were imported [4]. Migrants in Germany show higher sero-prevalence of hepatitis C (1.1%-1.9%) than the German general population (0.3%) [16,17]. However, these studies did not include sufficient samples of MisSA. In Germany, migration status is not collected for reporting of new diagnoses for hepatitis B and C.

### Sexually Transmitted Infections

According to the World Health Organization (WHO), there is an estimated annual incidence of 357 million new infections with one of four sexually transmitted infections (STIs): chlamydia, gonorrhea, syphilis, and trichomoniasis [23]. The African region contributed approximately 24% of the worldwide incidence of these four STIs in 2005 [24].

In 2010, the ECDC recorded only 11 countries that reported migration status for gonorrhea cases. In those countries, 11% of cases were in migrants and 50% were in nonmigrants. Studies from Europe show no significant differences between infection rates for gonorrhea and syphilis in migrants and native populations [3]. A total of 23 EU countries reported data on syphilis to the ECDC; of those, nine provided information on migration status. The proportion of migrant cases has remained stable around 8.5% [3].

There are no estimates on the incidence of STIs among MisSA living in Germany. Migration status is captured only in syphilis

reporting and only 0.3% of reported syphilis cases originated from sub-Saharan Africa [10].

### *HIV, Hepatitis B and C, and Sexually Transmitted Infection Testing in Germany*

Testing for HIV, HEP, and STIs in Germany is offered by the local public health departments (LPHDs), medical professionals (eg, gynecologists and HIV specialists), and other local testing and counseling centers (eg, nongovernmental providers). Special prevention services; counseling; and HIV, HEP, and STI testing services for MisSA are offered by AIDS foundations, other nonprofit organizations focusing on migrant health, and LPHDs. The LPHDs have a legal mandate to reach vulnerable populations with HIV, HEP, and STI prevention services and to offer free, anonymous testing. HIV testing is offered based on a personal risk assessment, whereas STI and HEP testing are only offered by the LPHD if patients are presenting with symptoms. However, LPHDs and nongovernmental organizations report problems in reaching migrant populations and, in particular, reaching MisSA with testing services [25].

### *Social and Structural Barriers to Prevention and Behavioral Surveillance Among Migrants From Sub-Saharan Africa*

Studies show that migrants, compared to the German general population, have an increased vulnerability for HIV infection because access to HIV prevention, testing, and care is often limited due to legal, cultural, socioeconomic, or language barriers [3,15,26]. In addition, the migration process itself can increase risk of HIV, HEP, and STI acquisition, as migrants might experience (sexual) trauma, discrimination, and problems with legal status [3,15,27,28]. Moreover, the lack of culturally sensitive services and language/translation capacities to reach different migrant groups, as well as migrants' lack of knowledge about existing services, might present important barriers to prevention. Other aspects are discrimination and stigmatization from outside migrant communities, as well as stigmatization of people living with HIV within migrant communities [15].

Therefore, in order to assess prevention needs and to tailor prevention to these specific needs in vulnerable migrant groups, the ECDC, the WHO, and the Joint United Nations Programme on HIV/AIDS strongly recommend monitoring of behavioral indicators [29], in addition to routine surveillance. Suggested indicators include access to testing, treatment, prevention, and care; knowledge on HIV and STIs; attitudes toward people living with HIV; and (sexual) protective and risk behavior [29,30].

In Germany, data on knowledge, attitude, behavior, and practice (KABP) of MisSA is scarce, and the population is not sufficiently reachable with surveys addressing the German general population [31]. The level of knowledge on HIV and STIs, as well as protective and risk behaviors of MisSA, have so far only been assessed in studies with small sample sizes (ie, <300 participants) [32,33], whereas HEP has not been addressed in any Germany-based study with MisSA.

### Community-Based Participatory Health Research

Community-based participatory health research (CBPHR) is a research approach that includes members of the group under study in the research process [34]. As seen on page 4 of the handbook by von Unger and Gangarova, CBPHR can be defined as a "collaborative approach to research [that] equitably involves all partners in the research process and recognizes the unique strengths that each brings. CBPHR begins with a research topic of importance to the community with the aim of combining knowledge and action for social change to improve community health and eliminate health disparities" [35].

Therefore, one important goal of CBPHR is social change and ultimately improving the situation of the group under study [34,36,37]. Part of this is a process of mutual learning from each other and the establishment of skills and relationships that promote self-esteem of community members [34-36]. The true involvement of community partners leads to a better understanding of the particular needs of community members, improves access to a particular community, and ultimately results in enhanced data quality in epidemiological research [34,38]. Moreover, this mutual working process is building valuable networks that can be utilized for intervention planning and dissemination of results [35,37,38]. Further benefits of utilizing CBPHR in epidemiological studies are the interpretation of results and development of practical recommendations with experts of the group under study as well as other stakeholders. Ideally, this dialogue will lead to concrete prevention activities that are feasible and accepted in the target population [38]. Thus, implementing CBPHR approaches into a behavioral survey with marginalized populations might result in higher quality of data and give an opportunity to understand the social context of the group under study [34,36,39]. In HIV/STI research with MisSA, CBPHR has been utilized for establishment of research design, survey development, data collection, and dissemination of results [32,33,40-44]. Experience from these studies showed the feasibility of this approach, in particular, regarding participant recruitment through trained members from the respective MisSA communities under study (peer researchers) [32,33,40-44].

### Objectives of the Study

Our research interest was to determine the specific HIV, HEP, and STI prevention needs of MisSA in Germany.

The specific objectives were as follows: (1) to identify behavioral determinants, risk, and protective factors in regard to these infections; (2) to determine the information needs on these infections; (3) to assess the utilization of existing testing services (ie, HIV, HEP, and STIs); (4) to sensitize MisSA communities for HIV, HEP, STIs, and other sexual health topics; and (5) to develop culturally sensitive recommendations for prevention with MisSA. This cross-sectional study was also intended to promote the inclusion and empowerment of MisSA communities and the establishment of local networks for prevention planning.

## *Methods*

### Study Design

We conducted a multicenter, cross-sectional, KABP survey regarding HIV, HEP, and STIs among MisSA living in Germany using convenience sampling. The study design was developed as a CBPHR project with persons working in HIV/STI prevention with MisSA, key persons from MisSA communities, and HIV/STI researchers; we conducted a pilot study to test feasibility of the study design in Hamburg before finalizing the study flow. Details on the description of the research process and the pilot study can be found elsewhere [44,45].

The study was funded by the German Ministry of Health and coordinated by the Robert Koch Institute (RKI), the national public health institute with the mandate for infectious disease surveillance and related research. Ethics approval was received as of November 25, 2014, from the ethics committee at the medical university of Charité, Berlin (EA4/105/14). The study protocol was approved by the Commissioner for Data Protection of the RKI without concern as of January 14, 2015.

### Selection of Study Cities

This study was conducted in six German cities with large MisSA communities (ie, >2000 MisSA residents according to population statistics). Other criteria for selection of study city were as follows: (1) availability of partner organization with well-established contacts to local MisSA communities, (2) willingness of a free and anonymous HIV/STI testing service (eg, the LPHD) to participate, (3) geographic region of city, and (4) no previous research on prevention needs of MisSA communities. After a kick-off meeting in 2014, the following study cities were selected: Munich, Essen, Cologne, Berlin, Frankfurt, and Hanover (see Figure 1). We chose two cities from the Rhine-Ruhr region, a densely populated area of North Rhine-Westphalia with a very big MisSA population. Given the close proximity of cities in this region, MisSA living here are well connected. The structure of the local communities in the respective cities varies, as is the case with Cologne, where the biggest MisSA subpopulation originates from the Democratic Republic of Congo. Essen, on the other hand, has a high number of MisSA from Ghana. By conducting the study in the two big cities in this region, we were able to show the heterogeneity of this area.

In each city, the selected partner organization identified a MisSA community member to work as local study coordinator. The local study coordinator supported the partner organization and the RKI with selecting the peer researchers. In addition, the study coordinator was the liaison communicating between the peer researchers, the RKI, key persons from the community, and study participants.

### Questionnaire Development and Measurements

An expert group consisting of MisSA community members, people working in HIV/STI prevention with migrant groups, representatives from HIV/STI clinics, HIV specialists, and researchers collectively developed the questionnaire used in this study. We included indicators suggested by the ECDC for behavioral surveillance with migrant populations [29]. As a draft, we utilized the survey instrument of a sexual health survey for African communities from the United Kingdom [41], translated the questionnaire into German, and added some questions on HEP and local HIV testing services. African community members conducted cognitive interviews with five migrants from sub-Saharan Africa to determine comprehensibility, recall strategy, issues with sensitivity, and social desirability, as well as understanding the response process [46,47]. Feedback from cognitive interviews was generally positive and only minor modifications were necessary. Before conducting the pilot study in Hamburg, we conducted pretesting of the questionnaire with 35 MisSA and discussed questions with low response rates and comments by participants with the expert group. MisSA community members translated the questionnaire into English and French. Translation was verified by independent native English and French speakers.

After the pilot study, we adapted the questionnaire, pretested it, and adjusted it again together with the expert group. Following data collection in the first study site, Munich, we changed the wording of three questions to improve recallability. We also included two questions on knowledge about female genital mutilation/cutting (FGM/C) suggested by the partner organization in the second study city, Essen.

The final questionnaire consisted of 51 questions and 23 knowledge items and covered the following sections: sociodemography and access to health care; testing behavior with regard to HIV, HEP, and STIs; sexual behavior and risk factors (ie, sexual violence and circumcision/FGM/C); stigmatization; and sources and preferred means of information and knowledge of infections and their transmission. For more details, see Table 1. We used true statements to determine knowledge on transmission and prevention of HIV and HEP (eg, "Hepatitis is a disease of the liver. Did you know this before?"). Participants had the following response options: "I knew this already," "I was not sure if that was true or not," "I didn't know this," or "I don't understand this statement."
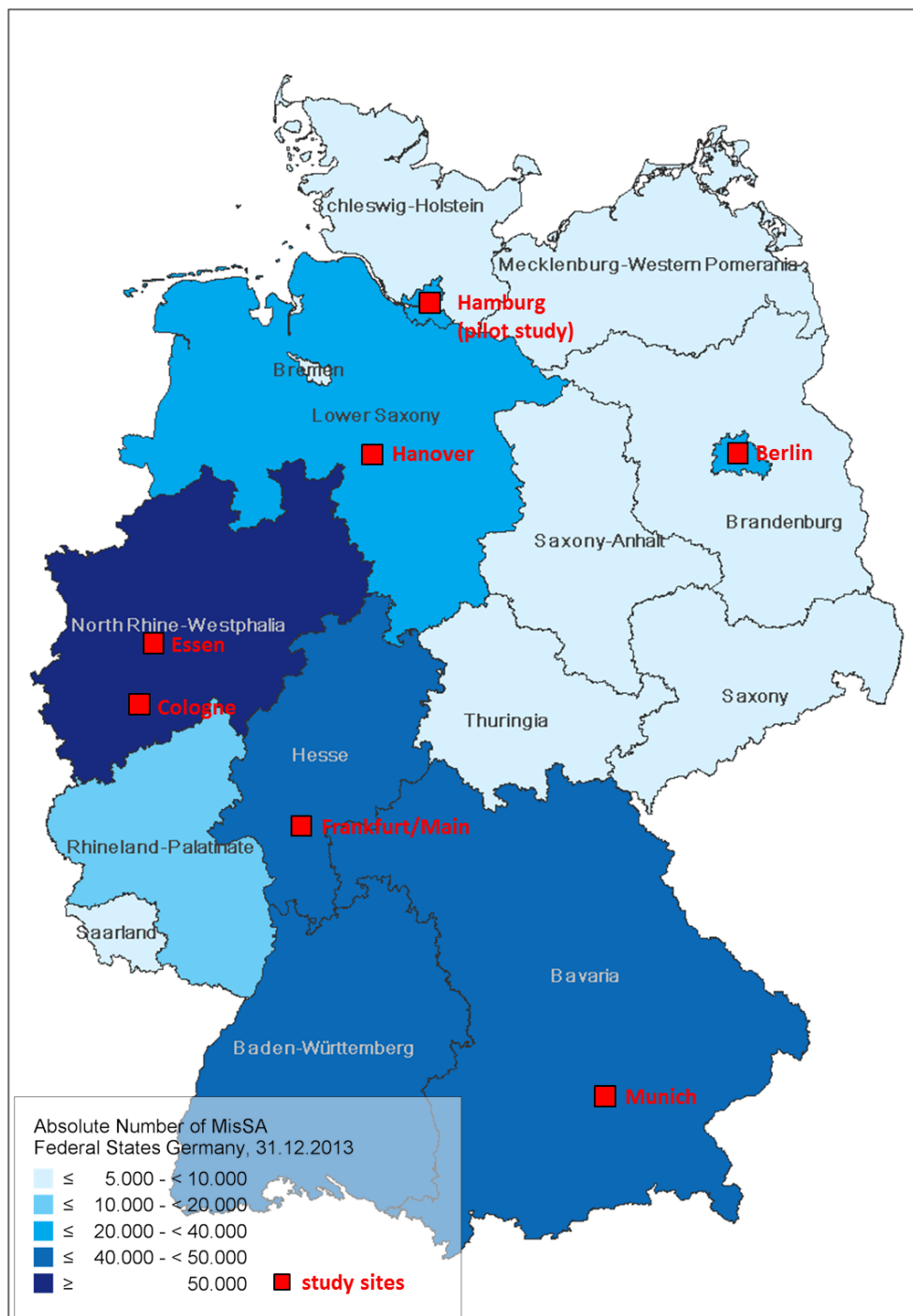
**Figure 1.** Map of study cities. MisSa: migrants from sub-Saharan Africa.

**Table 1.** Survey sections and operationalization.

| Section | Details and items (numbered) |
| --- | --- |
| Administrative information given by peer researcher | Peer ID, mode of administration of questionnaire, date of administration, and city where participant was recruited |
| Sociodemographic and personal characteristics | Sex, age, country of birth, country of birth of parents, time spent living in Germany, German language proficiency, visiting country of origin, living situation, steady relationship and time spent with steady partner, religious affiliation and participation in religious community life, level of education, sources of income and height of monthly net income, health insurance status, and health care utilization |
| Knowledge on hepatitis B/C: Use of informing statements "Did you know this before now?" | (1) Hepatitis is a disease of the liver. |
| | (2) Hepatitis B and C can be transmitted through blood or used needles. |
| | (3) Hepatitis B can be transmitted through sexual contact. |
| | (4) Hepatitis B can also be transmitted from mother to child. |
| | (5) Chronic hepatitis is a disease that often progresses unnoticed. |
| | (6) An untreated hepatitis can lead to cancer. |
| | (7) Chronic hepatitis can be treated successfully. |
| | (8) There is a vaccination to protect against hepatitis B. |
| | (9) There is no vaccination against hepatitis C. |
| Knowledge on HIV: Use of informing statements "Did you know this before now?" | (10) HIV and AIDS also exist in Germany. |
| | (11) AIDS is caused by a virus called HIV. |
| | (12) You cannot tell from someone's appearance whether he or she has HIV or not. |
| | (13) There is a test which shows whether someone is HIV positive or not. |
| | (14) Africans are NOT deported from Germany just for having HIV. |
| | (15) In [study site] you can get tested for HIV anonymously and for free, eg, at the LPHD[a] (see flyer). |
| | (16) People that have sexually transmitted infections have an increased risk of contracting HIV. |
| | (17) HIV is not transmitted through kissing or shaking hands. |
| | (18) HIV can be transmitted through sexual intercourse. |
| | (19) People with HIV have an increased risk of contracting tuberculosis. |
| | (20) There is no cure for HIV infection. |
| | (21) There are medications that can help people with HIV stay healthy. |
| Knowledge on STIs[b] "Have you ever heard of these STIs?" | (22) gonorrhea, (23) syphilis, (24) herpes, (25) genital warts, (26) chlamydia, (27) I do not know any of them |
| HIV, hepatitis C, and STI testing | Ever tested for hepatitis C or HIV, last time tested and results, country where last HIV test was done, testing for HIV without consent, last time tested for STI and last time diagnosed with STI, preferred HIV- and STI-testing sites |
| Sexual behavior and risk factors | Age at first sexual intercourse, sexual attraction, sexual activity within the last 12 months, number of male and female sexual partner(s) within the last 12 months, steady sexual partner(s) and origin of steady sexual partner(s), sex with nonsteady sexual partner(s) within the last 12 months, condom use with nonsteady sexual partner(s), condom use at last sexual intercourse, reasons for not using condoms, experience of sexualized violence and country where that happened |
| Circumcision and female genital mutilation/cutting (FGM/C) Knowledge on FGM/C: Use of informing statements "Did you know this before now?" | Circumcision and female genital mutilation/cutting (28) Did you know that a reconstruction of the female genitalia is possible for persons who have undergone female circumcision? (29) Did you know that the state health insurance in Germany can cover the cost for the reconstruction? |
| Behavior toward people living with HIV (PLWH) | Reaction and behavior toward PLWH, personal connection to PLWH, ever heard of PLWH being treated badly in community, HIV/AIDS as a topic discussed in community |
| Self-stated information needs | Relevant topics for prevention, preferred mode of dissemination |

[a]LPHD: local public health department.

[b]STI: sexually transmitted infection.

## Participants and Inclusion Criteria

Inclusion criteria for study participants were as follows: (1) 18 years of age or older, (2) born in sub-Saharan Africa or with at least one parent originating from sub-Saharan Africa, (3) currently residing in Germany, and (4) living in or near the respective study city. Peer researchers and local study coordinators were not allowed to take part in the survey.

## Sample Size

The calculated sample size was 3009. Differences in proportions of 10% (ie, 45% vs 55%) between men and women should be detectable with a significance level of .05 and accepting a beta error of .2. Additionally, the smallest group among MisSA (ie, MisSA from Southern Africa), making up about 10% of all MisSA in Germany, should make up at least 8.5% of the sample for stratified analysis, accepting a beta error of .2 and alpha error of .05 (both sided). We were aiming to recruit a minimum

of 2550 MisSA in six cities in Germany and were planning to include the sample of MisSA from the pilot study in Hamburg (N=569). We added an extra 110 persons to the calculated sample size to assure the achievement of the total sample size of 3009.

In addition to analysis of the total sample, we wanted to report results of study cities to the respective local partner organizations. Therefore, we decided on a minimum sample size of 350 MisSA per city to enable us to describe proportions of knowledge and sexual behavior as well as demographic characteristics accurately (significance level of .05 and accepting a beta error of .2). To determine the targeted sample size per city, we considered the size of the local MisSA community and the resources of the respective partner organization. Table 2 shows the targeted minimum sample size per city and the registered MisSA [48]. The total targeted sample size in this recruitment period was 2550.

**Table 2.** Expected sample size per study city.

| Study city/region | Registered MisSA[a](population statistics, 2010) [48] | Targeted minimum sample size |
| --- | --- | --- |
| **Rhine-Ruhr region** | | 1000 |
| Essen[b] | 8731 | 650 |
| Cologne | 5438 | 350 |
| **Berlin** | 12,086 | 500 |
| Munich | 7970 | 350 |
| Frankfurt am Main | 5605 | 350 |
| Hanover[c] | 3377 | 350 |
| Total | | 2550 |

[a]MisSA: migrants from sub-Saharan Africa.

[b]Recruitment in Essen (2229), Mulheim an der Ruhr (909), Oberhausen (911), Duisburg (1571), and Düsseldorf (3111).

[c]Recruitment in the administrative districts Hanover Region (2554), Hildesheim (239), and Brunswick (584).

## Data Collection

Data collection took place from October 2014 to November 2016.

### Selection and Training of Peer Researchers

The local partner organization selected 10-15 peer researchers for recruitment of study participants. Inclusion criteria for peer researchers were as follows: (1) well-established contacts within their communities, (2) availability during study period and training sessions, (3) interest in sexual health and community work, (4) basic German language skills (for training session), and (5) 18 years of age or older. Peer researchers were recruited by the local partner organization and in agreement with the RKI. They were selected based on the following characteristics: (1) country of birth (based on the biggest subpopulations according to population statistics), (2) gender, (3) age, and (4) spoken languages. In order to recruit a heterogeneous sample of MisSA living in the respective study city, it was important that the biggest subpopulations with regard to countries of birth were adequately represented within the group of peer researchers. Representatives from the RKI, the local study coordinator, and peer researchers from previous study cities conducted a 2-day

training session for peer researchers. Topics covered were as follows: (1) study flow, (2) survey administration, (3) ethical aspects of data collection, (4) recruitment strategy (eg, "How do I approach potential participants?"), and (5) basic information on HIV, HEP, and STI transmission and testing. We then conducted a community mapping exercise [33] to identify potential places for recruitment. Here, peer researchers discussed where they meet other MisSA. To explain possible recruitment strategies and their experiences with them, peer researchers from former study cities were invited to the training session. Recruitment of study participants started immediately after the training session and was scheduled to take 10-12 weeks per study city.

### Recruitment

Trained peer researchers recruited participants through outreach by convenience sampling in locations previously identified though community mapping. The possible modes of questionnaire administration were either face-to-face or telephone interview conducted by the peer researcher or self-completion of the questionnaire by the participant. Verbal informed consent for taking part in the survey was obtained by peer researchers. Peer researchers were asked to preferably offer

self-completion of questionnaires to reduce social desirability bias. Study participants received an addressed and stamped return envelope allowing them to mail the questionnaire directly to the RKI. Peer researchers and participants were encouraged to send the questionnaires promptly to the RKI. Participants received a give-away package consisting of a pen with the RKI logo, a shopping cart chip with a map of Africa, a referral to the local partner organization, a condom, and a flyer on the free HIV/STI testing services at the LPHD.

To steer recruitment and make sure the largest African communities were well represented, the RKI provided a weekly summary of the sociodemographic characteristics of the recruited participants to the local study coordinator. The following indicators were included: mode of administration, language of questionnaire, gender and age of participants, countries of birth, time spent in Germany, school education, religious affiliation, and health insurance status. Countries of birth and the gender proportion were compared to official data from population statistics. The local study coordinator forwarded this information to peer researchers on a weekly basis and encouraged peer researchers to reach out to the underrepresented groups.

After 4 weeks of field work, peer researchers, the respective partner organization, and the RKI met to evaluate the recruitment process. Peer researchers were encouraged to exchange experiences on recruitment strategies and support each other if they faced any difficulties. Furthermore, sociodemographic characteristics of the recruited study population were presented to discuss which groups might be underrepresented and to develop strategies on how to recruit these groups. After conclusion of data collection, a final meeting was scheduled with peer researchers, partner organization, and the RKI. Peer researchers received a certificate for their work as peer researchers, their participation in the training sessions, and the data collection. In addition, peer researchers, the local study coordinator, and RKI staff discussed experiences during training and fieldwork as well as the reception of the study within the MisSA community. Every peer researcher received a unique identifier, either an acronym or a number, to mark questionnaires of participants recruited by him- or herself. Peer researchers were compensated with €20 per questionnaire. Peer researchers were paid for 20 (30 in some cities) completed questionnaires only, even if they recruited more participants.

### Data From Local HIV, Hepatitis B and C, and Sexually Transmitted Infection Testing Sites

With completion of the questionnaire, participants were informed about the free and anonymous HIV, HEP, and STI testing service at the LPHD. We also included a flyer in English, German, or French with opening hours and language availabilities for counseling. For 6 months before data collection and 6 months after, the LPHD was sending the aggregated monthly numbers of MisSA attending the LPHD to assess whether the conduction of the study was leading to an increase of contacts and testing uptake among MisSA communities. Some LPHD agreed to send supplement aggregated information on countries of origin of their MisSA clients. Thus, it was possible to compare that data to population statistics to find out which groups were well reached or poorly reached. The study flow is shown in Figure 2.

Figure 2. Overview of the study flow and assigned responsibilities. LPHD: local public health department; STI: sexually transmitted infection; RKI: Robert Koch Institute.
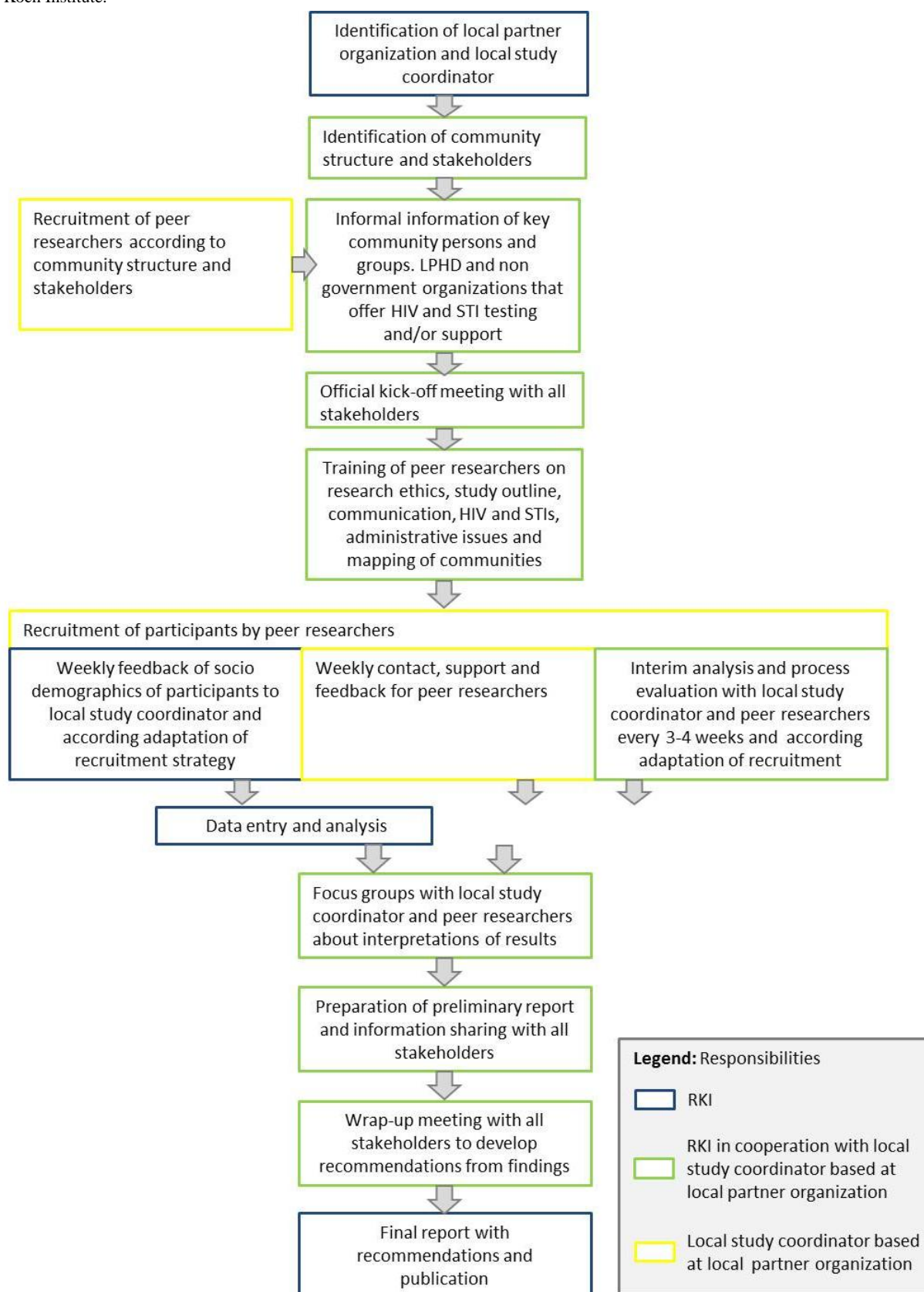


## Data Entry and Statistical Analysis

Upon arrival at the RKI, a consecutive unique identifier was assigned to all questionnaires. Administrative data (eg, ID of peer researcher and mode of administration) and selected sociodemographic data were entered into an Excel database. During that process, questionnaires were inspected for completeness, consistency, and meeting of inclusion criteria.

RKI staff entered data using Voxco Interviewer Web, an online survey and data collection software. A standard operation procedure for data entry and training was given to data entry personnel. A second person checked for correctness of entered data. We applied plausibility checks and excluded nonvalid cases from data analysis. Exclusion criteria were as follows: (1) missing data on country of birth and/or country of birth of parents, (2) missing data on sex, (3) participant not from sub-Saharan Africa or parents not originating from sub-Saharan Africa, (4) participant not living in or near study city, and (5) more than 40% of information missing.

Frequency distributions were tabulated for all variables, performing range checks and cross-validations. We described the characteristics of the study population in detail, for the whole sample, but also for each study city separately. We conducted stratified analysis of sociodemographic data and knowledge on HIV, HEP, and STIs; risk and protective behavior and attitudes toward people living with HIV and calculated unadjusted odds ratios. To identify subgroups with specific prevention needs, multivariable logistic regression was used to explore the associations between sociodemographic data and knowledge on HIV, HEP, and STIs; risk; and protective behavior and attitudes toward people living with HIV.

Per study city, we conducted a descriptive analysis of data directly after fieldwork and data entry. Variables on sociodemographics and sexual behavior, as well as potential risk factors, were stratified by gender; means, medians, and ranges were calculated where applicable. Variables on testing behavior and knowledge on HIV, HEP, and STIs were dichotomized to describe, in univariable analysis, differences in the following: gender, age ($\leq$ 30 vs >30 years of age), educational level (no certificate and primary/secondary school vs high school/vocational school and university/college), time spent in Germany (< 5 years vs $\geq$ 5 years including *since birth*), German language proficiency (mother tongue, very good, good vs average, little, not at all), monthly net income (<€1000 vs $\geq$€1000), health insurance status (health insurance card vs medical treatment voucher, no health insurance at all, and unsure), religious affiliation (Christianity vs Islam), partnership (yes vs no), and mode of administration (interview vs self-completion). Odds ratios and 95% confidence intervals were calculated.

Data submitted by the LPHD was analyzed descriptively. All analyses were performed using the statistical software SPSS Statistics for Windows, version 20 (IBM Corp); for the whole sample, Stata, version 14 (StataCorp LLC) was used as well.

## Focus Group Discussions With Peer Researchers

Following data analysis for the respective study city, we conducted a focus group discussion with peer researchers, partner organization, and the RKI. Participants interpreted the results of descriptive analysis and discussed ideas for further data analysis. In addition, they identified the most important prevention messages and determined appropriate strategies and interventions to disseminate results into the MisSA communities. Peer researchers were thus involved in data collection and in the interpretation of survey results. Following the focus groups, we prepared a report for each study city including basic results

of analysis and focus groups in order to disseminate these results to local organizations working with MisSA in HIV, HEP, and STI prevention; political decision makers; and to the MisSA community itself.

## Results

Data collection was completed in November 2016 when the last meeting with community partners and other stakeholders was conducted to discuss results and develop recommendations. Currently, data analysis is being conducted and we expect to publish first results by the end of 2017.

## Discussion

### Principal Findings

This study design was developed as a CBPHR project and people from different MisSA communities were involved in all stages of the research process. The active inclusion of research subjects results in higher acceptance of the research project in the target community and ultimately leads to increased accessibility and better quality of collected data [34,47,49,50]. Furthermore, the participation of MisSA in the development of study design and data collection assures a better understanding of the interests, needs, and living conditions of this group. Four of the MisSA who were part of the expert group became study coordinators in the local study cities and were thus involved in the complete research process. We chose to work with peer researchers for data collection to reach all relevant subgroups [37], including MisSA without (clear) legal status or people who might have faced discriminatory behavior by legal authorities in the past. Being able to reach "the unseen" with research is a major advantage of CBPHR [34,51]. We also included peer researchers in the discussion and interpretation of results as well in the development of recommendations to ensure relevance of findings for the local communities.

With the pilot study in Hamburg, we showed feasibility of study design for behavioral surveillance with MisSA. Peer researchers recruited 649 study participants within 2 months and overexceeded our aimed sample size of 350 MisSA. Working with peer researchers enabled us to reach particularly vulnerable groups, such as persons without health insurance (22% of participants) [44,45].

The described study design aimed to involve different stakeholders in the local study cities to establish new networks or expand existing collaborations for prevention planning and dissemination of results [34]. Thus, the utilization of CBPHR did not only allow better access to marginalized groups, but enabled us to get an enhanced understanding of the particular needs of the group under study and to develop research questions that were relevant to MisSA, stakeholders, and researchers. In addition, it will ultimately lead to concrete prevention messages for the group under study.

By providing true statements to assess knowledge on HIV, HEP, and STIs, participants can learn new information on these infections during questionnaire completion or interview. This is particularly helpful when reaching vulnerable subgroups that so far do not have access to prevention activities. When

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participants have questions about transmission or testing, peer researchers will refer them to either the partner organization or the LPHD. Gaining information about transmission and prevention of HIV, HEP, and STIs during survey completion, and being referred to counseling in the case of knowledge gaps, can be considered a preventive intervention.

## Limitations and Challenges

We used convenience sampling and, thus, cannot be sure that our sample will be representative for the MisSA population in Germany. Even though weekly feedback of sociodemographic data and subsequent adaptation of recruitment strategies were in place to steer sampling based on population statistics and to limit the effects of convenience sampling, these statistics did not include MisSA without legal status or MisSA who acquired German citizenship. When developing the study design, we had discussions with community partners who agreed that convenience sampling with peer researchers was the most feasible recruitment strategy to reach the MisSA community as well as MisSA with different living conditions.

Due to the cross-sectional nature of this survey, we will not be able to deduce direct causal relationships between sociodemographic, knowledge, and behavioral factors or the impact of prevention programs on behavior change.

The utilization of true statements might lead to an overestimation of knowledge on these indicators. In this context, we considered it ethically more important to inform participants who might belong to vulnerable hard-to-reach subpopulations about HIV, HEP, and STIs than to get exact information on level of knowledge. Additionally, expert group members highlighted the fact that taking part in a survey that actually provides information might be particularly motivating.

There might be social desirability bias in the answers of the respondents, especially when reporting the degree of condom use or talking about sexual practices and sexual violence. In addition, mode of administration might influence responses and social desirability.

The questionnaire was only available in English, French, and German; thus, MisSA who did not speak or read any of these languages can only be reached with interviews and simultaneous translation by peer researchers.

## Authors' Contributions

CSH and CK designed the study and were supported by VB, AK, and AT. CSH, CK, and VB are the scientific coordinators of the study. The manuscript was drafted by CK and CSH and critically revised by VB, AT, and AK. All authors read and approved the final manuscript.

## Conflicts of Interest

None declared.

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## Abbreviations

**CBPHR:** community-based participatory health research
**ECDC:** European Centre for Disease Prevention and Control
**FGM/C:** female genital mutilation/cutting
**HEP:** hepatitis B and C
**HET:** heterosexual contacts
**KABP:** knowledge, attitude, behavior, and practice
**LPHD:** local public health department
**MisSA:** migrants from sub-Saharan Africa
**PLWH:** people living with HIV
**RKI:** Robert Koch Institute
**STI:** sexually transmitted infection
**WHO:** World Health Organization

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Original Paper

# eMindLog: Self-Measurement of Anxiety and Depression Using Mobile Technology

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## Abstract

**Background:**  Quantifying anxiety and depressive experiences permits individuals to calibrate where they are and monitor intervention-associated changes. eMindLog is a novel self-report measure for anxiety and depression that is grounded in psychology with an organizing structure based on neuroscience.

**Objective:**  Our aim was to explore the psychometric properties of eMindLog in a nonclinical sample of subjects.

**Methods:**  In a cross-sectional study of eMindLog, a convenience sample of 198 adults provided informed consent and completed eMindLog and the Hospital Anxiety and Depression Scale (HADS) as a reference. Brain systems (eg, negative and positive valence systems, cognitive systems) and their functional states that drive behavior are measured daily as emotions, thoughts, and behaviors. Associated symptoms, quality of life, and functioning are assessed weekly. eMindLog offers ease of use and expediency, using mobile technology across multiple platforms, with dashboard reporting of scores. It enhances precision by providing distinct, nonoverlapping description of terms, and accuracy through guidance for scoring severity.

**Results:**  eMindLog daily total score had a Cronbach alpha of .94. Pearson correlation coefficient for eMindLog indexes for anxiety and sadness/anhedonia were r=.66 ($P<.001$) and r=.62 ($P<.001$) contrasted with the HADS anxiety and depression subscales respectively. Of 195 subjects, 23 (11.8%) had cross-sectional symptoms above the threshold for Generalized Anxiety Disorder and 29 (29/195, 14.9%) for Major Depressive Disorder. Factor analysis supported the theoretically derived index derivatives for anxiety, anger, sadness, and anhedonia.

**Conclusions:**  eMindLog is a novel self-measurement tool to measure anxiety and depression, demonstrating excellent reliability and strong validity in a nonclinical population. Further studies in clinical populations are necessary for fuller validation of its psychometric properties. Self-measurement of anxiety and depressive symptoms with precision and accuracy has several potential benefits, including case detection, tracking change over time, efficacy assessment of interventions, and exploration of potential biomarkers.

**KEYWORDS**

mobile; anxiety; depression; internet; measurement

## Introduction

Quantified information is the basis of evidence in science and medicine. Objective measures are more easily validated with independent reference frames. Subjective measures, being self-referential in nature [1], have larger and variable errors in measurement. In mental health, subjective measures provide unique data but come with challenges. Measuring one's mental experiences requires the individual to demarcate the experience to be assessed, discern through self-reflection, provide an internal context for grading, and translate the experience into a numerical quantity.

Measuring the severity of signs and symptoms of mental experience can be performed by clinician interviews or self-report by subjects, each providing unique contributions [2]. While clinician and subject ratings are generally concordant, 44% of subjects reported scores more than 1 standard deviation from the clinician-rated scores in a study of recurrent depression [3]. Outcomes differed based on the measure used, raising inferential issues. While clinicians have a reference frame from their wealth of clinical experience, self-reporting may more accurately measure subjective experiences that are difficult to articulate in words and are also less influenced by interviewer relationships.

Use of scales have traditionally been distinct from diagnostic tools, though recently, diagnostic criteria and their frequency have been combined to gauge the severity dimension [4,5]. There is value in measurements that can assess severity while also providing proxies for diagnostic thresholds. However, diagnostic boundaries in psychiatry are arbitrary and thus are a limitation as diagnostic comorbidities are the norm in psychiatric populations. An unverified assumption is that the criteria for distinguishing diagnostic differences also provide a comprehensive measure of the disorder. An additional risk is that the diagnostic criteria may change with advancing knowledge.

There are several self-report scales available for depression and anxiety. These have significant limitations [6,7], including being solely based on psychological approaches and guided by theoretical formulations (eg, cognitive theories of depression) or by treatment response characteristics (eg, tricyclic antidepressants). An alternative is a neuroscience-based approach, which broadly distinguishes affective from cognitive neurosciences [8,9], with conscious expression elementally distinguishing emotions from thoughts, with behaviors as the output. A brain circuit based approach, the Research Domain Criteria (RDoC) initiative, emphasizes dimensionally oriented behavioral measures, aiming to validate them for eventual clinical work [10]. RDoC distinguishes domains of positive affect from negative affect as well as cognition. The RDoC effort has so far focused on behavioral measures (tasks) and has not yet moved to the level of self-report [11]. The development of the self-report measure reported here is such an effort founded on the domain distinctions in RDoC and thus underlying neurobiological processes. The aspiration is to provide more precise measures that provide enhanced clinical value.

Depressive biotypes based on neurobiological substrates have identified neurophysiological subtypes of major depression, reflecting distinct patterns of dysfunctional connectivity [12,13]. Rating scales derived from underlying neurobiology are necessary to optimally explore such depressive biotypes at a clinical level. Dividing symptoms based on neurobiology may better explain symptom heterogeneity and divergent responses to treatment [14]. To achieve this, symptoms need to be revisited in the framework of neurobiology.

### Web-based Mobile Technology

Web-based technology has advanced to where mobile devices are used by increasingly large proportions of the population. Additionally, there is growing interest in tracking a variety of information, from measures of well-being to clinically relevant markers that can monitor variables relevant to disease management. Measurement tools that use mobile devices can provide value in behavioral health interventions [15], particularly as willingness for self-disclosure is enhanced [16]. Mobile technology also permits more frequent assessment, addressing the recency bias in less frequent assessments [17]. In the domain of anxiety and depression, there is a need for measures that capture the enormous variability of mental phenomena in multidimensional space and flowing over time. Such massive data need to be reduced to global severity scores and indexes of value for personalized medicine, case detection, tracking over time, and potentially differential responses to interventions [14].

The aim of this study was to examine the internal consistency (reliability) of a new Web-based self-report measure of anxiety and depression and its convergent validity compared to a standard reference scale. The hypothesis is that the new measure would have an acceptable Cronbach alpha ($>.7$) and a large Pearson correlation coefficient ($>.5$) with the reference scale.

## Methods

### Measure

eMindLog [18] is a self-report measure of anxiety and depression, associated symptoms, and functioning. eMindLog is administered on a mobile device or computer in a platform-independent manner. To provide clarity and enhance precision, terms used in the scale are succinctly described before the corresponding question—a unique approach in self-report measures. Accuracy of scoring by the subject is enhanced by scoring guidance. The time and burden of assessment are taken into consideration in choosing which symptoms need daily assessment (ie, they commonly fluctuate), versus those that can be reliably condensed for weekly assessment. Thus, eMindLog has two components: a daily set of items and a weekly set. A daily total score provides a global measure, useful in differentiating treatment groups and for global decisions at the individual level. Specific item scores and derivative index scores can provide granularity for various analyses, particularly for unique profiles at the individual level, necessary for personalized medicine. Algorithms can derive boundaries that reflect *Diagnostic and Statistical Manual of Mental Disorders-5* (DSM-5) diagnostic thresholds for Major Depression and Generalized Anxiety Disorder. Content validation data from a

discontinued scale provided guidance for the current scale items and their descriptions.

The version of the scale used in this report had 20 questions in the daily set and 14 in the weekly set (see Multimedia Appendix 1). Based on the results reported below, 3 items in the daily set were removed. These items were subsequently restructured and added to the weekly set and the process discussed below. Thus, the final version of eMindLog has 17 items in the daily component measuring emotions, thoughts, and behaviors from which 4 indexes are derived: anxiety, sadness, anger, and lack of pleasure. The weekly component (also 17 questions) addresses associated symptoms, interpersonal relations, quality of life, and functioning.

Why are emotions, thoughts, and behaviors so critical to measure? Emotions are subjective, felt experiences that are often difficult to describe in words. Emotions are bathed in internal body states, often reflecting somatic characteristics [19]. Emotions are associative, often independent of their temporal sequence in explicit memory. Intense emotions are immediate, not deliberate or willful. Elegant experiments demonstrate that the correlates of emotions are initiated by pattern recognition before conscious awareness of their trigger [20], with a later, conscious capacity to either let them be, inhibit, or embellish them. Primary emotions such as anxiety, anger, and sadness are mediated by the threat (negative valence) system, and anhedonia by hypoactivity of the reward (positive valence) systems [20,21].

Thoughts are subjective ideas and concepts capable of being transduced into words and articulated as speech [22]. Thoughts are capable of being reasoned, logical, proportionate, and flexible to changing situations. The focus of thinking may be narrow and detailed or broad and strategic. The sequence of thoughts, when smooth, may be linked to a theme without digressions. Thinking may be active and effortful or passive and repetitive as in habitual ways of the mind or automatic thoughts [23]. Thoughts are the conscious output of the cognitive system—much of the neuroscience effort studying cognition has focused on the process of components such as selective attention, working and declarative memory, and effortful control [11]. In a self-report, the focus is on thoughts as the conscious output of cognitive systems.

The content of thoughts is tethered by emotions. Intense emotions make thoughts captive, inducing certainty or disorganization (unsettled and turbulent). When emotions control thinking, they are hard to regulate, making deliberate and considered decisions difficult. Thus, anxious emotions make thoughts worrisome, and sad feelings biases one into beliefs of failure. Thinking can flow with emotions, embellish them if they are consonant, or counter them, which requires active effort. Cognitive therapy aims to enhance the control of thoughts over emotions. Changes in beliefs and processing routines are critical for benefit with cognitive therapy.

Behaviors are observable actions. They are in response to sensory stimuli (reflexive), emotions (conditioned), and thoughts (chosen). In situations when emotions are not intense, behaviors can be autonomous, voluntary, intentional, and willfully chosen.

Behaviors in the repertoire of anxiety and depressive disorders are limited. To achieve higher resolution in the measurement of behaviors relevant to anxiety and depression, their motivational drivers need to be considered in parceling out the pathways to their external manifestation (see Figure 1).

eMindLog leverages mobile technology to take advantage of ease of repeated measurement and tracking ability. At a subsequent stage of development, the relationship between eMindLog scores and RDoC-based behavioral tasks can be explored.

The items in the eMindLog daily and weekly measures can be examined in an exploratory manner, to indicate potential diagnostic thresholds. For such purposes, an item is marked as present if the score is 4 or greater (moderate or above). The DSM-5 criteria for Major Depressive Disorder and Generalized Anxiety Disorder were matched with items in eMindLog in algorithms based on these criteria.

## Protocol

This validation study protocol and informed consent form were approved by the East Carolina University Institutional Review Board, and the study was compliant with the Declaration of Helsinki code of ethics. A sample of 198 English-speaking adults provided informed consent. They were a convenience sample recruited from four expedient public locations (ie, a bookstore, wellness center, psychiatry clinic staff, and college commons) on different days during September through November 2015.

The informed consent process on paper was separate from the subsequent data gathered on laptops, maintaining data anonymity. Each subject provided demographic information (ie, age, sex, race/ethnicity, socioeconomic information, and educational level) and whether they were receiving professional care (ie, psychotherapy and/or medication) for anxiety or depression. Subjects viewed a 5-minute introductory video and completed the eMindLog daily and weekly sections. Subjects also took the Hospital Anxiety and Depression Scale (HADS) [24] as a reference and answered a series of questions to provide feedback on eMindLog. The HADS was chosen as it has anxiety and depressive subscales, permitting a comparison with the eMindLog indexes. Subjects rated the eMindLog daily and weekly items, as well as the HADS on only one occasion in this study. Each received a US $25 gift card for their time and effort. An individual could participate only once.

**Figure 1.** Emotions, thoughts, and behaviors - items from the threat and reward systems.



| | Enhanced Negative Valence | | | Diminished Positive Valence |
|---|---|---|---|---|
| **EMOTIONS** | Anxiety | Anger | Sadness, Numb | Lack of pleasure |
| **THOUGHTS** | Worry | Blame | Sad thoughts, Suicidal thoughts | Lack of thought, Futility |
| **BEHAVIORS** | Agitation, Avoidance | Hostility, Impulsivity | Withdrawal | Lack of approach |

The version of eMindLog used in the study had 20 daily questions and 14 weekly questions. The daily questions addressed anxiety (emotion: anxiety; thought: worry; behavior: physical agitation, avoidance), anger (emotion: anger; thought: blaming; behavior: hostility, impulsivity), sadness (emotion: sadness, emotionally numb; thought: sad thought, suicidal thought; behavior: withdrawal), anhedonia (emotion: lack of pleasure; thought: lack of thought, futility; behavior: lack of approach), and asocial (emotion: lack of compassion; thought: distrustful; behavior: asocial). Thus, there were 6 items related to emotions, 7 related to thoughts, and 7 related to behaviors. Each item was described (eg, "Anxiety is feeling nervous, uneasy, apprehensive or panicky") before the question was posed (eg, "During the past 24 hours, how anxious have you felt?"). Scoring used a discretized analogue scale (0-10) enhanced with descriptive anchors and color [25]. The descriptive guidance provided was 0 labeled as none and 10 as extreme, 1-3 as mild, 4-6 as moderate, and 7-9 as severe.

The weekly questions ask the individual to rate their experiences during the past 7 days. The weekly questions were divided into 8 questions related to associated symptoms: well-being, fatigue, emotional pain, memory, concentration, appetite, sleep, and stress; a single question on quality of life; and 5 questions on functioning in the domains of social, work, school, home, and hygiene/grooming.

The scores for the daily questions were totaled for a total score and divided by the number of questions to provide a total average score. Index scores for each of the 5 indexes (ie, anxiety,

anger, sadness, anhedonia, and social) were calculated as the average of 3 items including one each from emotion, thought, and behavior. When there were two items for a category (ie, physical agitation and avoidance as behaviors in the anxiety index), the higher score was used as the behavior score in calculating the index. This approach provided equivalent weighting for emotions, thoughts, and behaviors in each index. The score for functional restriction was the highest score among the 5 questions related to functioning.

**Statistical Analysis**

The item scores were computed for $t$ tests and analysis of variance (ANOVA). Being a study based on a general population sample, skewness was expected. One below 2 was considered acceptable by convention as too small to have a practical impact [26].

The statistical analysis assessed the internal consistency (reliability) for the eMindLog daily total score and the index scores, as well as the HADS scores. A Cronbach alpha .7 is considered the threshold for acceptability.

Convergent validity of the eMindLog was assessed by examining the relationship between specific eMindLog index scores and the HADS Anxiety and Depression subscale scores. A Pearson correlation coefficient .5 was considered a large strength of association.

The diagnosis of Generalized Anxiety Disorder and Major Depression are based on symptom criteria, all of which are assessed in eMindLog. The items in eMindLog daily and weekly

were matched to DSM-5 diagnostic criteria for Major Depressive Disorder (MDD) and Generalized Anxiety Disorder (GAD) using an exploratory algorithm. Since this study was a one-time assessment, the time requirements for MDD (2 weeks) and GAD (6 months) could not be considered, though the requirement for impaired functioning was included. To assess whether this approach was valid, a sensitivity analysis was performed using the HADS subscale score cutoffs defining valid cases [24,27].

The eMindLog Daily scores were subjected to analyses to determine the number and nature of the subscales that exist. The structure of the eMindLog daily items was explored with a maximum likelihood factor analysis with an oblique rotation (SAS Proc Factor, Promax).

## Results

### User Statistics

A total of 198 subjects provided informed consent. One subject provided incomplete data and was excluded. Two subjects' data were considered invalid—they filled out the scale with a degree of inconsistency that was random or due to illiteracy, and their data were excluded. Thus, data from 195 subjects were analyzed. Software challenges prevented 3 subjects from completing the HADS.

Demographic information is provided in Table 1. The average age was 39.8 (range 18-83), over half (112/195, 57.4%) were female, and over half (115/195, 59.0%) were married or in a committed relationship. Race and ethnicity, education, and economic status are also reported below. The proportion reporting professional care for anxiety/depression was 24.1% (47/195) with 9.7% (19/195) in psychotherapy and 17.9% (35/195) on medications.

**Table 1.** Demographic features of subjects (N=195).

| Characteristics | n (%) |
|---|---|
| Age, mean (SD), range | 39.8 (18.66), 18-83 |
| Female | 112 (57.4) |
| **Race** | |
| White | 139 (71.2) |
| African American | 41 (21.0) |
| Asian | 5 (2.6) |
| Other | 10 (5.1) |
| **Ethnicity** | |
| Hispanic | 7 (3.6) |
| **Marital status** | |
| Single | 80 (41.0) |
| Married/Committed | 115 (59.0) |
| **Education** | |
| Attended high school | 8 (4.1) |
| High school graduate | 77 (39.5) |
| College graduate | 110 (56.4) |
| Post-graduate degree | 0 (0) |
| **Economic status** | |
| Lower | 19 (9.7) |
| Middle | 149 (76.4) |
| Upper | 27 (13.8) |
| Disabled | 17 (8.7) |
| **Receiving professional care for anxiety/depression** | 47 (24.1) |
| Psychotherapy | 19 (9.7) |
| Medications | 35 (17.9) |

**Table 2.** Pearson correlation coefficient between eMindLog daily average total scores with selected eMindLog weekly items (N=195).

| Item | Mean (SD) | $r$ ($P$) |
|---|---|---|
| Stressed | 3.84 (2.338) | .60 (<.001) |
| Restricted quality of life | 2.59 (2.625) | .62 (<.001) |
| Restricted functioning | 3.38 (2.764) | .59 (<.001) |

The descriptions offered for each item in eMindLog were reported as helpful by 190/194 (97.9%) of the subjects. The daily eMindLog differentiated items into emotions, thoughts, and behaviors. The proportion of subjects who reported being able to differentiate emotions from thoughts was 159/194 (81.5%), and behaviors from emotions/thoughts was 175/194 (90.2%).

The mean eMindLog daily average total score was 1.76 and the median was 1.45. The suicidal thoughts item score had the largest skew (and the only one above 2), with 174 (89%) reporting none (score 0). The daily score was not significantly different between the sexes and racial/ethnic groups. The daily score was negatively correlated with education ($P<.001$) and economic status ($P=.02$). Being single was associated with higher scores than couples ($P=.002$). Those receiving therapy ($P=.006$) and medications ($P=.03$) also had higher scores. Those receiving therapy had a poorer quality of life ($P=.003$) and poorer functioning ($P=.008$), but not those receiving medications.

Only a small number (17/195, 8.7%) of subjects reported being disabled. Disabled individuals had nonsignificantly higher daily scores ($P=.074$). However, disabled individuals reported a poorer quality of life ($P=.046$) and restricted functioning ($P=.043$).

Table 2 reports the correlation between the eMindLog daily total scores and the weekly item scores for "Stressed," "Restricted Quality of Life," and "Restricted Function.". They are each correlated in the 0.6 range ($P<.001$).

Cronbach alpha for eMindLog daily average total and index scores are reported in Table 3. Cronbach alpha was .94 for eMindLog daily score and .86 for the HADS total score. The Social index had a Cronbach alpha of .63, below the .7 acceptable threshold, and thus the questions comprising that index were discarded from further analyses. This reduced the eMindLog daily to 17 questions with 4 indexes (anxiety, anger, sadness, and anhedonia). The other eMindLog index scores had Cronbach alpha in the .81-.83 range.

Pearson correlation coefficients between eMindLog and HADS scores are presented in Table 4. eMindLog anxiety index scores and HADS anxiety subscale score Pearson $r$ was .66 ($P<.001$). eMindLog combined sadness and anhedonia index score was correlated with the HADS depression subscale score at $r=.62$ ($P<.001$).

### Diagnostic Thresholds

Table 5 reports the number of subjects (35/195, 17.9%) who met cross-sectional criteria for MDD (29/195, 14.9%) or GAD (23/195, 11.8%). MDD was strongly associated with concurrent GAD ($\phi=.61$, $\chi^2_1=71.80$, $P<.001$). Among those with MDD, the odds of also having GAD (1.417) were 37.8 times higher than the odds among those without MDD (.0375). Subjects with GAD or MDD were more likely to be receiving psychotherapy compared to those without (odds ratio 5.19). However, they were not more likely to be receiving medications for anxiety/depression.

**Table 3.** Cronbach alpha for 17-item eMindLog daily and HADS.

| | Mean | SD | Range | Cronbach alpha |
|---|---|---|---|---|
| eMindLog daily total | 1.76 | 1.451 | 0-7.35 | .94 |
| Anxiety index | 2.50 | 1.771 | 0-7.50 | .83 |
| Anger index | 1.76 | 1.831 | 0-9.00 | .82 |
| Sadness index | 1.46 | 1.767 | 0-8.50 | .82 |
| Anhedonia index | 1.48 | 1.494 | 0-7.33 | .81 |
| HADS total | 11.5 | 6.20 | 0-31 | .86 |
| HADS anxiety | 7.79 | 3.79 | 0-19 | .81 |
| HADS depression | 3.7 | 3.25 | 0-16 | .81 |

**Table 4.** Pearson correlation coefficient for eMindLog daily and HADS scores.

| | HADS anxiety, $r$ ($P$) | HADS depression, $r$ ($P$) |
|---|---|---|
| HADS depression | .55 (<.001) | |
| eMindLog anxiety index | .66 (<.001) | .49 (<.001) |
| eMindLog sadness & anhedonia indexes | .58 (<.001) | .62 (<.001) |

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**Table 5.** Subjects meeting eMindLog thresholds for GAD and MDD (N=195).

| | GAD, n (%) | No GAD, n (%) | Total, n (%) |
|---|---|---|---|
| MDD | 17 (8.7) | 12 (6.2) | 29 (14.9) |
| No MDD | 6 (3.1) | 160 (82.1) | 166 (85.1) |
| Total | 23 (11.8) | 172 (88.2) | 195 (100.0) |

A sensitivity analysis performed using binary logistic regression from the HADS subscale scores to evaluate the validity of the algorithms for GAD and MDD were supportive (see Multimedia Appendix 2).

### Factor Analysis

The eMindLog daily scores were subjected to analyses to determine the number and nature of the subscales that exist. The structure of the eMindLog daily items was explored with a maximum likelihood factor analysis with an oblique rotation (SAS Proc Factor, Promax). Much (60%) of the variance in the 17 items was captured in four factors. Tucker and Lewis' reliability coefficient indicated good fit, with a value of .93. Cluster analysis (SAS, Varclus) was also used to group the 17 items into four clusters. The partitioning of items into clusters matched exactly the partitioning of variables into factors. Cronbach alpha was computed for each of the four subscales. As shown in Table 6, internal consistency/reliability was good, with values ranging from .80-.86.

**Table 6.** Oblique factor analysis of the daily items.

| Factor | Item | Greatest beta | Cronbach alpha |
|---|---|---|---|
| 1. Anhedonia | 14. During the past 24 hours, how lacking in pleasure have you felt? | .73 | .86 |
| | 15. During the past 24 hours, how lacking in thoughts have you been? | .64 | |
| | 17. During the past 24 hours, how lacking in approach have you been? | .62 | |
| | 16. During the past 24 hours, how futile have your thoughts been? | .51 | |
| | 9. During the past 24 hours, how withdrawn have you been? | .44 | |
| | 13. During the past 24 hours, how impulsive have you been? | .39 | |
| 2. Sadness | 7. During the past 24 hours, how sad have your thoughts been? | .83 | .86 |
| | 5. During the past 24 hours, how sad have you felt? | .70 | |
| | 8. During the past 24 hours, how suicidal have your thoughts been? | .59 | |
| | 6. During the past 24 hours, how emotionally numb have you felt? | .52 | |
| 3. Anxiety | 2. During the past 24 hours, how worried have your thoughts been? | .55 | .85 |
| | 1. During the past 24 hours, how anxious have you felt? | .48 | |
| | 4. During the past 24 hours, how avoidant have you been? | .43 | |
| | 3. During the past 24 hours, how physically agitated have you been? | .41 | |
| 4. Anger | 10. During the past 24 hours, how angry have you felt? | .83 | .80 |
| | 12. During the past 24 hours, how hostile have you been? | .63 | |
| | 11. During the past 24 hours, how blaming have your thoughts been? | .56 | |

We hypothesized that distinct factors would match the theoretically derived indexes. There were 2 items in the factor/cluster analyses that were discrepant with the theoretically derived index categorizations—the "withdrawal" and "impulsive" items were included in the anhedonia factor. In the theoretically derived index categorization, "withdrawal" falls into the sadness index and "impulsivity" in the anger index.

## Discussion

### Principal Results

eMindLog is a self-measurement tool for tracking anxiety and depression with several unique features. The basis of eMindLog is a hybrid approach that incorporates the clinical perspective and knowledge from the neurosciences . It assesses emotions, thoughts, and behaviors relevant to anxiety and depression, as well as associated symptoms, quality of life, and functioning. Subjects reported the ability to differentiate emotions from thoughts (82%) and behaviors from emotions/thoughts (90%). eMindLog minimizes assessment burden by differentiating daily from weekly assessments. eMindLog daily has 17 items reflecting 4 indexes—anxiety, anger, sadness, and anhedonia (lack of pleasure)—as noted previously, the 3 items in the social index were removed as their Cronbach alpha score fell below the .7 threshold. The 3 items were revised based on a re-reading of the relevant literature and moved to the weekly set due to the importance of capturing a measure of interpersonal relationships in assessing anxiety and depression. eMindLog weekly thus has 17 items in 5 domains: associated symptoms, stress, interpersonal, restricted quality of life, and functional

impairment. The interpersonal items were not tested in this study but will be particularly scrutinized in future validation studies.

eMindLog enhances measurement precision by describing clearly what the term encompasses and boundaries of an item being assessed, so they are nonoverlapping. Subjects (98%) found value in the items descriptions. eMindLog uses a standard 0 to 10-point scoring system, with descriptive guidance for differentiating severity to enhance accuracy. eMindLog gathers information electronically, using mobile technology to enhance ease of use with dashboard reporting of scores to graphically track scores over time. The individual owns their own data with privacy, confidentiality, and security assured. The user has the ability, if they choose, to share information with their clinician.

This cross-sectional validation study is in a nonclinical, general population convenience sample. The demographics of the study population, including the proportion with clinically significant symptoms, disability, and receiving professional care, support inferential statements from the data. Sex, race, and ethnicity do not impact the eMindLog daily total scores. Higher scores are associated with lower economic status, less education, being single, and receiving professional care. This is consistent with the known adverse effects of low socioeconomic and educational status, and social isolation on mental health. Individuals who reported being disabled (9%) had poorer quality of life and more functional impairment.

eMindLog daily scores had a Cronbach alpha of .94. An alpha score above .7 is considered acceptable for group comparisons for research purposes and an alpha above .9 as supporting reliability for monitoring individual scores [28]. This supports the value of eMindLog for individual patient care in clinical practice.

The daily version of the scale used in this study had 20 questions from which 5 indexes were derived. However, the social index, derived from 3 questions fell below the acceptable Cronbach alpha threshold and the 3 questions and social index were excluded. eMindLog thus has 4 index scores: for anxiety, anger, sadness, and anhedonia, with Cronbach alpha in the .81-.83 range. While the daily total score would suggest the unidimensional nature of the scale, studies in clinical samples are necessary to explore the value of eMindLog index scores in distinguishing biotypes of depression [12,13].

eMindLog index for anxiety had a Pearson correlation coefficient of .66 with the HADS anxiety subscale, and eMindLog sadness/anhedonia indexes with HADS depression subscale was .62. A score above .5 is considered a large convergent validation.

An algorithm derived from the DSM-5 criteria for MDD and GAD suggested that 12% met criteria for GAD and 15% for MDD cross-sectionally. The validity of these algorithms will need to be tested prospectively in studies that use clinician-based diagnoses. These proportions are, however, consistent with what would be expected in the general population. Additionally, the high comorbidity of GAD and MDD is to be expected. GAD and MDD were associated with receiving psychotherapy, but not medication. The more immediate and robust benefits of

medications may have obscured demonstrating a relationship here.

Cluster and factor analyses generally support the index structure of the daily eMindLog for anxiety, anger, sadness, and anhedonia. Two items failed to statistically match the theoretically derived formulations. However, this study is in a nonclinical population with the majority of subjects having few symptoms. Hence, such analyses are better performed in data obtained from clinical populations.

eMindLog has unique features. The items measured daily separate emotions, reflective of positive and negative valence systems, from thoughts, derived from cognitive systems. Both drive behavior, the former from bottom-up, and the latter potentially from top-down processing. The neuroscience distinctions of the threat and reward systems guided the indexes, such that the anxiety, anger, and sadness indexes are reflective of functional states of the threat system, while the anhedonia index reflects underactivity of the reward system. Studies of the cognitive system generally focus on standardized batteries assessing attention, working memory, and executive function, but these fail to address the content of thoughts, which are clinically relevant in anxiety and depression. Emotion, thought, and behavior items are weighted proportionately and contribute equally in the construction of index scores, permitting the comparison of index scores with each other. Future studies in clinical populations will examine the validity of these constructs. Each item is described in brief, distinct, nonoverlapping terms, to enhance measurement precision. The symptoms being assessed are placed in a neuroscience framework—thus, unlike some scales that measure items such as hopeless and worthless thoughts independently, enhancing the influence of thoughts in the total score, eMindLog asks the user to capture all such thoughts in a single item called sad thoughts. Guidance is provided to the user in choosing a score reflective of their experience [25]. Assessment burden is taken into consideration, so that ancillary symptoms needed for imputing diagnostic thresholds are not assessed daily, but every 7 days. Quality of life and functioning are measured separately, since these may provide a different perspective from symptom measures.

## Limitations

While eMindLog has features that positively differentiate it from other self-report measures in anxiety and depression, there are still limitations to be acknowledged. To reflect the flow of mental life, eMindLog entails the daily self-assessment of emotions, thoughts, and behaviors. The average time in the study to score the daily eMindLog was 7.3 minutes and 6.0 minutes for the weekly eMindLog; subjects were using this measure for the first time. Repeat eMindLog users report a time commitment around 3 minutes for each of the daily and weekly components. However, this still requires effort and ongoing adherence. The degree of adherence necessary to provide a minimum threshold for appropriate signal detection remains to be explored.

Somatic components of anxiety and depression are minimally assessed in eMindLog. "Lack of well-being," defined as generally feeling ill or unwell, is the only item that addresses somatic symptoms. Somatic symptoms can either reflect

emotional expression or a general medical condition. Such a distinction is difficult to make, and whether it can be made accurately and reliably in a self-report measure without a clinician's judgment, is uncertain.

eMindLog requires a level of sophisticated awareness of subjective processes, breaking down complex experiences into component parts. The precision of the measure is reported by users to be enhanced with practice and experience. An initial practice period is useful for the maturing of self-observation and while terms and their descriptions are harmonized with a user's subjective experiences. Data from further validation studies, particularly in clinical populations, are needed to explore whether eMindLog has superior signal detection properties than alternatives.

eMindLog has the promise of using mobile technology to gather data that reflect the richness of mental phenomena for use in case detection, monitoring severity, evaluating therapeutic interventions, and clinical trials. Confirmation in clinical populations, particularly the ability to separate the ill from the non-ill is essential. Additional studies will need to explore the

responsiveness to interventions with adequate precision and to document delineations for remission in anxiety and depressive disorders.

While eMindLog demonstrates strong unidimensional characteristics in this validation study, only studies in clinical populations with different diagnoses and in those with general medical conditions, can examine whether index scores have differential utility in specific populations. If eMindLog demonstrates enhanced measurement precision, it may be a useful tool for drug development in anxiety and depression. Enhanced measurement precision may also assist in the discovery of disease biomarkers.

## Conclusions

A novel self-measure of anxiety and depression using mobile technology, is presented. Data from a validation study of eMindLog in the general population demonstrates excellent reliability and a large convergent validity against a standard measure. Future studies in clinical populations will provide an assessment of the full potential for eMindLog.

## Conflicts of Interest

TMP is a Scientific Advisory Board member and equity holder of eMind Science Corp (license holder for eMindLog). PTN is a consultant to Lundbeck (reviewer for grants), and Founder, Chairman, Chief Scientific Officer, and equity holder of eMind Science Corp (license holder for eMindLog).

## Multimedia Appendix 1

Screenshots of website used in the study.

[PDF File (Adobe PDF File), 3MB - resprot_v6i5e98_app1.pdf ]

## Multimedia Appendix 2

Sensitivity analysis of diagnostic algorithms using Hospital Anxiety and Depression Scale (HADS).

[PDF File (Adobe PDF File), 256KB - resprot_v6i5e98_app2.pdf ]

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## Abbreviations

**DSM-5:** Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition
**GAD:** Generalized Anxiety Disorder
**HADS:** Hospital Anxiety and Depression Scale
**MDD:** Major Depressive Disorder
**RDoC:** Research Domain Criteria

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Original Paper

# Using Text Messaging in Long-Term Arthroplasty Follow-Up: A Pilot Study

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## Abstract

**Background:** Patient-reported outcome measures (PROMs) and mobile technology have the potential to change the way patients are monitored following joint replacement surgery.

**Objective:** The aim of this study was to determine the feasibility of text messaging to record PROMs in long-term follow-up of hip and knee arthroplasty. Our participants were 17 patients 2-years-plus post hip or knee arthroplasty attending clinic with a mobile telephone number on record.

**Methods:** A simple PROM (Oswestry Very Short Form) was texted to the patient. Responses were compared to clinical, radiographic, and existing PROM findings. Patients were interviewed to discover their opinions on this use of texting.

**Results:** A total of 11 patients engaged with the text messaging. Reasons for not engaging included wrong numbers, physical barriers, and lack of understanding. A total of 8 patients attending clinic allowed comparison of text messaging with clinical findings. The average age was 70 years. A total of 4 patient text messaging responses matched clinical and radiographic findings; 3 also matched PROM scores collected in clinic. The 3 patients with mixed responses had abnormal clinical, radiographic, or PROM findings. One patient's text responses conflicted with clinical outcome. Analysis of patients' views showed a generally positive opinion: patients were happy to communicate with surgeons by text. Practical problems, PROM limitations, and trustworthiness of texting were highlighted.

**Conclusions:** Engaging with changing technology creates challenges for patients and health care professionals. Despite this, our results suggest text messaging is a promising way to communicate with arthroplasty patients. Earlier integration of text communication in the patient pathway may be important and needs further research.

## Introduction

In an ideal world, every patient who undergoes joint replacement surgery should be followed up for the remainder of the life of the prosthesis or the patient. Failure rates in modern implants are low, but revision surgery is demanding, expensive, and distressing for the patient. An increase in primary procedures potentially creates a large revision burden [1]. Previous work investigating arthroplasty follow-up using technology has looked at short-term follow-up (less than 1 year) [2] and Internet- and computer-based evaluation [3].

Long-term follow-up of all arthroplasty patients in clinic would probably outstrip the capacity of most orthopedic outpatient departments in the National Health Service (NHS). Patient-reported outcome measures (PROMs) are common in arthroplasty surgery [4]. PROMs may have the potential to transform health care by measuring outcomes, prioritizing treatment and reimbursement. There are challenges to widespread PROMs use: minimizing the time, cost, collection, and analysis of data and maximizing patient participation. The adaptation of technology and Medicine 2.0 principles could be a way of encouraging widespread use of PROMs [5]. Studies outside of orthopedic surgery have noted that simple, short message service (SMS) interventions are as effective as more complex ones in modifying patient behavior [6]. Remote collection of PROMs and their comparison to results collected in outpatient clinics has been assessed previously, finding no difference between remote and on-site scores [7].

Mobile technology has developed since the early 2000s from simple, 2-way pagers to smartphones and tablet computers using wireless networks [8]. In the United Kingdom, 93% of adults own and use a mobile phone and 63% own a smartphone. Text messages or SMS are a common form of communication; the average number of text messages sent per person, per month in the United Kingdom was 117 in 2014 [9]. The literature on text messaging in health interventions is generally positive. It highlights good acceptance and efficacy, but the evidence base is limited [10]. Studies have shown that text messaging is a valid method of reminding patients about outpatient appointments [11] and that patients up to 75 years old show confidence with reading messages [12]. The issue regarding age and mobile technology uptake is evolving. Mobile technology itself presents challenges to older patients but these are likely to be practical (such as poor dexterity and vision) rather than due to attitudes and perceptions [13]. Further, older patients of tomorrow will be more familiar with and reliant on mobile technology than the current older generation [14]. For the target population in this study (60 years and older), the success of communication using mobile technology depends on how it is adapted and tailored to their needs [15].

Text messaging is a basic form of mobile communication. If shown to be a feasible way of communicating with arthroplasty patients, it has the potential to decrease the outpatient burden, collect PROMs data, and extend communication with patients beyond existing capabilities. This study aimed to determine the feasibility of text messaging as a means of communicating PROMs with long-term arthroplasty patients. We intended this study to be the first step to further research into mobile technology and PROMs.

## Methods

We investigated how patient text message PROMs responses compared to their clinical and radiological findings, and we elicited patient opinions on communicating with their surgical team by text message. This project was approved by the Cardiff and Vale University Health Board (CAVUHB) Continuous Service Improvement group as a service evaluation on January 9, 2015. Permission was granted to perform a small-scale pilot study comparing a text messaging assessment to clinical evaluation of patients attending continuing outpatient care by their operating surgeon.

The Cardiff and Vale Orthopaedic Centre (CAVOC) currently uses an email-based PROM monitoring system (Amplitude Clinical, Worcestershire, UK) to collect patient-generated joint scores, standard health outcomes, and "family and friends" [16] measures (how likely the patient would be to recommend the hospital). This has been in place since January 2015 and has no long-term results yet, so for our pilot study the principal change was to replace email with a short PROM delivered and responded to by text message.

The sample population was patients of two arthroplasty consultants at CAVUHB (RMJ/AG) who were more than 2 years following a primary hip or knee joint replacement, were already attending a follow-up appointment, and had a mobile telephone number on the electronic patient record system.

Eligible patients were sequentially texted using a smartphone (Apple iPhone 3GS), 2 to 3 days prior to their clinic appointment, a message of introduction, explanation, reminder of their surgery and appointment, and consent to participate. Patients who responded were then sent the PROM, developed at the Robert Jones and Agnes Hunt Orthopaedic Hospital and named the Oswestry Very Short Form (VSF). It consists of 2 questions: "Are you happy with your joint replacement?" and "Would you have it done again," with the responses "yes" or "no." The principle of the VSF is to measure patient satisfaction (happiness). This measure provides 3 outcomes: a positive response (yes/yes), a negative response (no/no), and a mixed response (yes/no or no/yes). A positive response should indicate satisfaction; a negative, dissatisfaction with the joint replacement; and a mixed response would indicate a need to investigate further. Patient text message responses were then compared to the consultant surgeon's assessment of them in clinic and their radiographic findings (signs of loosening or wear of the prosthesis). The patients also were assessed using existing, validated PROMs. The hip arthroplasty patients were assessed using the physician-derived Harris Hip Score (HHS) [17], and the knee arthroplasty patients completed the patient-derived Oxford Knee Score (OKS) [18]. As patients were unevenly distributed over 8 clinics spanning 2 months, inclusion was cumulative.

Data collected were anonymized and transposed from the survey tool to CAVUHB systems to ensure data security and confidentiality. Patient age, gender, prosthesis, surgeon, and

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year of surgery were recorded. The text messaging engagement and PROM responses were recorded as well as the PROM completed in clinic. Radiographs were analyzed by the consultant surgeon and recorded alongside the patient symptoms and signs in their clinic letter. After completion, the mobile device was wiped of all information.

For qualitative data collection, face-to-face survey techniques were used by the principal investigator (OB). The patients who attended were met on arrival to the outpatient clinic, where OB introduced himself as the author of the text messages, explained the study to the patients, and gained their consent to be interviewed during their visit to the clinic. The intention was to follow a semistructured interview guide, shown in Textbox 1.

**Textbox 1.** Semistructured interview guide.

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Interview questions

- Did you know we had your mobile phone number?

- What was your opinion on receiving the messages?

    - Prompt: Did you think it was appropriate to receive text messages from the Health Board?

    - Prompt: Were the messages clear and understandable?

    - Prompt: Did they allow you to express how you felt?

- What are your thoughts on receiving messages from us in the future?

- If you were unable to continue seeing your surgeon, would you be happy to use text messaging or other forms of communication?

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Closed and open questions were followed by prompts to maintain a conversation and elicit meaningful opinions. The prompts were flexible and were not always used.

## Results

### Overview

A total of 8 patients engaged with text messaging, attended clinic, and completed clinical evaluation, radiological assessment, and PROM scores. The average age was 70 years (range 59-85 years). The results are shown in Figure 1. The patient who did not answer the second question stated that it would have been yes, but as she was attending clinic she preferred "to tell you in person."

The typical values chosen by surgeons for the existing PROMs were an OKS of 24 or less (out of a total of 48) and an HHS of less than 70 (out of 100) as indicating a poor score needing surgical opinion [19]. Both of these values are subjective, decided by the surgeons' experience. The table shows that 4 binary VSF results (positive or negative) matched the clinical evaluation and in 3 cases related to the existing PROM. In 1 case, a positive VSF result did not match (a patient planned for revision surgery); 3 of 4 mixed responses did not match clinical or radiographic findings but had concerning PROM scores.

**Figure 1.** Summary of engaged and clinically assessed patient results.

| Age | Gender | Prosthesis | Year | Happy with joint? | Procedure again? | Clinical evaluation | Radiographic appearance | PROM |
|-----|--------|------------|------|-------------------|------------------|---------------------|-------------------------|------|
| 85 | Male | TKR | 2013 | No | No | Painful | Previously fine, recent bone scan normal | 11.00 (OKS) |
| 78 | Male | TKR | 2009 | No | Yes | Revision planned | Loss of joint space PFJ | 17.00 (OKS) |
| 64 | Female | TKR | 2013 | Yes | Yes | Revision planned | Eccentric patella component | 22.00 (OKS) |
| 59 | Female | TKR | 2008 | Yes | No | Painful | No abnormality (but abnormal bone scan) | 24.00 (OKS) |
| 74 | Female | TKR | 2011 | Yes | No | No problems | Previous valgus femoral position unchanged | 29.00 (OKS) |
| 72 | Female | TKR | 2011 | Yes | Yes | No problems | No abnormality | 44.00 (OKS) |
| 64 | Male | THR | 2011 | Yes | Yes | No problems | No abnormality | 52.25 (HHS) |
| 63 | Female | THR | 2011 | Yes | Yes (answered in clinic) | No problems | No abnormality | 73.85 (HHS) |

OKS: Oxford Knee Score          HHS: Harris Hip Score

**Figure 2.** Study participation flow diagram.
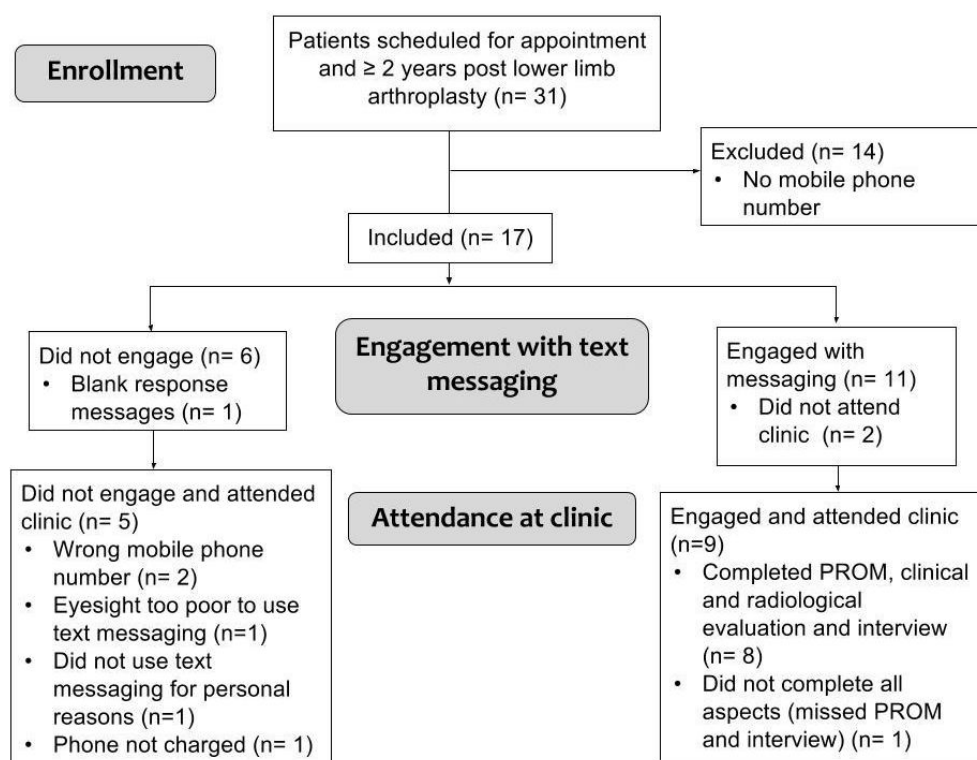
## Patient Views

The 5 patients who did not engage with messaging were questioned on their reasons for not responding, and the reasons are summarized in Figure 2. The 8 patients who engaged with the text messages were asked the questions as outlined in Textbox 1. The transcribed recordings were analyzed by OB.

## Opinions on Text Messaging

A total of 5 confirmed that it was appropriate to receive such messages, and 2 volunteered that it was a good idea. A total of 5 expressed surprise that they had received text messages from the Health Board, and 3 patients thought it may have been a scam; patients highlighted how important it was for a message sender to identify themselves. One suggested that instead of an unknown phone number they would prefer the message to be assigned a contact name, such as "(name of) Hospital." However, the clarity of the first message was praised for having identifiable names and knowledge of their surgeon and procedure.

## Views on the Oswestry Very Short Form

A total of 2 patients praised the VSF for being simple, and 2 said they would be happy to answer more questions by text message. Although all liked the brevity of the VSF, 5 patients wanted to expand on their answers, and 2 patients did provide additional information they thought was useful.

## Future Text Messaging

A total of 6 patients said they would be happy to receive further text messages from CAVUHB. The same number would be happy to communicate with their surgeon by text message if they were unable to see them in person, and 2 patients volunteered they would be happy to communicate with other members of the team instead of their surgeon. While 2 patients expressed a preference for communicating in future on a land line, 1 patient thought that text messaging would be "a good way for the NHS to save money."

A total of 2 patients said they would not be happy using email to communicate in the future, and 2 would be happy to "touch base" using text messages on an annual basis, especially when there were unexpected gaps between appointments.

> ...on another day like this it could say "Have you any problems"...."no everything is fine, or great" and "I would be in touch with you in the future."

Finally, 2 patients expressed dismay at the time spent attending or the distance travelled to an outpatient clinic when there were no problems.

> There is your afternoon or your morning gone for the sake of 2 minutes. But if it was just a matter of a text message, it is so much easier.

## Discussion

### Principal Findings

Appreciating the limitations of this study is an important part of its message. This was pilot study with a small sample to meet the requirements of ethical approval under Continuing Service Improvement. The Health Board does not routinely follow arthroplasty patients up in outpatient clinic more than 1 year postoperatively; our population of patients was more than 2 years after arthroplasty. The Health Board agreement was for a small scale pilot study only as prior patient consent had not been obtained; the patients were not informed of this study from the start of their surgical experience, which may have affected their opinions and engagement. Encouragingly, of the patients who did not respond, none refused to participate. Reasons for not engaging related to wrong numbers and physical or personal reasons related to mobile use more generally.

The methodology was pragmatic, sampling within the confines of existing patient clinics. Further work requires patients to be identified, consented, and involved from the outset of the study. This project focused on the patient-doctor communication and primarily the patients' views on text messaging. We have not considered other surgeons' views apart from those of the authors (who by definition are biased favorably toward the project). Investigation into other orthopedic surgeons' views, as well as those of administration staff who may be involved in the response and analysis of the text message communication, are required. Data security would need to be improved in the future (in line with Good Clinical Practice guidelines [20]). Texting patients sequentially from a smartphone is impractical for a large population as is transposing data from a survey tool to a spreadsheet. An ideal system would be a text messaging system allowing identification of patients, automatic sending and responding, and data capture with analysis and auditing. We suggest including applicable elements of the Checklist for Reporting Results of Internet E-Surveys, an existing matrix for designing Web-based surveys [21].

Our results show more than half of long-term arthroplasty patients have a mobile device and reported that they regularly used it. Of those, nearly two-thirds readily engaged with the text messaging intervention. In studies using Web-based surveys with orthopedic patients, less than half of patients (who had enrolled at the start of their patient experience) responded. In comparison, response rates in our study suggest text messaging may be a feasible option for long-term follow-up for at least a proportion of patients. This we believe could readily increase with better records of mobile numbers and increasingly prevalence in use of devices [22]. Texting is a limited format but short messages are attractive. There were conflicting opinions regarding communication via email and telephone. It is unlikely that there is a single method acceptable to all patients, and assumptions should not be made [13].

This was the first time the Oswestry VSF has been described in practice. The measure requires further validation as a clinical tool, which is beyond the scope of this paper. It was chosen specifically for its relevance, brevity, and ease of response. Patients made positive comments about its short length, although the results suggest it may be too brief for this group of patients. While some patients may be willing to complete an OKS by text message, the ideal orthopedic PROM for text message responses has yet to be devised. A text-based PROM should be designed to be useable by a patient who may have poor eyesight and arthritic fingers, who may take 25 minutes to read and respond to a single text message (as one patient described).

Of 4 positive VSF outcomes, 3 matched clinical and radiological findings. The one negative PROM matched clinical findings. PROMs delivered via mobile technology may play a useful role in filtering patients into groups: for example, satisfied patients who can be safely observed remotely, and unsatisfied patients who need clinical attention potentially more quickly than in existing outpatient formats. The problem, as seen from these small numbers, is that nearly half of the patients cannot be easily classified by the mobile PROMs. One author (JR) uses existing PROMs preoperatively and postoperatively to monitor trends in patient symptoms and satisfaction. The literature suggests that it is more useful to monitor the change in score than absolute values and that PROMs are more likely to identify satisfied patients [23]. Combining PROMs delivered by mobile technology with automated radiography reporting could allow trends to be monitored and changes correlated with radiographic findings. A combination of mobile messaging and radiographs has potential as a long-term, low-cost follow-up system for a large proportion of arthroplasty patients.

### Considerations for Future Research

As a result of our pilot study, we suggest future research into mobile technology delivered PROMs should do the following:

- Ensure engagement of the surgeon, hospital, and patient from the start of the process (preoperative assessment and patient education) to encourage participation, agree on a suitable communication method, gain consent, and ensure the probity of patient data
- Maintain accurate records of patient preferred contact details, which may not be limited to mobile or landline telephone numbers and email addresses. Patients, surgeons, and hospitals have a responsibility to keep patient information up to date and to use it to communicate effectively
- Consider physical barriers to using mobile technology and accept that such technology may not be suitable for all patients

### Conclusions

This pilot study on the use of text messaging to deliver PROMs to patients is an important first step to conducting rigorous research into new ways of monitoring outcomes in the long-term arthroplasty follow-up. Mobile technology, which is readily embraced by the arthroplasty demographic of today and could be universally used by the patients of tomorrow, should be engaged with and used by orthopedic surgery in the NHS. We have shown that many patients are willing and able to engage with mobile technology–delivered PROMs. Patient opinions on text messaging as a form of communication with their surgeons are generally positive, and text messaging could form an acceptable part of patient follow-up. For future research, we emphasize the importance of the involvement and engagement of patients and hospitals in these systems from the start of the arthroplasty pathway.

### Conflicts of Interest

None declared.

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## Abbreviations

**CAVUHB:** Cardiff and Vale University Health Board
**CAVOC:** Cardiff and Vale Orthopaedic Centre
**HHS:** Harris Hip Score
**NHS:** National Health Service
**OKS:** Oxford Knee Score
**PROMs:** Patient Reported Outcome Measures
**SMS:** short message service
**VSF:** Oswestry Very Short Form

Original Paper

# A Personalized and Interactive Web-Based Health Care Innovation to Advance the Quality of Life and Care of Patients With Heart Failure (ACQUIRE-HF): A Mixed Methods Feasibility Study

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## Abstract

**Background:** Heart failure (HF) is a progressive, debilitating, and complex disease, and due to an increasing incidence and prevalence, it represents a global health and economic problem. Hence, there is an urgent need to evaluate alternative care modalities to current practice to safeguard a high level of care for this growing population.

**Objective:** Our goal was to examine the feasibility of engaging patients to use patient-centered and personalized tools coupled with a Web-based, shared care and interactive platform in order to empower and enable them to live a better life with their disease.

**Methods:** We used a mixed methods, single-center, pre-post design. Patients with HF and reduced left ventricular ejection fraction (n=26) were recruited from the outpatient HF clinic at Odense University Hospital (Svendborg Hospital), Denmark, between October 2015 and March 2016. Patients were asked to monitor their health status via the platform using the standardized, disease-specific measure, the Kansas City Cardiomyopathy Questionnaire (KCCQ), and to register their weight. A subset of patients and nursing staff were interviewed after 3-month follow-up about their experiences with the platform.

**Results:** Overall, patients experienced improvement in patient-reported health status but deterioration in self-care behavior between baseline and 3-month follow-up. The mean score reflecting patient expectations toward use prior to start of the study was lower (16 [SD 5]) than their actual experiences with use of the platform (21 [SD 5]) after 3-month follow-up. Of all patients, 19 completed both a baseline and follow-up KCCQ. A total of 9 experienced deterioration in their health status (range from 3-34 points), while 10 experienced an improvement (range from 1-23 points). The qualitative data indicated that the majority of patients found the registration and monitoring on the platform useful. Both nursing staff and patients indicated that such monitoring could be a useful tool to engage and empower patients, in particular when patients are just diagnosed with HF.

**Conclusions:** The use of patient tracking and monitoring of health status in HF using a standardized and validated measure seems feasible and may lead to insights that will help educate, empower, and engage patients more in their own disease management, although it is not suitable for all patients. Nursing staff found the patient-centered tool beneficial as a communication tool with patients but were more reticent with respect to using it as a replacement for the personal contact in the outpatient clinic.

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## Introduction

Heart failure (HF) is the end stage of most heart diseases and a progressive, debilitating, and complex clinical syndrome characterized by dyspnea, edema, pulmonary congestion, decompensation, fatigue, impairments to daily functioning and quality of life [1,2], and risk of frequent hospitalizations and death [3]. Due to an increasing incidence and prevalence, which is expected to continue the next 20 years [4,5], HF represents a global health and economic problem at a time when health care systems worldwide are challenged. Hence, there is an urgent need to evaluate alternative care modalities to current practice to safeguard a high level of care for this growing population.

To date, HF care and disease management modalities that have been more clinically driven and relied on a mixture of telemonitoring, clinician monitoring and rating of symptoms based on more biometric measures and clinician-initiated contact have shown mixed results [6,7]. In addition, there is no close relationship between the vast majority of physicians' traditional objective indicators of HF severity (eg, New York Heart Association [NYHA] functional class, electrographic, and hemodynamic parameters) and patients' own assessment of their health status and quality of life [8]. By contrast, patients' rating of their own health predicts mortality and hospital readmissions in HF independent of somatic disease indicators and traditional biomedical risk factors [9-11]. However, no proxy measure for patient-rated health status can be captured from patient medical records nor is standard screening for patient-reported health status part of clinical cardiology practice in Denmark today.

Thus, patient-rated health status could be used with advantage as one of the patient-centered tools in clinical practice to monitor patients' health status, which may allow the timely detection of clinical deterioration in their HF condition and enable treatment recommendations to be tailored to individual patient needs and preferences [12-14]. This represents a systems review of the body beyond what traditional biometric measures can offer and is sustainable over time in contrast to technological solutions that may rapidly become outdated and replaced. A one-size fits all approach [6,15] and the absence of a patient-centered approach are likely to have contributed to the failure of available HF care and disease management modalities [16,17]. In addition, a recent study advocates a paradigm shift that moves away from "...individual blame toward an empowerment and systems approach that considers the big picture" [17].

Hence, we designed the ACQUIRE-HF study (a personalized and interactive Web-based health care innovation to advance the quality of life and care of patients with heart failure) to examine the feasibility of engaging patients to use patient-centered and personalized tools coupled with a Web-based, shared care, and interactive platform in order to empower and enable them to live a better life with their disease. The feasibility study is a precursor to a large randomized controlled trial that will open up for more features on the platform and include a psychological intervention for the subset of patients who score high on anxiety and depression. The results presented in this paper include both quantitative and qualitative data on experiences with the platform and the intervention both from the perspective of patients and nursing staff.

## Methods

### Study Design and Population

We used a mixed methods, single-center, pre-post design. Patients with HF (n=26) were recruited from the outpatient HF clinic at Odense University Hospital (Svendborg Hospital), Denmark, in the period between October 2015 and March 2016 as a convenience sample. Patients were asked to complete purpose-designed, standardized, and validated questionnaires at baseline and at 3-month follow-up. Nursing staff (n=6) from the outpatient HF clinic was involved in the study.

The qualitative study consisted of (1) observations during the workshop and training course of the nursing staff in use of the platform, which was provided by CGI Denmark, (2) observations during the workshop and training of 5 of the 26 patients on how to use the platform, which was provided by nursing staff, (3) semistructured telephone or face-to-face interviews with 10 patients after they had used the platform for 3 months (patients were interviewed toward the end of January 2016), and (4) focus group interviews with 3 of the 6 nurses, which were conducted at a time when the majority of the 26 patients had been included in the study.

The Health Innovation Centre of Southern Denmark was responsible for all observations and interviews. Nurses provided continuous feedback, and a midway evaluation was conducted with nursing staff, CGI Denmark, and the research team from the University of Southern Denmark.

### Ethics

We submitted the study protocol to the Regional Committees on Health Research Ethics for Southern Denmark. According to Danish law on ethics related to health research (Law 593 of June 14, 2011), ethical committee approval is not required for this kind of study. The study was performed according to the Helsinki Declaration. Permission was also sought and granted from the Danish Data Protection Agency under the umbrella agreement of the University of Southern Denmark (2015-57-0008).

### Platform Used for the Study

We used CGI's modular and cloud-based CommunityCare360 (CC360) platform in the study, with patients and nursing staff having access to the platform and its tools via a Web interface on a tablet, smartphone, or computer. CC360 makes it possible for patients, health care professionals, and other stakeholders to access, monitor, and update personal health data. It allows for (1) integration of information from various sources including health technology (eg, weight scale) that patients may use, electronic health record (EHR), labs, imaging, and prescribing; (2) relatives to gain access to patient data provided that patients give their permission; (3) patients to write messages to the HF team; (4) patients and caregivers and health care professionals to engage in video dialogs; and (5) setting targets for patients' medication, which may serve as a reminder to patients and

health care professionals if targets are not met. Manuals are available to support use for patients, clinicians, and other health care professionals. The platform has a health care classification toolkit (SNOMED, *International Classification of Diseases, 10th Edition* [ICD-10], ICD-10 procedure codes [ICD-PC], Nomenclature for Properties and Units [NPU] result codes, etc) and facilitates easy device integration through the Sensor engine, which supports the Continua Alliance standard. The platform gives instant feedback in a red-amber-green color state methodology, clearly showing the patient if the measurement is okay (green), if the patient should consult with a doctor (amber), or if the patient must consult with a doctor (red). This acts as a guideline both to patients and physicians to take action in the case of amber and red alerts.

We used only 2 features on the platform for the feasibility study: patient registration of their weight and completion of a health status measure, allowing for patients to monitor their weight and health status over time. We started out with only these 2 features as HF patients tend to be somewhat older and not necessarily used to using technology [18]. We chose these 2 specific features as a try out, as weight monitoring is an essential part of HF management because an increase in weight can be a sign of congestion and decompensation [19] and patient-reported health status has been shown to be an independent predictor of rehospitalization and mortality [9]. Figure 1 presents the interface of the CC360 platform as seen by patients in the feasibility study.

**Figure 1.** CommunityCare360 interface as seen by patients.
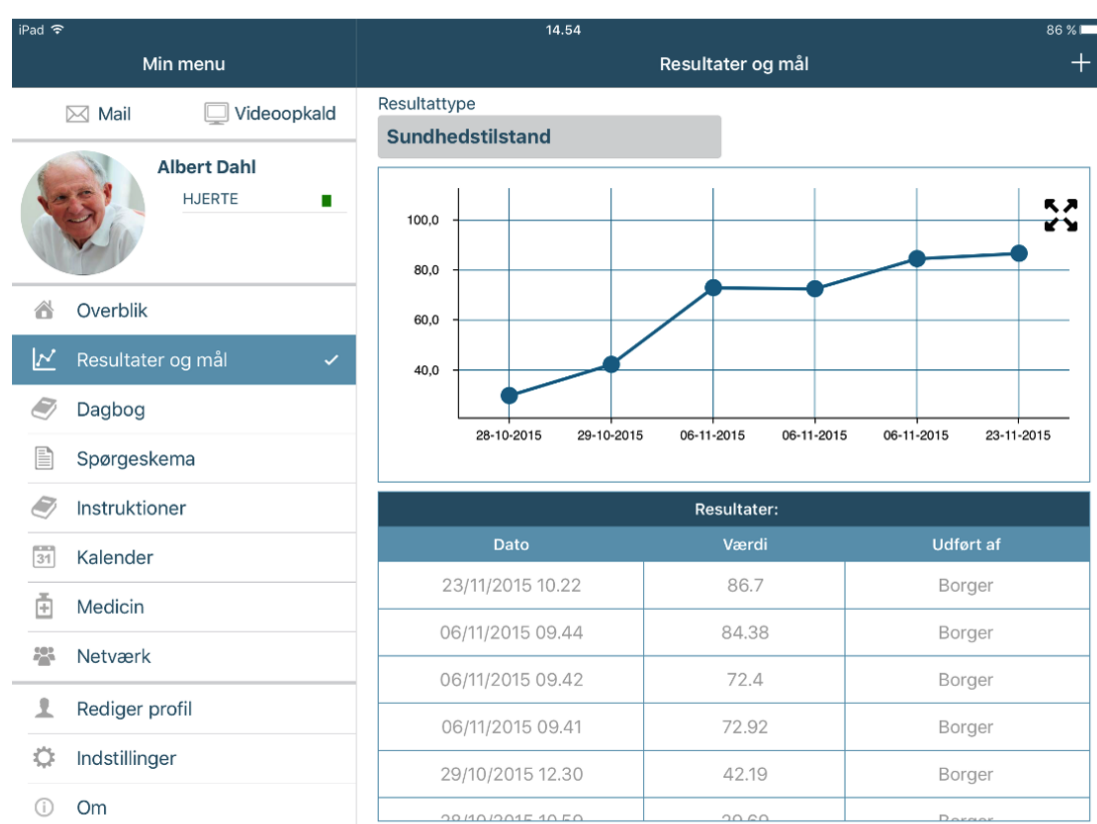


## Measures

Information on baseline demographic and clinical characteristics was either captured from purpose-designed questions in the questionnaire or from the patient medical records. Data on patient compliance with reporting their weight and health status on the CC360 was available from the platform. Patients were asked to complete the following measures pretest (ie, at baseline) and posttest (ie, at 3-month follow-up).

### Patient Expectations Toward and Experiences With the Platform

We developed a 11-item purpose-designed questionnaire to tap into patient expectations and experiences with the platform, with choice of items inspired by the standardized and validated Expectations Towards ICD Therapy (EXPECT-ICD)

questionnaire [20]. We used the same items to tap into patient expectations toward use of the platform pretest and their experiences posttest, with the only difference in the wording being the use of the present versus past tense (eg, pretest: "Do you expect that use of the platform will make you feel more safe?" versus posttest: "Do you feel that the platform has led to you feeling more safe?"). The questionnaire contained both negatively and positively worded items. Items were rated on a 5-point Likert scale from 0 (completely disagree) to 4 (completely agree). Negatively worded items were recoded prior to calculating a total score. The score range of the scale is 0 to 44, with 44 representing the highest level of expectations and best possible experience with the platform.

### Kansas City Cardiomyopathy Questionnaire

The Kansas City Cardiomyopathy Questionnaire (KCCQ) is a disease-specific, validated, patient self-report international standard used to quantify patient experiences with HF [21] that can capture clinical changes in patient condition and predict hospitalization and mortality [9,22] independent of N-terminal pro-brain natriuretic peptide, a biometric measure predictive of HF progression and mortality [23]. We used the 12-item version to reduce patient burden—an abbreviated version of the 23-item scale [24]—with equivalent validity and reliability [25]. Via an algorithm, KCCQ scores are converted to a score from 0 to 100, with 100 representing the best possible health status.

### European Heart Failure Self-Care Behavior Scale

The European Heart Failure Self-Care Behavior (EHFScB) scale is a 9-item standardized and validated questionnaire that assesses patient opinions on their ability to manage their HF (eg, "I take my medication as prescribed"), with items answered on a 5-point Likert scale from 1 (completely agree) to 5 (completely disagree) with a score range of 9 to 45, with 9 representing best possible self-care behavior [26].

### Study Procedure

Nurses from the outpatient HF clinic approached patients for study participation and provided them with written and oral information about the study. After signing an informed consent form, patients were asked to complete the baseline questionnaire. Patients were also asked if they would be willing to be interviewed about their experiences with use of the platform after 3 months. Nurses from the hospital set up patients on the platform, and patients received a log-in and password to gain access. Nurses also trained all patients how to use the platform and patients received a user manual for CC360 to take home to facilitate use. Patients could contact the outpatient clinic if they encountered any problems with use of the platform (eg, problems with logging in, questions related to the use of the platform) with the nurses being the first point of contact for technical support. CGI Denmark provided back-up support to the nursing staff. Patients were also informed that use of the platform was not a substitute for usual care and that they should contact the clinic if they felt unwell and experienced deterioration in their condition or contact emergency services outside office hours.

### Intervention

As part of the intervention, patients were asked to do the following:

- Weigh themselves every day in the morning on their own scale and enter the weight into the platform. The rationale was that both the patient and the nursing staff in the outpatient clinic could monitor the patient's weight and that

patients might gain more insight into their weight fluctuations.
- Complete the KCCQ every 2 weeks during the 3-month study period as an indication of their health status. Scores were plotted in a graph that was visible both to patients and the nursing staff. Patients were instructed how to interpret their score and could also see the evolution in their health status over time.

The nursing staff had the following responsibilities:

- Call patients 1 week after study inclusion to ensure that patients could log in to and use the platform and were able to comply with the tasks (ie, entering and monitoring their weight and health status) as indicated above.
- Check every time patients had completed the health status measure (KCCQ). A reduction in patient score by 20% or more as compared to their baseline value instigated a red alert, a reduction between 10% and 20% an amber alert, and a reduction of 10% or less a green alert. These alerts appeared in the nursing staff's module on CC360, which required them to contact the patient to discuss if the patient needed to be seen in the clinic.
- If patients would forget to enter their weight or to complete the KCCQ, a red light would appear on the nursing staff's module on CC360. They would then be required to contact the patient to remind the patient to complete the measures.

### Data Analysis

Results related to the quantitative data are reported as frequencies with percentages or as means and standard deviation. Pearson correlation coefficients were calculated to examine the relationship between continuous measures. Data were analyzed using RStudio version 0.99 (RStudio Inc) and SPSS Statistics for Macintosh version 22.0 (IBM Corp). The qualitative data were analyzed using thematic analysis, with the aim of grouping data and finding patterns that give insight into the user experiences with the platform [27].

## Results

### Quantitative Data

Baseline characteristics of the patient sample are presented in Table 1. The mean age was 67 (SD 11) years, and the majority of patients were men with an NYHA functional class I-II (ie, asymptomatic or mild symptomatic HF).

### Study Attrition

The 7 patients who did not complete the posttest questionnaire had a lower baseline mean score on expectations toward the platform (15 [SD 4] vs 16 [SD 6]), a better self-care behavior score (13 [SD 3] vs 18 [SD 5]), and a lower health status score (61 [SD 21] vs 69 [SD 21]) as compared to the 19 patients who completed both the pre- and posttest questionnaires.

**Table 1.** Baseline characteristics of the patient cohort (n=26).

|  | Total |
|---|---|
| Age (years), mean (SD) | 67 (11) |
| Men, n (%) | 21 (81) |
| Married/have a partner, n (%) | 20 (77) |
| Lower educational level (<14 years), n (%) | 15 (58) |
| Employed, n (%) | 7 (27) |
| **NYHA class[a] (severity of heart failure), n (%)** |  |
| I-II | 24 (92) |
| III-IV | 2 (8) |
| **Comorbidities (based on self-report), n (%)** |  |
| Stroke | 4 (15) |
| Diabetes | 2 (12) |
| Aneurism | 1 (4) |
| Liver disease | 0 (0) |
| Kidney disease | 0 (0) |
| Claudicatio intermittens | 0 (0) |
| COPD[b] | 3 (12) |
| Ulcer | 1 (4) |
| Cancer during last 5 years | 1 (4) |
| Other | 5 (19) |

[a]NYHA: New York Heart Association functional class (III-IV: most severe heart failure).

[b]COPD: chronic obstructive pulmonary disease.

**Table 2.** Pre- and posttest scores on the questionnaires.

|  | Baseline pretest | | 3-month follow-up posttest | |
|---|---|---|---|---|
|  | Valid cases (n) | Mean (SD) | Valid cases (n) | Mean (SD) |
| Expectations: use of the platform[a] | 25 | 16 (5) | — | — |
| Experiences: use of the platform[a] | — | — | 18 | 21 (5) |
| Health status: KCCQ[b] | 26 | 62 (21) | 19 | 68 (15) |
| Self-care behavior: EHFScB[c] | 26 | 17 (5) | 19 | 18 (6) |

[a]The same items were used to tap into patient expectations toward use of the platform pretest and their experiences posttest with the only difference in the wording being the use of the present versus past tense (see the Methods section). Score range was 0 to 44 (44 = highest level of expectations and best possible experience).

[b]Kansas City Cardiomyopathy Questionnaire (KCCQ) score range 0 to 100 (100 = best possible health status).

[c]European Heart Failure Self-Care Behavior (HFScB) score range 9 to 45 (9 = best possible self-care behavior).

## Patient Expectations and Experiences and Actual Use of the Platform

Patient scores with respect to expectations toward and experiences with the platform are displayed in Table 2. Patient actual use of the platform, as indicated by the number of times that patients were logged on to the platform, varied considerably from 2 to 210 times during the 3-month follow-up period, with total number of log-ins being 2968 and the mean being 114 (SD 72) times (median 140, interquartile range 131). A total of 3 patients never logged on to the platform. Patients with higher expectations toward use of the platform at baseline reported a higher score with respect to their experiences after 3 months (Pearson $r$=.41; $P$=.10), with expectations toward use of the platform accounting for 17% of the variance in patient experiences with the platform.

**Table 3.** Pre-, posttest, and change health status Kansas City Cardiomyopathy Questionnaire scores and weight entries on the platform for individual patients during 3-month follow-up.

| Patient ID | KCCQ[a] score baseline | KCCQ score 3-month follow-up | KCCQ change score | KCCQ platform entries (count)[b] | Weight platform entries (count)[c] |
|---|---|---|---|---|---|
| 1 | 85 | — | — | 0 | 1 |
| 2 | 72 | 63 | –9 | 4 | 84 |
| 3 | 76 | — | — | 0 | 0 |
| 4 | 87 | 92 | 5 | 6 | 65 |
| 5 | 46 | 51 | 5 | 6 | 84 |
| 6 | 31 | — | — | 2 | 14 |
| 7 | 69 | — | — | 5 | 77 |
| 8 | 37 | 57 | 20 | 6 | 84 |
| 9 | 43 | — | — | 1 | 1 |
| 10 | 98 | 64 | –34 | 5 | 82 |
| 11 | 51 | 74 | 23 | 5 | 85 |
| 12 | 81 | 75 | –6 | 6 | 78 |
| 13 | 48 | 50 | 2 | 6 | 75 |
| 14 | 45 | 60 | 15 | 6 | 76 |
| 15 | 72 | 62 | –10 | 6 | 64 |
| 16 | 93 | 90 | –3 | 5 | 85 |
| 17 | 76 | — | — | 4 | 51 |
| 18 | 46 | — | — | 6 | 85 |
| 19 | 74 | 52 | –22 | 6 | 84 |
| 20 | 96 | 92 | –4 | 2 | 21 |
| 21 | 100 | 88 | –12 | 1 | 1 |
| 22 | 65 | 57 | –8 | 6 | 83 |
| 23 | 52 | 55 | 3 | 6 | 78 |
| 24 | 58 | 66 | 8 | 4 | 86 |
| 25 | 84 | 85 | 1 | 5 | 84 |
| 26 | 50 | 58 | 8 | 6 | 79 |

[a]KCCQ: Kansas City Cardiomyopathy Questionnaire.

[b]Possible KCCQ entries during 3-month follow-up period = 6.

[c]Possible weight entries 3-month follow-up period = 90.

## Changes in Health Status and Self-Care Behavior and Weight Entries

Table 2 presents the mean and SD pre- and posttest scores on the questionnaires. Overall, patients experienced improvement in patient-reported health status but deterioration in self-care behavior between baseline and 3-month follow-up. The mean score reflecting patient experiences with use of the platform was higher than their expectations toward use prior to start of the study.

Pre-, posttest, and change health status scores and number of weight entries for individual patients are presented in Table 3. Of the 19 patients who completed the baseline and follow-up KCCQ, 9 experienced deterioration in their health status score (range 3-34), while 10 experienced an improvement (range 1-23). Of 26 patients, 4 patients entered their weight once or not at all, while 19 patients entered their weight 64 times or more (range 0-86).

## Qualitative Interview Data

Based on interview data and observations, patient and nursing staff evaluations of the platform are summarized below according to specific topics.

### Suitability of an Information Technology Solution to Patients With Heart Failure as Target Group

Given the demographics of patients with HF, one of the obvious questions to ask is whether an information technology (IT) solution as presented in ACQUIRE-HF is feasible. HF patients are typically older and do not necessarily have a lot of

experience with such solutions or the confidence or the energy to engage in digitization. Our experiences show that patients who are unfamiliar with iPads and touch screens were significantly challenged already when having to log on to the platform. These challenges included scrolling down too quickly, not knowing how hard to touch the screen, etc. The observer noticed in some cases an increasing sense of insecurity and decreasing motivation, in particular in patients who borrowed an iPad for the project (they were not used to using it). For patients using their computer, it was much easier for them to understand and use the platform irrespective of their IT experience and user level.

Technological problems and nursing staff uncertainty when introducing and teaching patients about the platform—particularly in the beginning of the study—increased patient insecurity and discouragement with respect to participating. Thus, it is important that training of nursing staff in use of the platform occurs close to study start so they still have benefits from the training. However, experience is also built up over time. Hence, more intensive use of the system will likely create more confidence when problems do occur about how to resolve them.

Patients with very limited IT experience need a more thorough introduction to the use of computer/tablet, and they have a need for troubleshooting particularly in the early stage as these patients might be more prone to dropping out.

> *I could not figure it out—I kept trying but I couldn't—but it is difficult. Nobody had the time to come and help me. They are all too busy—my children and grandchildren, they go to work and school. Then the nurse told me I could hand it in [the tablet]. ...I never really got into it. I didn't really feel like familiarizing myself with it—but they also did not spend a lot of time showing me. Perhaps had it been my grandchildren I would have been more motivated to try it.* [Patient, 83-year-old female]

### Patient User Manual on the Platform

Patients also indicated that more information is warranted on use of the platform and not just on the technical aspects. There are several concepts that they would have liked explained in more detail: "What is a reference value?" "What does health status refer to?" "What do the numbers mean?" "What can you use the diary for—how does that help me?"

> *I spent a lot of time reading the manual. I don't think that everybody can understand it. It should probably be more detailed and informative both with respect to text and pictures.* [Patient, 61-year-old male]

### User Friendliness and Customization of the Platform to the Individual Patient's User Level

Patient experiences with computers and technology vary considerably. Hence, there is a need to customize the platform such that patients who have less experience start with a very simple set-up, while more experienced and curious users might be able to use and have benefit from more features on the platform.

> *We also have patients who would like to receive it digitally.* [Nurse]

### Reminders via the Platform

Patients agree that it is important that the platform can send reminders to patients when they need to complete the health status measure and report their weight or if they have forgotten to do so. However, they prefer that the user is able to decide whether the reminder system should be switched on or off.

### Completion and Monitoring of Patient-Reported Health Status via the Platform

The majority of interviewed patients found the questions strange and criticized that they had to answer the same questions every time.

> *The questionnaires are too general. Who has come up with these questions? Is it at all people who know about patients with heart disease?* [Patient, 64-year-old male]

Despite this criticism, other patients found the questionnaires valuable because they made them reflect and think things through. Nursing staff feels that completion of the questionnaires 2 times a month is too frequent and that once a month might increase motivation.

> *The principles behind the questionnaires are fine—as a matter of fact I think it is nice.* [Patient, 82-year-old male]

Patients voice a preference for being able to have a complete overview and see the evolution in their weight and health status scores over time.

> *I would like to see the entire month. I use the graph, as I have experienced a drastic weight loss in the middle of the period.* [Patient, 70-year-old male]

### Patients' Perceived Value of the Platform

Patients have different views of the platform and its potential usefulness. Generally, as the interview progresses patients attribute more and more value to the rationale behind the platform as they voice their experiences during the last 3 months. However, there are patients at both ends of the acceptance and value continuum. Overall, patients find the rationale and the idea behind the platform good, but the questions as formulated in the questionnaires are considered a major drawback. A few patients—3 out of 10 interviewed—do not find the platform useful nor do they believe that it could be useful to them in the future.

### Increased Insight and Empowerment

Of the 10 patients interviewed, 7 patients either experience or believe that in the future the platform will help them better understand themselves, their body, and their disease and increase empowerment. They find both the insight but also the responsibility valuable.

> *I have been staying at home for many years. It was nice to have the platform to be able to monitor my own health. You gain knowledge about your disease*

*and get a feeling that you are more involved in the process.* [Patient, 82-year-old male]

*It is a nice tool that makes it possible to see how hard it has been. It is food for thought. It is nice to gain this insight. I become aware of things when I answer the questions—I can follow my own developments.* [Patient, 61-year-old male]

*I have become aware of what I gain from weighing myself daily with respect to fluid retention. It is nice to know that you can follow your own disease in such a simple way. But you can become worried! But it gives a sense of security that you know what is going on—this way you can quickly relate your condition to your weight.* [Patient, 60-year-old male]

### Better Communication

Patients feel that the platform is valuable as a communication tool and that the questions support their dialog with the nursing staff. In addition, it makes them remember important aspects related to their condition and health.

*We can talk better now. Because you can refer to the questions—and it makes it a more equal dialog with the nursing staff.* [Patient, 82-year-old male]

### Value for the Nursing Staff

The nursing staff feels that the platform is primarily valuable to patients, as the staff members already have dialogs with patients and their own way of monitoring patients' weight and methods of screening. When asked about the potential of the platform in the future for themselves and patients, they feel that they learn something new about the patients and gain new (and more honest) insight into patients' conditions. They experience that use of the KCCQ tells something new about patients' health status and also that it provides them with different information than what patients tell them when they are seen in the outpatient clinic.

*It is about how they deal with and accept their disease. We can have an opinion about how they feel, but here the questionnaire data can show a different and more true picture.* [Nurse]

Generally, the nursing staff felt that the platform facilitates a more equal dialog between patients and staff but that it cannot replace the personal contact in the outpatient clinic.

### Implementation of the Platform in Clinical Practice

It is paramount that the expectations of patients and nursing staff are aligned and that patients are aware that they need to take an active role and act on their own scores when clinically relevant changes occur. The majority of patients express that they thought there would have been more dialog and follow-up based on their scores. They feel that they did not know what was going on at the other end (the nurses' role).

*I thought that there would have been more dialog between me and the hospital, such as videoconferencing, et cetera. I wrote a remark on the platform in the comment field, but nobody saw it. So it felt like somewhat of a dead end.* [Patient, 60-year-old male]

Nurses are concerned that patients might have inexpedient expectations that nurses act as contact person.

*It is important to be prudent and not to cultivate the idea that we have to be part of their network.* [Nurse]

### Timing for Introducing the Platform

Both patients and nursing staff feel that the platform could be of considerable value to newly diagnosed HF patients as a tool to develop good routines from the beginning and to gain knowledge of oneself, one's disease, and the evolution of the disease.

*It would be good when you are first diagnosed to learn about your disease.* [Patient, 82-year-old male]

*It would give us important information about their level of functioning if the platform was used as part of the introduction to the outpatient clinic. Instead of us having to ask them, they could complete the questionnaire via the platform. Then patients would also have time to think about how they actually feel before they respond. Then we would have something to go on—then we know what the problem is without having to spend time on asking these questions... But it should probably not be digital—an IT platform is a bit overwhelming for most of our patients in the beginning.* [Nurse]

As such, nursing staff emphasizes that the platform should be viewed as a tool to support dialog, not as a replacement for contact with the outpatient clinic, and also a tool that patients can take with them and use once they are no longer seen in the clinic.

Based on the interview data and observations, recommendations for use of a platform and patient-centered tools in studies like ACQUIRE-HF are provided in Textbox 4.

**Textbox 4.** Recommendations based on the results of the feasibility study.

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Use of the platform and monitoring of symptoms:

- Should be customized to the individual patient's user level and preferences if feasible

- Should facilitate that patients can use the technology that they are familiar with

- Is not a one-size fits all solution

- Is not a replacement for clinical practice

- Could be a useful tool for newly diagnosed patients

- Is a useful communication tool

- Gives patients a more equal relationship with nursing staff

- Provide nursing staff with new, additional and more honest information about patients

- Might induce anxiety in some patients

Practical and logistic issues:

- Alignment of patient and nursing staff expectations is paramount

- Patients prefer to see total overview and evolution in scores

- Reexamination of questionnaire use for health status monitoring

- Train nursing staff in use of the platform close to recruitment and allow a few test cases to increase familiarization

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## Discussion

### Principal Findings

The ACQUIRE-HF study was designed to examine the feasibility of using a Web-based platform combined with patient-centered tools to empower and engage patients as more coactive partners in their own disease management. Despite concerns that such a solution might not be feasible to use in the HF population due to their higher age and risk of being inexperienced and challenged with respect to the use of a technology-based intervention, our results based on both quantitative and qualitative data show that such a solution is feasible but also that it is not a one-size fits all solution, with some patients (albeit a minority) never logging on to the platform or only using the platform a few times. Patients were not explicitly singled out for interviews if they did not enter their weight or use the platform. When patients were recruited for the study they were asked whether they would be willing to be contacted later for an interview. However, as indicated in one of the quotes included in the paper, insufficient coaching and familiarity with the platform could be one reason why this subset of patients did not engage with the platform. This was also supported in a recent study on extra device monitoring in patients with HF [28].

In this study, both patients and nursing staff recommended that patient health status tracking and monitoring could be used as a communication tool between the parties in clinical practice. This finding is similar to that of a recent study using participatory design methods, asking patients about their needs, values, and preferences with respect to the use of eHealth tools in the management of their disease [29]. In the latter study, patients advocated the use of such tools to support their preparation for consultations in clinical practice, in order to

empower them and make them more active comanagers of their disease.

When implementing a solution, as evaluated in ACQUIRE-HF, in clinical practice, it is important to emphasize that patient tracking and monitoring may induce anxiety in some patients, in particular if they see a significant reduction in their health status. This was mentioned by one of the patients in the post-hoc interviews. On the other hand, several of the patients who were interviewed also mentioned that tracking of their own health status was insightful, constituted a learning opportunity, and for some was an indication of how far they had come in managing their disease. The importance of patients gaining increased awareness about their disease and disease status through eHealth solutions is also supported by others [30]. However, in a recent study in patients with multiple chronic diseases, tracking of objective clinical parameters (eg, self-tracking of blood glucose level, results of blood tests received from the hospital) may not only have emotional but also moral implications, including feelings of guilt in patients who have not been compliant [30,31]. Although we did not explicitly ask patients whether they thought that a reduction in their perceived health status had moral implications and no patients mentioned it in the interviews, it is possible that asking patients to track their own health status is benign, as it provides an overall snapshot of patients' health [13] rather than specific values, such as blood glucose level and blood pressure. Designing a solution that also focuses on patient strengths and resources, such as optimism and willpower to overcome obstacles, may be paramount to balance the positives and negatives of such solutions at the patient level in future eHealth interventions [29].

For the purpose of the study, we designed a questionnaire to tap into patient expectations toward the platform prior to use and perceived experiences post use. Based on our results, patient expectations toward use of the platform prior to actual use were

at a lower level than their actual experiences with the platform at the end of 3 months, suggesting that patients generally experienced gains that they might not have anticipated. In future studies, it will be important to focus on patient expectations toward the eHealth intervention or tools that will be evaluated, as such expectations may not only influence patient engagement and user experience but also patient-reported outcomes [20].

## Limitations

The results of this study should be interpreted with the following limitations in mind. We recruited patients from only one center, and the majority of patients were men. Hence, the results may not necessarily be generalizable to the general HF population and in particular to women. Due to the small sample size, we were not able to perform sophisticated statistical analyses and thus are only able to report simple descriptive statistics. Although the focus of the feasibility study was to evaluate the experiences of patients with HF when tracking and monitoring their own health status and the potential value to nursing staff, we are not able to delineate whether use of the platform had a direct impact on patient HF symptoms, as there could be many alternative reasons as to why patients improved or deteriorated in their health status as measured by the KCCQ.

## Conclusion

The use of patient tracking and monitoring of health status in HF using a standardized and validated measure seems feasible and may lead to insights that will help educate, empower, and engage patients more in their own disease management. Nursing staff found the patient-centered tool beneficial as a communication tool with patients, indicating that the dialog might become more equal and that it might represent a more honest picture of patient cardiovascular health and disease status. However, they were more reticent with respect to using it as a replacement for the personal contact in the outpatient clinic. Further studies are warranted to examine how technology and a more elaborate intervention than provided in our study may facilitate the dialog between health care professionals and patients and improve patient outcomes.

## Conflicts of Interest

None declared.

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## Abbreviations

**ACQUIRE-HF:** Advance the Quality of Life and Care of Patients With Heart Failure
**CC360:** CommunityCare360
**EHFScB:** European Heart Failure Self-Care Behavior scale
**EHR:** electronic health record
**EXPECT-ICD:** Expectations Towards ICD Therapy
**HF:** heart failure
**ICD-10:** International Classification of Diseases, 10th Edition
**ICD-PC:** ICD-10 procedure codes
**IT:** information technology
**KCCQ:** Kansas City Cardiomyopathy Questionnaire
**NPU:** Nomenclature for Properties and Units
**NYHA:** New York Heart Association

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Original Paper

# Comparison of Ecological Momentary Assessment Versus Direct Measurement of E-Cigarette Use With a Bluetooth-Enabled E-Cigarette: A Pilot Study

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## Abstract

**Background:**    Assessing the frequency and intensity of e-cigarette use presents special challenges beyond those posed by cigarette use. Accurate measurement of e-cigarette consumption, puff duration, and the stability of these measures over time will be informative for estimating the behavioral and health effects of e-cigarette use.

**Objective:**    The purpose of this pilot study was to compare the accuracy of self-reported e-cigarette puff counts collected via ecological momentary assessment (EMA) to objective puff count data collected by a Bluetooth-enabled e-cigarette device and to examine the feasibility and acceptability of using a second-generation e-cigarette among adult smokers.

**Methods:** A total of 5 adult smokers were enrolled in a longitudinal parent study assessing how e-cigarette use affects cigarette use among e-cigarette–naïve smokers. Using a text message–based EMA system, participants reported e-cigarette puffs for 2 weeks. Participants were also given a Bluetooth-enabled e-cigarette (Smokio) that passively collected puff counts and puff duration. Comparisons between mean reports of Smokio (device-report) and EMA (self-report) use were evaluated using paired $t$ tests. Correlation and agreement between device- and self-reports were evaluated using Pearson correlation and the concordance correlation coefficient (CCC), respectively. A linear mixed effect model was used to determine the fixed effect of timing and Smokio-reported daily puffs on report accuracy. We examined the relationship between time of day and reporting accuracy using Tukey's test for multiple pairwise comparisons.

**Results:** A total of 5 African American participants, 4 men and 1 woman, who ranged in age from 24 to 59 years completed the study, resulting in 5180 observations (device-report) of e-cigarette use. At baseline, participants reported smoking for 5 to 25 years and consumed a mean of 7 to 13 cigarettes per day (CPD); 4 smoked within 30 minutes of waking. At the 30-day follow-up, CPD range decreased to 1 to 3 cigarettes; 4 participants reported past 7-day e-cigarette use, and 1 participant reported no cigarette smoking in the past 7 days. Over 2 weeks of e-cigarette use, participants took an average of 1074 e-cigarette (SD 779.0) puffs per person as captured by the device reports. Each participant took a mean of 75.0 (SD 58.8) puffs per day, with each puff lasting an average of 3.6 (SD 2.4) seconds. Device reports captured an average of 33.3 (SD 47.8) more puffs per person per day than the

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self-reported e-cigarette puffs. In 87% of days, participants underestimated the number of puffs they had taken on the Smokio. There was significant moderate correlation ($r=.47$, $P<.001$) but poor agreement ($p_c=0.31$, 95% CI 0.15-0.46) between the device- and self-reported data. Reporting accuracy was affected by amount and timing of e-cigarette use.

**Conclusions:**   Compared to self-reported e-cigarette use, the Bluetooth-enabled device captured significantly more e-cigarette use and allowed for examination of puff duration in addition to puff counts. A Bluetooth-enabled e-cigarette is a powerful and feasible tool for objective collection of e-cigarette use behavior in the real world.

## Introduction

There has been a rapid increase in lifetime and past 30-day adult use of e-cigarettes in the United States since their introduction in 2007 [1-3]. The highest prevalence of e-cigarette use is among current and former cigarette smokers [4-6], who most commonly report use to reduce cigarette consumption, quit smoking, or prevent smoking relapse [6-10].

Much of the scientific literature on e-cigarette use stems from national surveys and laboratory studies, which are limited by recall bias or are not generalizable to e-cigarette use behavior in the real world. Ecological momentary assessment (EMA) is an intensive longitudinal method that samples participant behaviors and experiences to reveal how individual differences and within-person processes interact to produce a behavioral outcome such as quitting smoking [11]. EMA reduces recall bias and threats to generalizability common to retrospective surveys and laboratory studies by sampling participant behavior and experience in the time and place where the behavior or experience occurs. In a comparison of methods to assess daily cigarette use, EMA best correlates with biomarkers of cigarette smoking, suggesting that this is a valid method to assess cigarette smoking frequency [12]. EMA has been extensively applied to tobacco control and smoking cessation treatment research to better understand phenomena such as smoking patterns, the smoking cessation process, and the interaction between the built environment and smoking craving [12,13].

Accurate measurement of e-cigarette consumption, puff duration, and the stability of these measures over time will be informative for estimating the behavioral and health effects of e-cigarette use. Because EMA has been applied in cigarette smoking research, EMA could also be a powerful tool to understand e-cigarette use in isolation and in combination with other tobacco products (dual use). To date, no studies have employed EMA assessment of e-cigarette use in analyses, and only one study has used daily reports to examine within-person variation in e-cigarette use among smokers; in that study, only the presence or absence of e-cigarette use in that day was assessed, without attention to frequency or intensity of use [14]. A more fine-grained assessment of e-cigarette use in its physiological, social, and environmental context will yield a better understanding of the individual differences and e-cigarette product features that promote or discourage use and will be informative of any future US Food and Drug Administration Center for Tobacco Products (FDA CTP) e-cigarette regulation.

Measurement of e-cigarette use poses challenges beyond those posed by measuring cigarette smoking. The term e-cigarette encompasses an array of products with different performance characteristics. Unlike cigarettes, which have a distinct beginning and end point, an e-cigarette could last several days before it needs to be refilled or discarded. Asking about the number of puffs in an e-cigarette use session may be an adequate measure of e-cigarette use intensity; however, it is unknown whether adult smokers can reliably report e-cigarette puff counts. The purpose of this pilot study was to compare the accuracy of self-reported e-cigarette puff counts collected via EMA to objective puff count data collected by a Bluetooth-enabled e-cigarette device and to examine the feasibility and acceptability of using a second-generation e-cigarette among adult smokers.

## Methods

### Study Design

Data from this study come from a pilot embedded in a longitudinal study (Mixed Method E-Cigarette [Moment] Study). Details on the study protocol and procedures are available elsewhere [15]. Briefly, the Moment Study was a 6-week intensive longitudinal study that employed a mixed methods design to yield an in-depth description of the e-cigarette initiation process among adult smokers. Participants completed 4 in-person visits, followed by an online follow-up survey at 30 days after the final in-person visit. Participants in the Moment Study were provided with NJOY King disposable e-cigarettes at the second in-person visit and self-reported their subsequent e-cigarette and cigarette consumption via text message EMA. For this pilot study, 5 participants were provided with a Bluetooth-enabled e-cigarette tank system (Smokio brand) that passively recorded puff count and puff duration data. Like participants in the parent study, pilot study participants also submitted self-reported e-cigarette and cigarette consumption data via text message EMA. The Moment Study's mixed method design featured concurrent collection of multiple data streams, including (1) EMA, (2) geotracking, (3) in-depth interviews, and (4) biosamples. Geotracking and biosample data are not reported in this study and will not be discussed further.

### Study Population and Recruitment

Eligible individuals were English-speaking adults aged 18 years or older residing in the Washington, DC, metro area who smoked at least 8 cigarettes a day for the past 5 years. To simplify EMA tobacco use reports, we excluded polytobacco

users, defined as having smoked a little cigar/cigarillo, large cigar, or hookah more than 5 times in the last 30 days or used smokeless tobacco in the past 30 days. Additional eligibility criteria included (1) no e-cigarette use in the last 30 days, (2) interest in trying an e-cigarette, and (3) report interest in quitting cigarette smoking in the next 30 days at the initial screening. To facilitate EMA data collection, participants were required to use a cell phone daily and have an unlimited text message plan. Participants were recruited via public online postings, paid advertisements, and physical flyers. Recruitment documents directed potential participants to an online screening survey (www.ecigstudy.org).

## Procedures

In-person procedures consisted of 4 office visits. During the baseline visit, participants completed the informed consent process and confirmed current smoking status with an exhaled carbon monoxide test. A research assistant (RA) registered participant phones to receive EMA text messages and trained participants on how to respond to the EMA random texts and self-initiated tobacco use reports. At the second office visit, participants were provided with 2 Smokio batteries (Figure 1) and 10 prefilled cartomizers (single coil, 1.5 ohm, 510-threaded,

Smok brand) of 1.8% nicotine fluid in tobacco (AVAIL VA Pure) or menthol flavor (AVAIL Port Royal), depending on their cigarette flavor preference. The RA trained participants on how to use the Smokio and asked participants to take a minimum of 3 puffs a day for the next week. Prefilled cartomizers were provided to participants rather than the Smokio tank and 10 mL of nicotine fluid to simplify use of the device. Nicotine fluid was purchased from AVAIL Vapor (www.availvapor.com) in a 70%/30% propylene glycol/vegetable glycerin mix and was independently verified by an analytic chemist at Virginia Commonwealth University as containing an average of 17.1 mg/mL of nicotine (6 vials with a range of nicotine concentrations between 16.8 and 17.7 mg/mL). At the third office visit, participants received an additional 10 prefilled cartomizers and instructions to use the device as desired. At the last office visit, participants were provided with an empty Smokio tank (Figure 1) but no additional nicotine fluid or cartridges. At 30 days after their last contact with the study, participants were sent a reminder email with an embedded Web link to take the online follow-up survey. All study procedures were reviewed and approved by Chesapeake Institutional Review Board (Pro00008526).

**Figure 1.** The Smokio battery/cartomizer combination (top) was given to participants during the study; the Smokio tank (bottom) was provided to participants at the end of the study.



## Measurement Instruments

This study employed 2 types of active EMA data collection: (1) participant-initiated cigarette and e-cigarette use reports and (2) system-initiated random prompts to assess mood and craving. Random prompt data are not reported in this manuscript; more information on these methods is available elsewhere [15]. Participant-initiated reports collected information on cigarette consumption (weeks 1-3), e-cigarette consumption (weeks 2-3), satisfaction derived from the reported product (weeks 1-3), and desire to use the opposite product (eg, desire to smoke after using the e-cigarette; weeks 2-3). Participants were instructed to self-initiate an e-cigarette puff report when they "put down

the e-cigarette and did not intend to pick it up again in a while." Participants texted #cig (to report cigarette use in week 1) or #both (to report cigarette or e-cigarette use in weeks 2-3) to the study system phone number, which initiated a short series of questions about the recent cigarette or e-cigarette use. Questions included "About how many drags did you take on the e-cig?" and "How many minutes ago did you finish using the e-cig?" Participants could initiate an unlimited number of reports in a day and could report cigarette or e-cigarette use at any time. As participants had to smoke at least 8 cigarettes per day to be eligible for the study, they were encouraged to make an average of 6 cigarette or e-cigarette reports per day and incentivized

with an additional $10 per week if they self-initiated at least 42 reports each week.

Both streams of data were collected via text messages on participant personal cell phones. The EMA data collection system returned an error message to prevent participants from skipping items or entering out-of-range values. All EMA entries were stamped with the time, date, and geolocation of the report and were uploaded to Truth Initiative's secure server via an encrypted representational state transfer application program interface.

Smokio (Figure 1) is a Bluetooth-enabled e-cigarette that records puff counts (ignition button clicks) and puff duration (span of time in milliseconds that the ignition button is depressed). Devices were paired with the Smokio app on participant cell phones, which pushed data from the Smokio to the Cloud. If the paired cell phone was not within range of the Smokio, the device cached data until the phone was nearby. Participants indicated that Smokio could share their puff data with the study by entering the study's email address into the Smokio app. After obtaining permission, the RA downloaded a .csv file of participant puff data from Smokio's Web portal. Participants removed the study's permission to access their puff data at the last study visit.

An RA conducted in-depth interviews with all participants at week 1, 2, and 3 office visits. Among other topics, the RA asked participants about their sensory and social experience using the e-cigarette and any difficulties they had using the device, such as remembering to keep it charged. Interviews did not exceed 30 minutes. Both the baseline and follow-up surveys were computer-assisted self-interview surveys. Survey questions assessed sociodemographics, tobacco and e-cigarette use history, tobacco and e-cigarette use beliefs and cognitions, tobacco product and e-cigarette harm perceptions, alcohol use, and health status.

### Analyses

Descriptive statistics were used to characterize the sample in terms of demographic characteristics (sex, age, race, and education), baseline factors (years smoked, cigarettes per day, nicotine dependence, and other tobacco use) and follow-up smoking/e-cigarette use (cigarettes per day, e-cigarette use, and point prevalence abstinence). All EMA e-cigarette puff reports (self-reports and device-reports) were aggregated at the day level. Comparisons between day-level mean reports of e-cigarette device-recorded puffs and self-reported puffs were evaluated using paired $t$ tests. Correlation and agreement between e-cigarette device reports and self-reported puff counts were evaluated using Pearson correlation and the concordance correlation coefficient (CCC), respectively. The CCC is a statistic to assess interrater reliability and was used to assess agreement between the device-reported and self-reported puff counts at the day level. The CCC ranges from –1 (complete negative agreement) to 1 (complete agreement), with 0 indicating no agreement.

After checking the descriptive statistics, we examined the extent to which timing and device-reported daily puffs influenced self-report accuracy. A linear mixed effect model was used to determine the fixed effect of timing and Smokio-reported daily puffs on report accuracy by taking the random effect of each individual into consideration. To find out the best and worst timing under each time window cases, Tukey's test was used for multiple pairwise comparisons. All statistical analyses were performed in R (The R Foundation) and SAS version 9.4 (SAS Institute Inc); figures were created in R, SAS 9.4 and JMP version 10.0.2 (SAS Institute Inc). Statistical significance was set to a $P$ value of .05.

## Results

### Participant Characteristics

A total of 5 African American participants, 4 men and 1 woman, with an age range of 24 to 59 years completed this pilot study (Table 1). At baseline, participants reported having smoked for 5 to 25 years and consumed between 7 and 13 cigarettes per day; 4 out of 5 participants smoked within 30 minutes of waking. All participants used his or her Smokio throughout the 2-week e-cigarette observation period, and no one lost a device. At the 30-day follow-up, cigarettes per day (CPD) range decreased to 1 to 3 cigarettes, with 4 participants reporting any past 7-day e-cigarette use and 1 participant reporting no past 7-day cigarette smoking.

### E-Cigarette Puff Data

Over 2 weeks of e-cigarette use, the Smokio device captured 5180 e-cigarette puff observations. Participants took an average of 1074 (SD 779.0) e-cigarette puffs per person, with a mean of 75.0 (SD 58.8) puffs per day and 536 (SD 377.9) puffs per week, with each puff lasting an average of 3.6 (SD 2.4) seconds (device data). The average number of device- and self-reported puffs per person per day did not vary by week.

Table 2 presents average e-cigarette puffs per day, comparing the 2 data collection methods. Smokio captured an average of 33.3 (SD 47.8) more puffs per person per day than the self-reported e-cigarette puffs. Smokio identified significantly more daily puffs per person than self-reports overall ($P<.001$), at week 2 ($P<.001$), and at week 3 ($P<.001$). In 87% of daily reports, participants underestimated the number of puffs they had taken on the Smokio. Across individuals and days, there was a significant moderate correlation ($r=.47$, $P<.001$) between the device-reported and self-reported puff count data; however, there was poor agreement ($p_c=0.31$, 95% CI 0.15-0.46) between device-reported and self-reported puff counts. Given the variability in puff counts by participant, CCC was further assessed at the individual level; the CCC ranged from virtually no agreement (Participant 2; $p_c=0.001$, 95% CI –0.10 to 0.11) to high agreement (Participant 3; $p_c=0.91$, 95% CI 0.76-0.97) between the device-reported and self-reported puff counts.

**Table 1.** Participant characteristics at baseline and 30-day follow-up (n=5).

| Characteristics | Number |
|---|---|
| **Sociodemographics** | |
| Female, n | 1 |
| Age, range | 24-59 |
| African American, n | 5 |
| **Education, n** | |
| High school or less | 1 |
| Some college or more | 4 |
| **Tobacco use (baseline)** | |
| Years smoked, range | 5-25 |
| CPD[a], range | 7-13 |
| Smoke within 30 minutes of waking, n | 4 |
| **Tobacco use (follow-up)** | |
| CPD, range | 1-3 |
| Past 7-day e-cigarette use, n | 4 |
| 7-day cigarette smoking PPA[b], n | 1 |
| **Change in cigarette use, n** | |
| Increase | 0 |
| No change | 1 |
| Decrease | 4 |
| **Change in e-cigarette use, n** | |
| Increase | 1 |
| No change | 0 |
| Decrease | 4 |

[a]CPD: cigarettes per day.

[b]PPA: point prevalence abstinence.

**Table 2.** Descriptive statistics of e-cigarette use by week of study, comparing e-cigarette use captured by the Smokio device to self-reported e-cigarette use.

| Puffs per person per day | Device-reported | Self-reported | % difference | $P$ value[a] |
|---|---|---|---|---|
| Overall, mean (SD) | 75.0 (58.8) | 48.0 (32.6) | 56.25 | <.001 |
| Week 2, mean (SD) | 69.9 (53.1) | 47.3 (31.0) | 47.78 | <.001 |
| Week 3, mean (SD) | 80.1 (64.1) | 48.7 (34.6) | 64.48 | <.001 |

[a]Paired $t$ test results.

Figure 2 presents number of e-cigarette puffs per day by participant, comparing device-reported puffs to self-reported puffs. These plots reveal significant variability in within- and between-person daily e-cigarette consumption and highlight participants' tendency to underreport e-cigarette puffs. For example, Participant 2 consumed the greatest number of puffs but did not accurately report his puffs via EMA; in contrast, Participant 4 was a light Smokio user and his EMA puff reports closely followed his Smokio-recorded puffs. Participant 3, a moderate Smokio user, was remarkably accurate in her e-cigarette puffs. In an examination of prediction accuracy by the number of Smokio-reported daily puffs, the percentage difference between Smokio and self-reported e-cigarette puffs increased by 4.5% for every 1-puff increase captured by the Smokio ($P$<.001). Comparing reporting accuracy by time of day (day divided into 12 2-hour increments), participants' self-reports were most accurate from 4 PM to 6 PM and least accurate from 6 AM to 8 AM. In this small sample, reporting accuracy depended on the amount and timing of e-cigarette use.

**Figure 2.** Panel plot of e-cigarette puffs per day by participant and study day comparing device-reported puffs (orange line) to self-reported puffs (blue line).
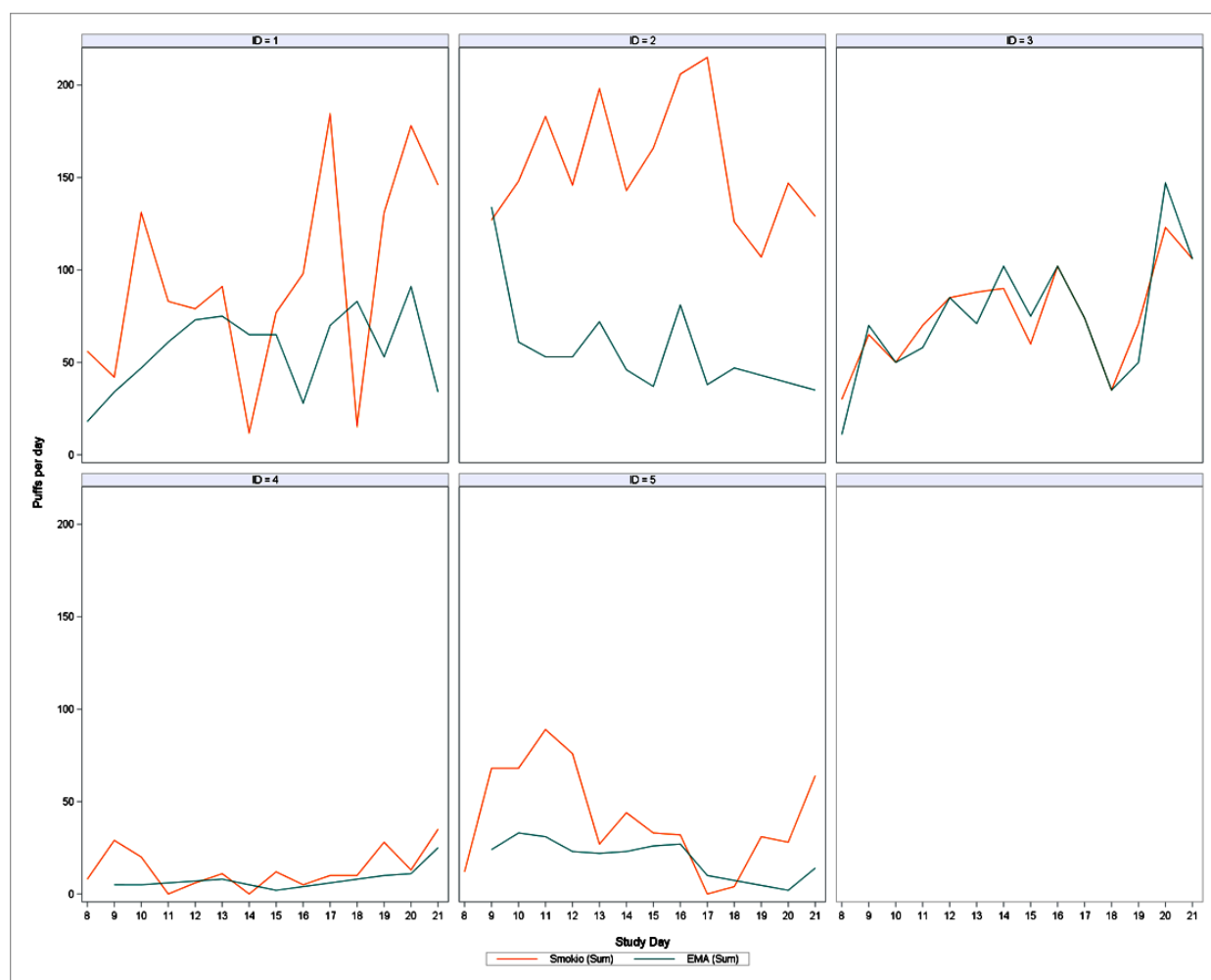


## Device Acceptability

All 5 of the participants felt the device was convenient and acceptable, with none reporting problems with turning the device off/on or keeping it charged. Participants were struck by their ability to use the Smokio in places where they could not smoke a cigarette.

> I kind of like the fact that I can kind of stay in the crowd and still get my nicotine without offending other people. [Participant 2]

> I could smoke it like absolutely anywhere…it didn't bother anybody. [Participant 5]

Participants also positively described the taste of the AVAIL e-liquid.

> It tasted menthol-y enough to where it satisfied the nicotine taste, my body's craving. [Participant 2]

> It was a pretty good experience for first time using. [It gets]…that sweet menthol taste out of it. So it's pretty good actually. [Participant 3]

Participant 1 stated that it "was weird trying to get used to the taste of it." While Participant 2 reported "holding it was kind of odd because it wasn't the size of a cigarette," no one disliked the Smokio because of its size or weight. All participants felt that using the device suppressed their urge for a cigarette.

> When I did smoke the Smokio, it took away a lot of cravings and urges, made me feel better. [Participant 1]

> It satisfies my craving when I need it. [Participant 4]

## Discussion

### Principal Findings

Compared to self-initiated e-cigarette puff reports, the Smokio proved to be a far superior method to collect e-cigarette puff data. However, the moderate correlation ($r$=.47, $P$<.001) and high agreement between device-reported and self-reported puff data for some participants (eg, Participant 3; $p_c$=0.91, 95% CI 0.76-0.97) demonstrate that self-reported e-cigarette puff data may be a feasible method for collecting naturalistic e-cigarette use data, especially among low-level users. Self-initiated puff reports may not be an optimal data collection method for high-level e-cigarette users. However, the exceptional agreement between Participant 3's Smokio-captured and self-initiated reports suggests that research participants may be able to improve their self-report precision with training. Future

investigation of how to improve the validity of self-reported puff counts would be of great utility to the field. It may be that other approaches to understanding naturalistic use, such as an EMA coverage approach, collection of used cartomizers, or assessment of weekly or usual consumption may outperform the self-initiated puff report used in this study.

In comparing device-reported to self-reported data, other consistent trends were revealed. First, we observed that participants underestimated the number of e-cigarette puffs consumed in nearly 90% of study days. While missing data is never preferred, a consistent pattern to missing data can be accounted for in the analyses and interpretation of results. Second, despite a burdensome design, participants did not reduce their average self-reported e-cigarette puff counts between weeks, indicating that there was minimal fatigue in EMA e-cigarette reporting. While Smokio captured more e-cigarette puff data than self-reports, the between-person average difference between the two methods remained steady between the second and third weeks of data collection. If objective measurement of e-cigarette use using a device like Smokio is cost prohibitive or otherwise not feasible (eg, participants are provided with "cigalike" e-cigarettes, or e-cigarettes with small batteries that are often disposable), self-reported e-cigarette puffs may be an acceptable alternative as long as the research question and design allow for underreporting of e-cigarette use and variation in the accuracy of reporting between individuals by heaviness of e-cigarette use.

Data from in-depth interviews with our 5 pilot participants demonstrate that the Smokio device and e-liquid choices were acceptable and convenient. Participants reported liking the taste and experience of using the Smokio, although one individual initially found using the device awkward. Participants also commented on the Smokio's ability to alleviate craving and the appeal of feeling free to use the device in places where they could not smoke cigarettes. None of our participants reported trouble with keeping the device charged nor did they find operation of the device challenging. Continued use of an e-cigarette at follow-up also suggests that the device was acceptable, although we cannot be certain that participants continued to use the Smokio from the study or some other e-cigarette device. At the 30-day follow-up, it is notable that all participants reported that they smoked fewer cigarettes than when they enrolled in the study, with the average CPD dropping from 9 to 1.8.

## Limitations

This pilot study has several limitations. First, as a pilot study, conclusions are based on only 5 individuals. Results are intended to inform measurement of e-cigarette use in EMA studies and should not be interpreted beyond this purpose. Second, we assumed that the device-recorded puffs were the gold standard method for assessing naturalistic e-cigarette use; however, we did not conduct a formal laboratory assessment of the Smokio puff counter or puff duration measurement and thus cannot be certain of the precision of the device. Additionally, as of summer 2016, the Smokio (now called Vap.io) is no longer available for purchase in the United States. Other devices, such as several Joytech products, collect puff count data but do not currently sync data and push to a remote server, which allows real-time monitoring of e-cigarette use behavior and reduces data loss if a participant misses an in-person visit. Future collaboration with private companies or independent developers will be necessary to create a product with capabilities similar to the Smokio. Research funders should consider supporting the development of a range of e-cigarette device types that passively capture user data, including puff counts and puff duration. We also note that Participant 3 was remarkably accurate in her self-reports. We did not collect information that explains why her self-reports outperformed those of the other participants; however, participants did know that the Smokio counted their puffs—that awareness could have encouraged counting. It is also possible that novel users are more aware of their puff patterns than more established users; thus, these conclusions may not transfer to established e-cigarette users. We also did not collect information on the amount of e-liquid consumed by each participant, which would be an additional helpful source of data to compare against the Smokio-reported puffs. Finally, our instruction to participants to initiate an e-cigarette self-report when they "put down the e-cigarette and did not intend to pick it up again in a while" may not translate to established vapers who "graze" on their devices throughout the day. In this population, an EMA coverage approach or, ideally, provision of a Smokio-like device would be the best option to capture puffing data.

## Conclusions

Compared to self-reported e-cigarette use, the Bluetooth-enabled device captured significantly more e-cigarette use and allowed for examination of puff duration in addition to puff counts. A Bluetooth-enabled e-cigarette is a powerful and feasible tool for objective collection of e-cigarette use behavior in the real world. As e-cigarette users adopt more sophisticated devices, researchers should consider harnessing the existing capabilities of these devices to aid data collection.

Zhou conducted the analyses. B Das, S Smiley, L Rubin, T DeAtley, E Harvey, R Niaura, and D Abrams contributed to the analysis plan, interpretation of results, and manuscript writing. S Smiley was project director of the parent study. L Rubin was the research assistant for this pilot.

## Conflicts of Interest

None declared.

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## Abbreviations

**CCC:** concordance correlation coefficient
**CPD:** cigarettes per day
**CTP:** Center for Tobacco Products
**EMA:** ecological momentary assessment
**FDA:** Food and Drug Administration
**RA:** research assistant

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Original Paper

# Crowdsourced Identification of Possible Allergy-Associated Factors: Automated Hypothesis Generation and Validation Using Crowdsourcing Services

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## Abstract

**Background:** Hypothesis generation is an essential task for clinical research, and it can require years of research experience to formulate a meaningful hypothesis. Recent studies have endeavored to apply crowdsourcing to generate novel hypotheses for research. In this study, we apply crowdsourcing to explore previously unknown allergy-associated factors.

**Objective:** In this study, we aimed to collect and test hypotheses of unknown allergy-associated factors using a crowdsourcing service.

**Methods:** Using a series of questionnaires, we asked crowdsourcing participants to provide hypotheses on associated factors for seven different allergies, and validated the candidate hypotheses with odds ratios calculated for each associated factor. We repeated this abductive validation process to identify a set of reliable hypotheses.

**Results:** We obtained two primary findings: (1) crowdsourcing showed that 8 of the 13 known hypothesized allergy risks were statically significant; and (2) among the total of 157 hypotheses generated by the crowdsourcing service, 75 hypotheses were statistically significant allergy-associated factors, comprising the 8 known risks and 53 previously unknown allergy-associated factors. These findings suggest that there are still many topics to be examined in future allergy studies.

**Conclusions:** Crowdsourcing generated new hypotheses on allergy-associated factors. In the near future, clinical trials should be conducted to validate the hypotheses generated in this study.

## Introduction

This study aims to generate hypotheses for clinical research by querying the general public through a crowdsourcing service, which is one of the new services and research styles that have emerged with advances in information and communication technology. Hypothesis generation is one of the most essential tasks for clinical research. A good hypothesis can bring about insightful and applicable results, whereas an unreasonable hypothesis may not only hinder research efforts, but also waste time and money. As it can require years of experience to produce a single meaningful research hypothesis, it is usually the *experts*, such as medical researchers and clinical doctors, who usually propose hypotheses for study. However, it has recently been suggested that hypotheses remain that even these experts have

yet to address [1]. Applying the knowledge of the general public and the wisdom of crowds has drawn attention as a means to delve into these unexplored themes. This study does not provide an ultimate cost- and labor-cutting means for removing inadequate candidate hypotheses. However, the aim of the study is to acquire broader and more flexible possibilities of detecting possible novel risk factors for allergies with very quick and costless means, which would take much more money and time if practiced in traditional manners. This approach may also reduce the first step of validation by calculating odds ratios (ORs). Thus, this study is not intended to revise the traditional approach to research, but is capable of adding and accelerating the research of allergies with little cost and effort. We must note that for the final and concrete validation of hypotheses, we still require traditional medical diagnoses.

In this study, we investigated possible allergy-associated factors from hypothesis generation to questionnaire-based validation. An allergy occurs when a person's immune system reacts to substances in the environment that are harmless to most people. These substances are known as allergens and are found in house dust mites, pets, pollen, insects, foods, and some medicines. It has been estimated that approximately 1 of every 3 people in Japan suffers from some type of allergy, and this number is thought to be increasing [2]. According to a government research survey [3], 35.9% of survey respondents reported experiencing allergy symptoms during the year of the survey; among those, 14.7% were diagnosed by a physician as having an allergic reaction. This result indicates that less than half of the people who claimed to experience allergy symptoms actually sought treatment from a physician. The survey results also showed that respondents wanted more reliable information about dealing with allergies.

The causes of allergies can be classified into two general categories: (1) the patient's genetic factors, and (2) environmental factors [4]. Genetic factors include the patient's gender, race, age, and perhaps most importantly, their hereditary determinants. However, the recent increases to the number of allergic disorders cannot be explained by genetic factors alone [5]. Other causes may include major environmental factors such as air pollution, allergen levels, dietary changes, as well as exposure to infectious diseases during early childhood. Sifting through the vast numbers of different possible environmental factors places a heavy burden on researchers when identifying allergy-associated factors, but this task may be suitable for crowdsourcing research. In this paper, we call a factor that has a causal relation to the allergy a *risk factor*. Cases in which the causal relation is ambiguous, we call the factor an *associated factor*. Many allergy sufferers have to work to manage their allergies throughout their lives, and they can become well-informed on their own allergies in the process.

Existing epidemiologic literature indicates that the standard process of disease risk studies usually follows two phases. First, a researcher identifies a possible associated factor (hypothesis generation phase). Second, more experts analyze statistical data to shed light on the relationship between the candidate risk factor and the target disease, using methods such as interventions, observations, and questionnaire investigations (hypothesis validation phase). In contrast, crowdsourcing-based

studies conduct both the hypothesis generation phase and the validation phase relying only on efforts by the general public, with little input from experts and their knowledge. This approach can substantially reduce the costs, time, and effort required by more conventional research methods.

In this study, we have developed a questionnaire consisting of three sections. The first section addressed the presence or absence of allergy symptoms in the respondent. The second section asked questions regarding known allergy risk factors, such as, "*Do you wear piercings?*" The third section was specifically designed for hypothesis generation, and respondents were asked to post new hypotheses using the question, "*Please submit some of your own questions that you feel may help to detect the cause of an allergy. Were/Do/Did you _____?*" The new hypotheses provided by the participants were then included as new risk question candidates (in the second section) for the subsequent round of the questionnaire. Repeating this cycle enabled automatic hypothesis generation and validation.

Crowdsourced hypothesis generation is a creative production task that is distinct from many previous crowdsourcing tasks for clinical or medical studies. Many previous crowdsourcing studies have requested the public to fulfill a relatively simple task [6,7]. These tasks have included crowdsourcing-based endoscopic video image annotation [8], medical document annotation for information retrieval [9], and evaluation of a surgical operation performance [10,11]. However, a few studies have already undertaken the challenge of generating medical hypotheses via crowdsourcing services. At present, new risk hypotheses for obesity [12,13], eczema [14], and acne treatment [15] have been generated through crowdsourcing-based procedures. Our study offers the following three novel features that distinguish it from previous studies:

This paper proposes a new methodology for crowdsourcing service-based risk research.

Unlike the diseases addressed in previous studies [12-14], allergies (the target subject of this study) covers a broad range of diseases. Simultaneously focusing on multiple diseases is a novel feature in our study.

While several previous studies have developed and used original crowdsourcing services, this study utilizes a standard commercially available Web service (Yahoo! Crowdsourcing Service [16]).

## Methods

### Ethics Statement

All participants provided written informed consent before participating in this study, and agreed to the terms of the Ethics Statement provided by Yahoo! Japan crowdsourcing service when they proceeded to the task page. All participants were informed of the aim of the questionnaire, and were told that their responses could be published in the future as part of a research study.

This study did not require the participants to be involved in any physical and/or mental intervention. Participants' information was unlinkable, anonymized, and deidentified prior to analysis.

This research did not obtain identifiable private information, meaning that it was exempt from Institutional Review Board approval according to the Ethical Guidelines for Research of the Japanese national government.

## Materials

Most materials for this study were gathered through crowdsourcing. However, 24 known allergy risk factors were initially cited from a previous study [17] and used as seed questions. Sample questions of our study questionnaire (hereinafter referred to as *questions*) are listed in Multimedia Appendix 1. The questionnaire consisted of 3 types of questions: (1) profile-related questions (*profile questions*); (2) risk questions, including known risks (*risk questions*); and (3) a question asking participants to propose questions regarding novel allergy risk factors (*novel risk-proposal questions*). We repeated the crowdsourcing process for 5 iterations (rounds), and the number of risk questions and their content were modified after each round as the hypotheses increased and evolved due to the crowdsourcing procedures.

### Profile Questions

This section comprised questions regarding the basic profile of the participants, such as their allergy status, gender, and age. In this study, we examined the following allergy types: asthma, pollinosis, allergic rhinitis, atopic dermatitis, food allergy, drug hypersensitivity, and sick building syndrome. Pollinosis is regarded as a subgroup of allergic rhinitis. In the questionnaire, however, we divided these two concepts as different diseases so that the crowdworkers could easily understand. We

investigated each of the aforementioned allergies independently, as well as in total (as some participants had more than one allergy type).

### Risk Questions

This section comprised questions regarding each participant's environmental (and partly genetic) situations. The initial risk questions consisted of 8 known risks (randomly selected from 24 known risks), which were used as seed questions. The questions in the second and third rounds contained both seed questions and the newly proposed questions by participants. The ORs for each associated factor and allergy (7 different allergies and overall) were estimated.

### Novel Risk-Proposal Question

We asked the participants to suggest novel hypotheses for proposing associated factors in the form of questions, which were provided as risk questions in the subsequent round. Some of these questions were hard to match with the known risk factors of previous studies; we refer to such factors as *associated factors* in this study. At least one answer was required, with a maximum of five answers accepted

## Participants

All participants were recruited via Yahoo! Crowdsourcing Service. A total of 502 adults (303 men, 199 women) aged 20-69 years participated in this study, and their allergy types are shown in Table 1. The approximate sample size (n=500) was chosen according to a previous study [13], which gathered 532 samples via a crowdsourcing service.

**Table 1.** Number of participants for each allergy type (some having more than one type).

| Allergy Type | Reported Prevalence Rate | Allergy, n (%) |
| --- | --- | --- |
| Total (n=502) | 50% [18] | 298 (59.4%) |
| Asthma | 5.4% [18] | 38 (7.6%) |
| Pollinosis | 26.5% (particularly for cedar pollen) [18] | 183 (36.5%) |
| Allergic rhinitis | 39.4% [19] | 130 (25.9%) |
| Atopic dermatitis | 9.4% (age: 20s), 8.3% (age: 30s), 4.8% (age: 40s) [18] | 59 (11.8%) |
| Food allergy | Insufficient sampling surveys [18] | 26 (5.2%) |
| Drug hypersensitivity | Insufficient sampling surveys [18] | 13 (2.6%) |
| Sick building syndrome | Insufficient sampling surveys [20] | 12 (2.4%) |

## Procedure

Figure 1 illustrates the crowdsourcing process. We repeated this process five times. Notices were posted on the Yahoo! Crowdsourcing job offer site [16] in both the *Easy Task* category and the category for those without particular professional skills.

After running an iteration of the procedure, we calculated the ORs of each answer for all risk questions. Based on these ORs, only the potentially promising top 99 (or fewer, if not applicable) questions of that round were retained for the subsequent round

as risk factor questions; questions whose answers failed to score adequately high ORs were discarded. The detailed procedures are listed in Textbox 1. For the newly created questions provided by the participants in Round 1 that appeared suitable, we manually sorted these questions and combined similar questions (synonymous check) to make them more general. We also selected a candidate question if it was more general than other similar questions, and discarded the others (eg, when the questions were, "*Do you have a cat?*" and, "*Do you have pets?*" we discarded the former question and kept the latter).

**Textbox 1.** Procedure for the generation of research questions.

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**Round 1**: We asked 5 profile questions, 8 seed questions, and a question in which participants were required to provide 1 to 5 hypotheses of possible risks or causes of allergies (in a format that was similar to that of the 8 seed questions).

**Round 2**: We calculated the ORs of the answers for the 8 seed questions. From this round, we utilized the novel risk-proposal questions (ie, hypotheses) provided by the participants. The answers to these questions were manually filtered to eliminate inadequate questions. Questions were determined to be inadequate if they fulfilled either of the following criteria:

- A question that did not require a "yes" or "no" response (eg, "*How many cats do you have?*")

- A question that required participants to divulge personal information (eg, requires an answer such as "*I work at the XX Company.*")

**Round 3**: This round was similar to Round 2, but the ORs of the newly proposed hypotheses, as well as those of the seed questions (known risks), were calculated.

**Rounds 4 and 5**: These rounds were similar to Round 3, and were conducted to validate the crowdsourced hypotheses.

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**Figure 1.** Experiment flow.
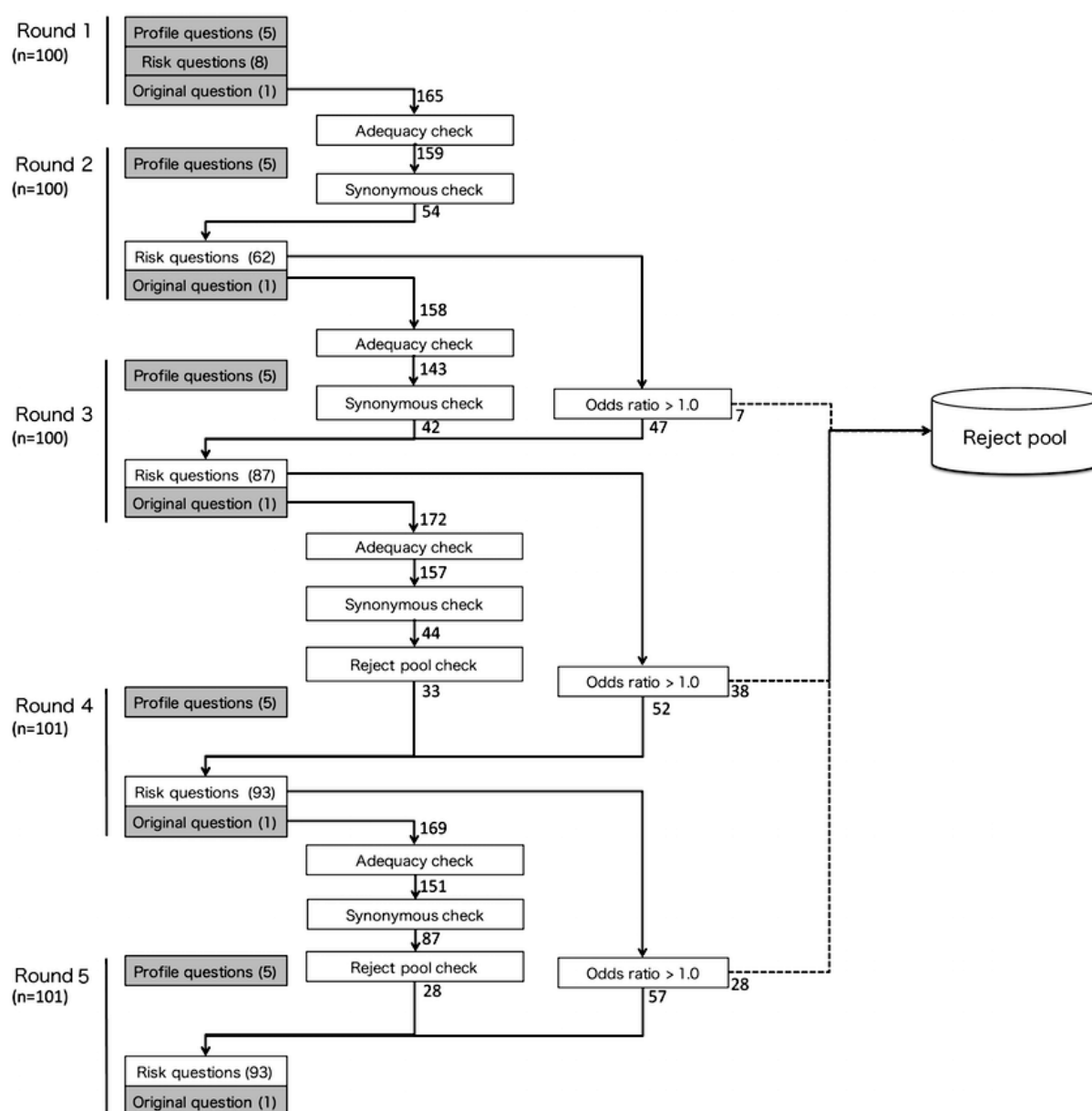
# *Results*

## Allergy Distribution

A participant was classified as *allergy negative* when he or she checked the *none* box in Profile Question 5, and classified as *allergy positive* in the other cases. Allergy negative or positive fully depends on the crowdsourcing participants' decision; false negative or false positive results are sometimes included in the results. As shown in Table 1, 298 of the 502 participants (59.4%) reported having allergies, which is slightly higher than government-reported estimates [3]. There were 38 participants (38/502, 7.6%) with asthma and 183 participants (183/502, 36.5%) with pollinosis, both of which are higher than government statistics [3]. In contrast, there were 130 participants (130/502, 25.9%) with allergic rhinitis, which was lower than the government estimate of 39.4% [3]. The number of participants with atopic dermatitis was 59 (59/502, 11.8%), which was above the government estimate for adults [3]. With regard to the other allergy types (food allergy, drug hypersensitivity, and sick building syndrome), there was insufficient statistical data from previous studies. In our study, there were 26 participants (26/502, 5.2%) with food allergies, 13 participants (13/502, 2.6%) with drug hypersensitivities, and 12 participants (12/502, 2.4%) with sick building syndrome.

## Hypotheses Generation

A total of 157 new hypotheses were proposed from the five-round crowdsourcing procedure; from these, 75 hypotheses showed significant ORs, as shown in Multimedia Appendix 2 A. Hypotheses were regarded as significant if the lower limits of their 95% confidence intervals were >1.0. Approximately

22% of the participants took part in multiple rounds. The participants of multiple rounds are identified by their identification numbers in the Yahoo! Crowdsourcing Service.

## Hypotheses Evaluation

The evaluation of these hypotheses was difficult because the aim of this study was to identify new risks. When a new candidate associated factor was initially identified, we were unable to evaluate it immediately, as its validity was still unclear. Therefore, instead of evaluating new associated factors, we evaluated the performance of reidentified ratio of the known risks. These known risks were identified from a review study [17] and government guidelines on allergies [21]. The relationship between participant answers and known risks are illustrated in Figure 2. By using these relationships, we evaluated the results for the following four aspects: Rediscovered Known Risk Ratio (RKRR), Significant Known Risks Ratio (SKRR), Significant Seed Risks Ratio (SSRR), and Significant Unknown Answer Ratio (SUAR).

### *Rediscovered Known Risk Ratio*

The RKRR is the ratio of known risk factors within the participants' answers. This ratio represents the coverage of crowdsourcing, and is defined as follows:

> *RKRRParticipant answers that are known risksKnown risks*

Thirteen (8+5) of the participants' answers out of 16 known risk factors were derived from preceding studies and guidelines. This indicates that approximately 81% (13/16) of the hypotheses were reconfirmed by crowdsourcing. The number of new suitable hypotheses decreased steadily in later rounds.

**Figure 2.** Relationship between participants' answers and known risks.
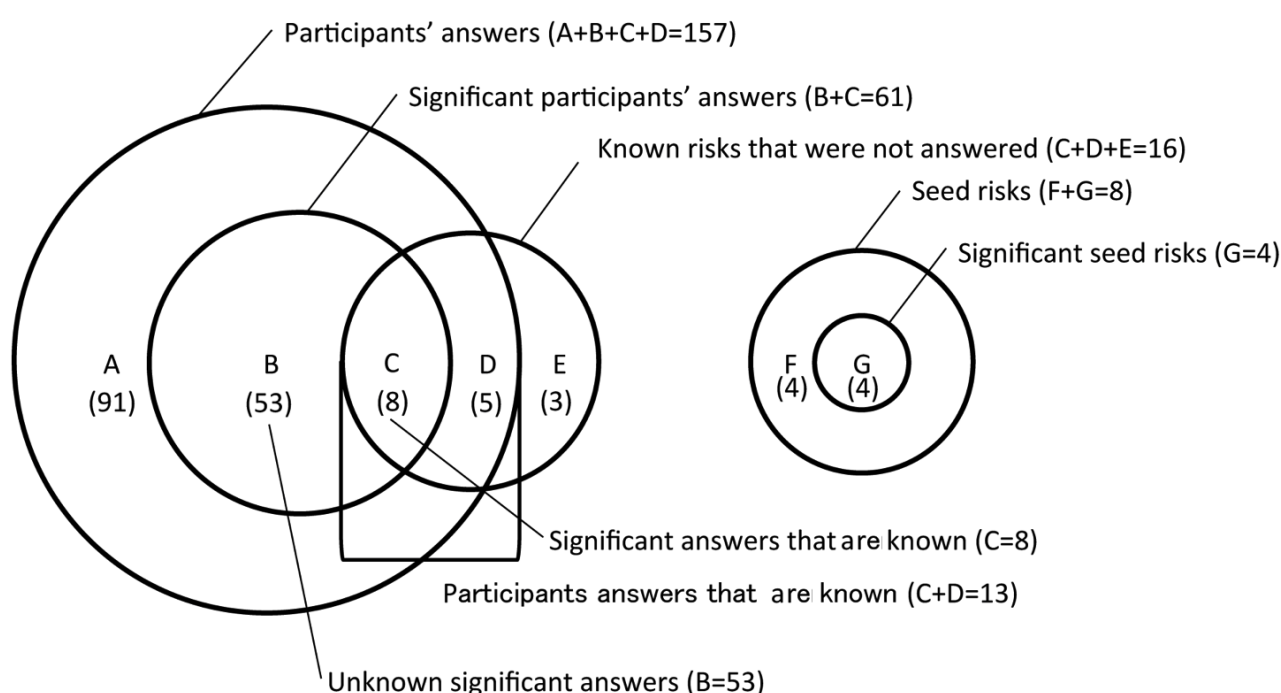
### Significant Known Risks Ratio

The SKRR is the ratio of significant risk factors within the ratio of known risk factors. This ratio represents the validity of crowdsourcing, and is defined as follows:

*SKRRSignificant answers that are known risksParticipant answers that are known risks*

Eight of the 13 known risk factors were statically significant, indicating that more than half (61%) of the risks had validity.

### Significant Seed Risks Ratio

The SSRR is the ratio of significant risk factors within the known seed risk factors. This ratio also corresponds to the validity of the method, and is defined as follows:

*SSRR = Significant seed risks / Seed risks = 4/4+4 = 0.50*

Four of the 8 initial hypotheses (seed risk factors) were statically significant. Similar to the SKRR, this result also indicated that approximately half of the crowdsourced hypotheses had validity.

### Significant Unknown Answer Ratio

The SUAR is the ratio of previously unknown significant associated factors within the participants' significant answers. This ratio represents potential future topics for allergy research:

*SUAR = Unknown significant answers / Significant answers = 53/53+8 = 0.86*

This value (86%) indicates that there still remain many hypothesized associated factors that should be investigated in the future. In the context of the SSRR and SKRR results, half of these hypotheses may be valid risk factors.

## Types of Allergies

This study addressed 7 types of allergies: (1) asthma, (2) pollinosis, (3) allergic rhinitis, (4) atopic dermatitis, (5) food allergy, (6) drug hypersensitivity, and (7) sick building syndrome. Multimedia Appendix 2 shows the possible associated factors for overall allergies (Multimedia Appendix 2 A) and each of the 7 allergy types (Multimedia Appendix 2 B-H): 17 associated factors were identified for asthma (Multimedia Appendix 2 B); 31 associated factors were identified for pollinosis (Multimedia Appendix 2 C); 43 associated factors were identified for allergic rhinitis (Multimedia Appendix 2 D); 24 associated factors were identified for atopic dermatitis (Multimedia Appendix 2 E); 6 associated factors were identified for food allergies (Multimedia Appendix 2 F); 9 associated factors were identified for drug hypersensitivity (Multimedia Appendix 2 G), and 4 associated factors were identified for sick building syndrome (Multimedia Appendix 2 H).

Allergies are considered as, "exaggerated immune reactivity (hypersensitivity) to certain environmental substances (allergens) that normally have little effect on most people" and the, "hypersensitivity is established on initial exposure to the allergen (the sensitizing *dose*); subsequent exposure causes the hypersensitivity reaction" [22]. There are various types of allergies known to exist, and in this study we have focused on 7 of the most well-known allergy types in Japan. Allergies have

become a serious national disorder in Japan, and the Japanese government has set up several boards for preventing allergies. The governmental guidelines of 2011 listed the major allergic symptoms, and we have used these symptoms in this study [23]. The current concepts, causes, and risk factors known for each specific allergy type are detailed below.

### 1. Asthma

Asthma shows episodic reversible airway obstruction, increased bronchial reactivity, and airway inflammation. Causes of asthma can be divided into allergic and nonallergic etiologies. Allergies play an important role in asthma. For example, exposure to dust mites is associated with the development of asthma [24]. Mite and cockroach antigen exposures have been shown to increase asthma morbidity [24]. In this study, all types of possible asthmatic symptoms are included.

### 2. Pollinosis

Pollinosis, commonly called *hay fever* (a term used in the past to describe farmers with symptoms occurring during *haying season* felt to be caused by the hay, but later determined to be caused by ragweed) is defined as the appearance of respiratory symptoms (rhinoconjunctivitis and/or asthma) resulting from the inhalation of pollen to which the individual is sensitized [25]. In this paper, the term is primarily applied to individuals reacting to Japanese red cedar, a seasonal form of allergic rhinitis. According to the Japanese government guideline of allergies, there are more than 60 kinds of possible major seasonal causes of pollinosis in Japan (eg, locust, Japanese cypress, birch, Japanese alder) [15]. In this study, we have included symptoms caused by all such possible allergens as *pollinosis*, and did not differentiate mono- or poly-sensitization during the season.

### 3. Allergic Rhinitis

"Allergic rhinitis is a very common disorder that affects people of all ages, peaking in the teenage years. It underlies many complications, is a major risk factor for poor asthma control, and affects quality of life and productivity at work or school" [26]. Allergic rhinitis is frequently caused by exposure to perennial or seasonal allergens that exist in our indoor and outdoor environments [5]. Among the most common allergens, pollens (grass, trees, and weeds) are the predominant causes of seasonal allergic rhinitis [5]. House dust mites, pets, and molds are the major causes of perennial allergic rhinitis. However, in tropical and subtropical areas pollen may become a perennial allergen [5].

### 4. Atopic Dermatitis

Atopic dermatitis is a skin condition characterized by a complex, heterogeneous pathogenesis, including skin barrier dysfunctions, allergy/immunology, and pruritus. When the skin barrier is disrupted, the skin is predisposed to being penetrated by external stimuli. Foreign antigens can be subdivided into two subsets by size: haptens (including metals) and protein antigens [27].

### 5. Food Allergies

Food allergies are immunologically mediated adverse reactions to foods. Any food protein can trigger an allergic response, and allergic reactions to many foods have been documented. Many

individuals have allergic reactions to food through mechanisms that are elusive [28,29].

### 6. Drug Hypersensitivity

Drug hypersensitivity is an immune-mediated reaction to a drug. Symptoms range from mild to severe and include rash, anaphylaxis, and serum sickness. Symptoms and signs vary by patient and drug, and a single drug may cause different reactions in different patients. The most serious reaction is anaphylaxis; exanthema, urticaria, and fever are common. Fixed drug reactions—reactions that recur at the same body site each time a patient is exposed to the same drug—are uncommon [30].

### 7. Sick Building Syndrome

Sick building syndrome, or building-related illness, is a heterogeneous group of disorders whose etiology is linked to the environment of modern airtight buildings. Such buildings are characterized by sealed windows and dependence on heating, ventilation, and air conditioning systems for the circulation of air. Most cases occur in nonindustrial office buildings, but cases can occur in apartment buildings, single-family homes, schools, museums, and libraries [31].

## Discussion

### Number of Diseases and Hypotheses

The number of participants with a particular disease (allergy) was found to be related to the number of hypotheses for that disease. Among the 7 types of allergies addressed in our questionnaire, many of the participants (n=130) reported suffering from allergic rhinitis, which produced the high number of significant possible associated factors (43 associated factors). Pollinosis, which had the highest number of sufferers (n=183), produced the second highest number of significant possible associated factors (31 associated factors). In contrast, sick building syndrome, reported by only 12 participants, produced 4 significant associated factors. Similarly, drug hypersensitivity, reported by only 13 participants, produced 9 significant associated factors. One of the possible reasons for this observation is that the high number of patients with an allergy may result in increased generation of hypotheses. This finding suggests that common diseases with many patients may be more suitable for crowdsourcing-based investigations.

### Genetic Factors Versus Environmental Factors

The results showed that most allergy types (with the exception of sick building syndrome) were associated with the genetic factor of *having family member(s) with an allergy*, which suggests a genetic basis for allergies. This, however, may also be interpreted to some degree as an environmental factor, as family members often share similar environments. In addition, participants who reported suffering from 5 types of allergies (except for atopic dermatitis and food allergies) were significantly associated with the condition of *often falling ill*, which may also suggest an environmental component to allergies. It is difficult to determine whether some environmental factors are the cause of an allergy, or its outcome.

### Disease Relationship: Pollinosis and Allergic Rhinitis

Among the 7 allergy types, pollinosis and allergic rhinitis shared many possible associated factors. These two diseases had 20 possible associated factors in common (out of 31 possible associated factors for pollinosis and 43 possible associated factors for allergic rhinitis), and also shared similar factors. Of the 183 participants (approximately 38%) with pollinosis and 130 participants (approximately 53%) with allergic rhinitis, 69 participants reported having both diseases. Interestingly, those with both diseases showed high ORs for exposure to emotionally stressful environments (*feeling temperamental or moody*; *feeling fatigued or stressed*; *having a traumatic and stressful experience*; *experiencing considerable environmental changes, such as moving and changing jobs*; and *having trouble with family relationships*) and food-related factors (*eating between meals* and *having a lot of ready-to-eat food/instant food*). These results corroborate the relationship between nasal-related allergies and emotional reactions that has been considered by recent allergy researches [32-34].

Conversely, it has been reported that preservatives can induce rhinitis (but this effect appears in very few cases associated with food), and this result somewhat indicates the relationship between eating habits and pollinosis/allergic rhinitis, which has been described in several previous studies [35,36].

### Asthma

Thirty-eight of the 502 participants reported suffering from asthma. The associated factor hypothesis of *often falling ill* (OR 6.81) may indicate that asthma itself implies a more delicate state of health. Some participants reported that they *have a harder time breathing during a typhoon* (OR 13.35), and this supports the theory that the typhoon season can worsen the asthma condition [37]. In addition, some individuals with asthma also experience *the onset of itching when touching certain metals* (OR 4.49). This result supports the relationship between asthma and metal allergy; especially as both may have been affected by the Asian Dust event [38]. Individuals with asthma appeared sensitive to their environment, such as *sensitive to smells* (OR 3.62), *sensitive to temperature change* (OR 2.88), as well as sensitivities to *the climate* and *typhoons*. Considering the asthma mortality rate for adults in Japan is still higher than in many Western countries [39], there is an urgent need to investigate the factors that contribute to the development of asthma. It was also noteworthy that those who *had measles during childhood* also tended to suffer from asthma. While a previous study reported that having childhood measles may reduce the diagnosis of asthma [40], another study claimed the opposite outcome [41]. This disparity requires further investigation.

### Pollinosis

Pollinosis is one of the most common diseases in Japan, and 183 of 502 participants in our study reported suffering from this disease. The hypothesized associated factor with the highest OR for pollinosis was that participants *sneeze often* (OR 3.64), but this is also one of the major symptoms of pollinosis. In the future, it will be necessary to determine causal directionality in such relationships, and identify whether a factor is a disease risk or a symptom/outcome. The results also indicated close

relationships between this disease and stressful environments, including: *being in a very stressful environment* (OR 3.52); *experiencing considerable environmental changes, such as moving and changing jobs* (OR 3.26); *having a traumatic and stressful experience* (OR 2.56); *not feeling satisfied with life in general* (OR 3.41); *feeling temperamental or moody* (OR 2.08); and *having trouble with family relationships* (OR 1.85). These factors had higher ORs in pollinosis and allergenic rhinitis than in the other allergy types.

It is also notable that the participants with these two allergy types have experienced *eating food that had been prechewed by someone else* (OR 2.96) as a child, which used to be customary in some areas of Japan. This possible associated factor should be explored in greater depth, as this may indicate the possibility of a transmitted disease. In addition, *having family member(s) with an allergy* (OR 2.81) was significant in both of these types of allergies, indicating that genetic factors should also be investigated further. The hypothesis with the fifth highest OR was *being suntanned* (OR 3.46), and these participants may be more likely to spend time outdoors. Being suntanned and being exposed to pollen allergens may share a common primary factor, and further investigations are needed. Similarly, the results showed that individuals with pollinosis tended to be *habitually wearing facemasks* (OR 2.87), but this behavior may be used to avoid pollen exposure after the onset of symptoms. As stated earlier, the causal directionality of this relationship should be investigated further.

## Allergic Rhinitis

Allergic rhinitis is also a major common disease in Japan. In this study, 130 participants reported suffering from allergic rhinitis. As in pollinosis, the hypothesized associated factor that showed the highest OR for this allergy type was that participants *sneeze often* (OR 10.93), which is also a symptom of this allergy type. The results also indicated a possible relationship between *eating between meals* (OR 4.07) and allergic rhinitis. It is noteworthy that this allergy type showed similar possible associated factors with those of pollinosis. However, *being suntanned* was not significantly associated with allergic rhinitis, but *having birds as pets, and/or having close contact with birds* (OR 1.98) was unique to this allergy type. Although crowdworkers were assumed to have regarded pollinosis and allergic rhinitis as different diseases, we obtained similar possible associated factors. If the difference of the possible associated factors between these two diseases is meaningful, this should be validated externally in future work. Another novel finding was that *never been stung by a bee* (OR 2.73) and *habitually removing body hair* (OR 2.30) were shown to be related to allergic rhinitis, and both of these unique possible associated factors should be investigated further. Moreover, participants with allergic rhinitis showed significant relationships with the experience of *having been a target for bullying* as well as *living in apartments in higher floors when they were young*. This study, however, cannot distinguish between individuals who think they are allergic and those who have a nonallergic form of rhinitis (idiopathic rhinitis, nonallergic rhinitis with eosinophilia syndrome). A mechanism to remove these individuals from the grouping of allergic rhinitis needs to be established.

## Atopic Dermatitis

Fifty-nine participants reported suffering from atopic dermatitis in this study. The hypothesized associated factor that showed the highest OR was *suffering from atopic dermatitis as a child* (OR 30.25). This result shows that many individuals who suffered from this disease as a child continued to suffer as adults. Another hypothesized associated factor that showed a high OR was *often experiencing skin trouble (itching, rashes, etc.)* (OR 21.98), which is also a symptom of atopic dermatitis. A conspicuous and serious possible atopic dermatitis associated factor was *having sexual interactions since the participants were minors or in their teens* (OR 8.57). A similar hypothesis has been proposed by a previous study [42]. Discovery of this hypothesized associated factor may have been made possible by the high level of privacy afforded by crowdsourcing, which allowed the participants to honestly respond to highly private matters. Research that uses crowdsourcing may therefore have great potential for studies dealing with highly personal conditions.

Another possible associated factor was *not reading used books* (OR 6.32), which may be related to the fact that many participants with atopic dermatitis considered themselves to be *clean freaks* (OR 3.01); these individuals tend to avoid allergens as much as possible after they become aware of their allergy. Similarly, behaviors such as *preventing mite infestation (eg, on carpets, mattresses, beddings)* (OR 8.75), *being particular about using additive-free skin care products* (OR 5.77), and *wearing gloves when using detergents* (OR 5.48) may have been reactive countermeasures to their atopic dermatitis symptoms. Participants who reported *having close relationships with others who had allergies as a child* (OR 3.43) suggests that individuals with atopic dermatitis may have gathered with others who were also suffering allergic symptoms, indicating some psychological care for children with atopic dermatitis. This associated factor may have a possible influence on character development. In addition, those with atopic dermatitis showed some unique associated factors such as *not feeling sick when traveling abroad* (OR 9.75) and *not using contact lenses or glasses* (OR 3.97). Further investigation is needed for these factors.

## Food Allergy

Twenty-six of 502 participants reported having a food allergy, and the hypothesized associated factor of *having family member(s) with an allergy* (OR 3.71) showed a relatively high OR in these individuals, and in those with drug hypersensitivity (OR 16.21). This result may suggest a strong genetic influence in these allergy types. However, between these two allergy types, only food allergies showed a significant relationship with *suffering from atopic dermatitis as a child* (OR 4.69), which supports the findings from previous studies that indicated a relationship between these two allergy types [28,43]. The low number of participants who reported having drug hypersensitivity may also have influenced these findings (we did not observe any relationship with *suffering from atopic dermatitis as a child*), and further studies that compare these two particular allergy types are needed to shed light on this topic.

Those with a food allergy were associated with *often suffering from hives* (OR 3.44), which may also be one of their symptoms. Another possible associated factor was *frequent cleaning of the house* (OR 5.22), which may be a behavioral response to their allergy, as individuals with food allergies frequently attempt to remove allergens from their house after they become aware of their disease. Conversely, this result may support the so-called *hygiene hypothesis*, which states that childhood exposure to allergens can reduce susceptibility to allergies. However, two other possible associated factors identified in our study may be contrary to the hygiene hypothesis: *played at vacant lots during childhood* (OR 5.71) and *played in mountains and bushes during childhood* (OR 3.45). Further investigations should therefore be conducted on the relationship between food allergies and the hygiene hypothesis.

### Drug Hypersensitivity

Thirteen of 502 participants reported suffering from drug hypersensitivity, which was half the number of those with a food allergy. Similar to food allergies, this type of allergy had a significant relationship with the genetic factor of *having family member(s) with an allergy* (OR 16.21). However, unlike food allergies, drug hypersensitivity showed more environmental factors as possible associated factors, including: *often wearing cosmetics* (OR 5.07); *experiencing considerable environmental changes, such as moving and changing jobs* (OR 5.22); and *owning pets or having general contact with animals* (OR 4.09). The relationship between drug hypersensitivity and cosmetics should be investigated, especially on the specific types of cosmetics that may have influenced this allergy. In addition, those who experienced *often falling ill* (OR 0.96) and who *often caught colds during childhood* (OR 3.65) also showed significant relationships with this allergy type. Such individuals may have increased exposure to medications, which may be an associated factor for drug hypersensitivity [44].

### Sick Building Syndrome

Twelve of 502 participants reported suffering from sick building syndrome, making this the least represented allergy in our study sample. This allergy type also produced the fewest number of hypotheses. The hypothesized associated factor with the highest OR was *having felt sick after changing wall paper* (OR 48.50). This, however, can be one of the symptoms of this allergy type and is not considered to be a novel associated factor. The factor of *often falling ill* (OR 7.37) had the third highest OR for this allergy type. This finding may indicate possible allergies due to exposure to medications and a symptom resulting from this allergy. Similarly, other hypothesized associated factors that were significantly associated with sick building syndrome were *using cotton towels* (OR 12.92) and *habitually wearing facemasks* (OR 5.57), which are both very likely to be countermeasures against this allergy. As a result, this research could not identify any useful hypotheses for sick building syndrome, which suggests that research using crowdsourcing may have problems with small sample sizes.

### Optimal Stopping of the Algorithm

There were difficulties in determining the optimal stopping of the algorithm (questionnaire rounds) because more data would ostensibly give rise to more accurate results with negligible increases in cost. A strong indication for the optimal end time was the number of new hypothesized associated factors. In this experiment, Round 1 produced 54 hypotheses, Round 2 produced 42 hypotheses, Round 3 produced 33 hypotheses, and Round 4 produced 28 hypotheses. This steady decrease indicated that there may be few novel hypotheses generated in further iterations of the algorithm. Other indications for optimal stopping of the algorithm included the steady decrease in the number of significant hypotheses and the number of hypotheses that were identical to those previously proposed. In the near future, these aforementioned statistics may support the development of an optimal stopping theory for studies such as this.

### Limitations

This study had several limitations. A major limitation is the possible sampling bias due to the use of Web-based participants. Age, gender, and other background characteristics may differ from the general population, and thereby reduce the representativeness of our findings. While Internet usage for people aged <50 years is over 90% in Japan, half of those aged >70 years do not have significant access to the Internet [8]. This study used one crowdsourcing company (Yahoo! Japan [16]) for sampling, and the users of other crowdsourcing companies were not included. This limitation may have resulted in sampling error. Current methodologies make it difficult to avoid such biases, and new techniques are needed.

Another limitation is the difficulty in determining the causal directionality of relationships. For example, one of the hypothesized associated factors for pollinosis is *sneeze often* but this can be a symptom of pollinosis itself. In fact, the new hypothesis generated in this study contained many of these types of associated facts. Ultimately, if we have already obtained enough knowledge on a disease, we could classify the results in three ways: (1) a symptom/outcome of the allergy (eg, *sneeze often*); (2) a behavioral response to the allergy (eg, *clean your house frequently*); and (3) a potential causal relationship, which is a target of this study. However, such classifications tend to be subjective and difficult to distinguish. For example, several studies have indicated that environments that are *too clean* during childhood may cause a risk of allergies [45,46]. Such a hypothesis causes difficulty for classification, partly because the terminology and granularity of the descriptions are different between the crowdsourced results and existing known risks. For example, a crowdsourced result, " *Do you often undergo illnesses?* " does not match the existing findings, because some words, such as *often* and *illnesses*, are not well-defined. Crowdsourced results often contain various vague words. Further studies are required to fill this gap, which makes the obtained hypotheses suitable for external validity.

Furthermore, most of the crowdsourcing participants lack in-depth knowledge about allergies, presumably lack detailed medical knowledge, and the concept of allergies may be misunderstood by some individuals. To deal with this problem, we could use an alternative questionnaire to ask, " *Have you ever been diagnosed by a physician with X?* " which is based

on a physician's expertise. This study has room to improve the credibility of participants' answers.

Finally, it was labor-intensive and costly to remove inadequate candidate hypotheses generated by the participants. Many participants submitted the hypotheses individually, and we found that many hypotheses overlapped with one another. To avoid these overlaps, we had to manually check the newly proposed questions, which required a great deal of effort and time. For every 100 questions, this checking process incurred the cost equivalent to hiring one person per day (on average). In the near future, advances in natural language processing techniques are expected to contribute to easing the demands of this labor-intensive and potentially costly process. This study cannot provide medical diagnoses for individual participants (ie, it is not possible to definitively tell an individual that they have allergic rhinitis or a food allergy). Detailed diagnoses and precise medical studies are awaited to determine the novel medically-qualified allergy risk factors.

## Conclusions

The aim of this study was to utilize and apply a Web crowdsourcing service to collect and test hypotheses for possible allergy-associated factors. We crowdsourced for unknown allergy-associated factors for seven different allergies, and calculated their ORs. This study was unique in that it also asked the participants to generate original hypotheses to allow the general public to contribute to identifying possible causes of allergies that even an experienced physician may have difficulties conceiving. This task identified more than 157 new hypotheses, including 53 significantly associated factors that were previously unknown. These novel factors warrant further in-depth investigation, and clinical trials should also be conducted in the future to validate these hypotheses.

## Authors' Contributions

EA and SS conceived and designed the experiment, analyzed the data, and prepared the manuscript. SS performed the experiment. SA and SK contributed materials and analytical tools.

## Conflicts of Interest

None declared.

## Multimedia Appendix 1

The questionnaire used in the crowdsourcing survey.

[PDF File (Adobe PDF File), 33KB - resprot_v6i5e83_app1.pdf ]

## Multimedia Appendix 2

Questions (hypothesized associated factors) with significant odds ratios (95% CI: over 1.0).

[PDF File (Adobe PDF File), 109KB - resprot_v6i5e83_app2.pdf ]

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## Abbreviations

**OR:** odds ratio
**RKRR:** Rediscovered Known Risk Ratio
**SKRR:** Significant Known Risks Ratio
**SSRR:** Significant Seed Risks Ratio
**SUAR:** Significant Unknown Answer Ratio

Original Paper

# Recruitment of Community College Students Into a Web-Assisted Tobacco Intervention Study

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## Abstract

**Background:** United States college students, particularly those attending community colleges, have higher smoking rates than the national average. Recruitment of such smokers into research studies has not been studied in depth, despite a moderate amount information on study recruitment success with smokers from traditional four-year colleges. Recruitment channels and success are evolving as technology evolves, so it is important to understand how to best target, implement, and evaluate recruitment strategies.

**Objective:** The aim of this paper is to both qualitatively and quantitatively explore recruitment channels (eg, mass email, in-person referral, posted materials) and their success with enrollment into a Web-Assisted Tobacco Intervention study in this priority population of underserved and understudied smokers.

**Methods:** Qualitative research methods included key informant interviews (n=18) and four focus groups (n=37). Quantitative research methods included observed online responsiveness to any channel (n=10,914), responses from those completing online screening and study consent (n=2696), and responses to a baseline questionnaire from the fully enrolled study participants (n=1452).

**Results:** Qualitative results prior to recruitment provided insights regarding the selection of a variety of recruitment channels proposed to be successful, and provided context for the unique attributes of the study sample. Quantitative analysis of self-reported channels used to engage with students, and to enroll participants into the study, revealed the relative utilization of channels at several recruitment points. The use of mass emails to the student body was reported by the final sample as the most influential channel, accounting for 60.54% (879/1452) of the total enrolled sample.

**Conclusions:** Relative channel efficiency was analyzed across a wide variety of channels. One primary channel (mass emails) and a small number of secondary channels (including college websites and learning management systems) accounted for most of the recruitment success.

**Trial Registration:** ClinicalTrials.gov NCT01692730; https://clinicaltrials.gov/ct2/show/NCT01692730 (Archived by WebCite at http://www.webcitation.org/6qEcFQN9Q)

**KEYWORDS**

XSL·FO
**RenderX**

## Introduction

Community colleges are a unique setting with an understudied population consisting of distinct subpopulations, including young adults, older nontraditional students, armed services veterans, individuals with full time jobs, and single parents. Rates of nonwhite students and students with low socioeconomic status (SES) are higher in community colleges compared to traditional colleges and universities [1-3]. Of all college students, nearly half (42-45%) attend community colleges [4,5]. The total number of enrollees at community colleges in the United States was approximately seven million during the 2013-2014 academic year, and according to a recent report, it is estimated that enrollment at community colleges is projected to increase by 21 percent to 8.2 million students between 2014 and 2025 [6].

Community colleges have increasingly become more popular for many groups: young adults, as a pathway to costlier traditional colleges and universities; veterans, as an increasingly available option upon returning from active duty; and nontraditional older adults seeking to improve their job market qualifications [7]. President Barack Obama launched the American Graduation Initiative in 2009 and America's College Promise in 2015 to increase enrollment and provide new avenues for persons to successfully enter the work force [8,9].

Cigarette smoking prevalence is higher among community college students (as high as 34%), compared to their traditional college and university counterparts [10-12]. Although the community college population is projected to grow, research studies that target this diverse student body remain limited [13-16]. Community college students are more vulnerable to health risks compared to other college students [3,17], yet limited research has been undertaken on smoking cessation interventions in this population [13,18]. Most of the relevant research on smoking cessation has focused on traditional colleges and universities, or those institutions in combination with community college populations [14].

The limited studies that are available indicate that community college students (compared to other college students) are more likely to smoke, describe themselves as regular smokers, and be unsuccessful at quitting [14,19]. Community college students report being less concerned about smoking-related health problems than other college students [11], and nearly half (45%) state that quitting smoking would have little or no impact on their health [20]. Such findings strongly support the need for research in this vulnerable population to explore effective smoking cessation interventions.

Challenges exist when applying research from traditional college and university environments to the environments of community colleges, which can be underscored by distinct characteristics of the community college mission, organizational capacity, and student population [21]. Although published literature reports demographic differences between students at community colleges and traditional colleges and universities, little is known about the nature of successful recruitment strategies to engage such students into randomized controlled trials (tobacco cessation intervention or otherwise).

An updated review of Web-assisted tobacco interventions in The Cochrane Database of Systematic Reviews included a total of 28 studies with over 45,000 participants for interventions that varied in intensity and outreach [22]. Studies were included with information on recruitment of various populations, including adults from the general population, adolescents, and university students. In most studies, recruitment was Web-based (search engines and browsing), while several trials also used press releases, billboards, television advertisements, posters, and flyers, in addition to Web-based strategies. Using these recruitment methods, participants included in these trials were smokers who were motivated to quit and chose the Internet as a tool for smoking cessation support.

Recruitment channels that have demonstrated particular success vary greatly by study design and population, and data on direct comparisons of channel performance are not often reported. As reported in the 2013 Cochrane review [22], online recruitment accounts for most participants in online cessation studies, whereby participants find the studies through search engines and browsing. These studies reported a wide variety of other recruitment channels, including: traditional materials (flyers, posters, brochures, school newspaper ads and articles, school-wide announcements, newspapers, health plan magazine advertisements, press releases, billboards, bus interior posters), engagement with champions (classroom presentations, school liaison referrals, employee mailings, physician referrals), face-to-face (lunch-hour sign-up tables, word of mouth, medical clinics), and electronic media (website banners and links, purchased email addresses, electronic newsletters, social network sites and campaigns, online smoking cessation forums, television, radio, online research panels, search engines, central telephone numbers, and mass emailing).

The present study explored research study recruitment strategies in two phases of a randomized controlled trial (ClinicalTrials.gov NCT01692730). The initial qualitative phase (Phase 1) provided key formative evaluation information to aid in the design of the study's specific recruitment methods. The quantitative phase (Phase 2) assessed the study's success with these methods from initial reach to ultimate enrollment via recruitment channels by examining (1) initial recruitment of potential participants, (2) those who were recruited and consented, and (3) those who consented and were ultimately enrolled and randomized.

## Methods

Proposed research study recruitment channels (traditional channels such as flyers and posters; digital channels such as mass emails, digital bulletin boards, and websites) were initially examined qualitatively with community college students and staff. The Phase 1 study protocol, conducted as planned formative research, was approved by the principal investigator's institutional review board (IRB), and informed consent was obtained from all participants. Phase 1 qualitative monetary incentives included US $15 for key informant interviews (KIIs), and US $25 for focus group (FG) participation, while Phase 2 randomized trial monetary incentives included no payment for baseline enrollment (in order to minimize recruitment of

individuals who might falsify smoking status and/or cessation intent in order to receive a payment), and increasing incentivization for follow-up outcome questionnaires (in order to maximize retention of valid participants) at 1-month (US $10), 6-month (US $15), and 12-month (US $20) timepoints.

## Phase 1: Qualitative Methods

Research sites included four Western New York community colleges, selected through purposive sampling to include two in rural areas, one in a middle-class suburb, and one in a central urban area. Qualitative research methods based on our previous research protocols, and consistent with evidence-based strategies [23], included KIIs (n=18) and four FGs (n=37) with a total of 55 students, administrators, and staff. Potential respondents were reached via emails from campus champions, courseware postings, and hard-copy flyers with IRB-approved wording. All respondents who presented at prearranged times were provided with information sheets describing the goals of the research, and how the Phase 1 qualitative work would inform key elements of the Phase 2 randomized trial. Each participant provided informed, signed consent.

Purposive sampling was utilized for the KIIs, which were conducted with students (n=11; smokers and ex-smokers, traditional, nontraditional, and veteran students), and with faculty and staff (n=7). Two male PhD level senior researchers (SM, AW), each with more than 10 years of experience conducting qualitative research methods, participated in all KIIs: one acted as a facilitator while the other was a cofacilitator/note taker. Semistructured KII interview guides were developed, pretested, and pilot tested (as were guides for FGs), with domains including smoking, smoking cessation, campus tobacco-free policies, and the study's specific proposed research recruitment channels. Qualitative data collection progressed iteratively, with early interview responses used to refine subsequent KII and FG interview guides, and protocols for interviews and FGs. Open-ended questions in the guides were designed to elicit qualitative responses related to the targeted domains. Each KII and FG was audio recorded, and researchers made field notes before and after all contact with participants. Most of the students interviewed were daily commuters living off-campus. Seven KIIs were conducted with nonstudent campus opinion leaders, including student health center directors, administrators, educators, an associate dean, and a director of residential life. Faculty and staff were interviewed in seven KII sessions (n=9; two of these were conducted with two interviewees in attendance), which consisted of two health center directors, one residential life director, four student service administrators, one faculty from the department of nursing, and one associate dean. Only researchers and respondents were present at all KIIs (lasting between 30 and 60 minutes each) and FGs (lasting 90 minutes each).

The four FGs, assembled with purposive sampling as described above and whose members were similarly provided with information sheets and informed consent procedures, were conducted with 8-12 students each, inclusive of students who were smokers or ex-smokers varying in race, age, gender, and student type (traditional young adults, nontraditional older adults, and veterans). The FGs addressed similar topics as those

in the KIIs. Although all KII participants were invited to the FGs, per our previous protocols and for the purposes of efficient outreach and iteratively building on qualitative findings, only five of the FG participants had previously participated in KIIs. Aside from these five individuals, no other repeat interviews were carried out. One FG consisted of students who lived on-campus.

The KIIs and FGs used iteratively refined interview guides with open-ended questions addressing the domains of tobacco use, campus polices, and cessation resources that are described elsewhere [24], as well as domains addressing recruitment strategies, materials, and channels, which are examined in the present analysis. See Multimedia Appendix 1, Multimedia Appendix 2, Multimedia Appendix 3, and Multimedia Appendix 4 for examples of the key recruitment materials that were refined during this process and later used in the Phase 2 randomized trial. See Multimedia Appendix 5 for an example of a KII interview guide and Multimedia Appendix 6 for an example of an FG guide.

### Materials Presented in Key Informant Interviews and Focus Groups

Materials were presented during KIIs and FGs to elicit reactions, opinions, and recommendations for recruitment success (ie, success in recruiting and enrolling participants into an online research study) with a population of community college students. Examples of recruitment channels were identified from the limited literature available for this population, and from the study team's previous research recruitment strategies [18,25-30]. Multimedia presentation of materials included hard-copy mock-ups of passive recruitment materials (flyers, tent-cards), and overhead displays of pictures of various recruitment channels, including electronic methods (eg, Quick Response [QR] codes, email invitations, electronic bulletin board displays). Samples of visual materials included variations of persons' faces, *no smoking* signs, and other iconic images, to elicit feedback and discussion. These proposed mock-ups, displays, and associated procedures were considered initial drafts, and participants were informed that their feedback was a vital component of the overall research by helping to make the study methods maximally relevant to the intended participants.

### Analysis of Qualitative Data

The Grounded Theory Approach guided the present analysis, specifically employing a Constant Comparative Method, in which data collection and analysis progressed iteratively [31-34]. The content for the KII and FG guides began with open-ended supposition-building questions concerning research participant recruitment (specifically, community college student interest in, and likely methods for, successful recruitment into a randomized trial). After each KII, questions were refined based on new suppositions informed by the analysis of the rich content provided by respondents. As the analysis progressed, iteratively gathered data supported the ongoing theoretical sampling of general subgroups of participants (young adults, midlife and older students, and military veterans). Data saturation that supported emerging themes was observed to have been reached in both the KII and FG processes.

Five project team members conducted open coding and then axial coding of each recorded interview. After establishing a broad framework for data analysis (open coding of themes and specific quotes related to recruitment channels and to features of online smoking cessation interventions), axial coding (a structured process to associate self-reported constructs) led to the development of specific categories and subcategories [31]. Following code creation, quotations of text with codes were placed in a spreadsheet to aid in analyses. Project staff debriefed and compared emerging data patterns to solidify codes, categories, and subcategories, and resolved discrepancies. Two coders then independently coded quotations of text per identified theme categories (eg, perceptions of potential effectiveness of a given recruitment channel), and Cohen κ was run to quantify the agreement between these two independent raters.

## Phase 2: Randomized Trial

### Participants in Web-Assisted Tobacco Intervention Trial

To be eligible for the Web-Assisted Tobacco Intervention (WATI), participants had to be enrolled in a community college, smoke at least 5 cigarettes per week, and desire to quit smoking within the next 3 months. All potential participants reached an online survey with a description of the study, followed by an online consent process, enrollment instructions, the study's baseline questionnaire, and access to the appropriate study intervention website (see below).

The Phase 2 study protocol was approved by the principal investigator's IRB, and informed consent was obtained from all participants. The parent IRB-approved process, and the nature of the study design, did not require each participating campus to complete their own site-level IRB approval process (it was not considered a partnering research initiative, as recruitment could occur outside of campus environments). However, some community colleges (individually, or via larger organizational review in systems with multiple community colleges) deemed this necessary, resulting in successful IRB approval (or exemption) obtained from eight community college systems, representing over 30 campuses. IRB requirements included a combination of (1) the provision of a copy of the parent IRB approval letter for review, (2) submission of a short application, and (3) the provision of all materials previously reviewed and approved by the parent IRB.

### Baseline Questionnaire

A baseline questionnaire was developed from our previous smoking cessation studies that used technological interventions, understudied populations, and multiple recruitment channels [21,27,29]. The questionnaire was pretested with multiple versions that were improved iteratively with feedback from: (1) a group of students from a local community college (a health class of approximately 40 students); and (2) for comparison purposes and ongoing feedback from young adult college age students, a convenience sample of three local university students working as independent study students on the parent study. Pretesting instructions elicited feedback with respect to length of time, understandability, and recommendations for changes.

### Recruitment

All online data were captured using Research Electronic Data Capture (REDCap), a widely-used data capture application developed for large-scale research projects [35]. Those who qualified and consented proceeded to the baseline questionnaire, after which they were randomized and enrolled in one of two intervention arms of the parent WATI study, as described elsewhere [13]. Interventions varied in level of interactivity, but both included Public Health Services Guideline-based tobacco cessation information [36], and information and formatting used successfully in other studies [37].

Process evaluation strategies for the recruitment phase of the parent study primarily involved monitoring dates of implementation of various channels (eg, the date a community college would send a mass email to their student body, or a campus website began recruitment advertising for the study), and rates of accrual to study enrollment. Based on the slower than expected rate of recruitment from an initial sample of 16 community colleges in Western New York, the target sample of colleges was expanded to recruit participants from any community college in the state of New York, and eventually from any US state (except the 27 states whose tobacco cessation websites were developed by the same vendor in the parent study).

Channel efficiency was defined as the percentage of those reached who ultimately enrolled for each channel. Individual channel reach and efficiency are reported, including all channel exposures as self-reported by participants and including only the single most influential channel per self-report.

### Recruitment Categories and Channels

#### Traditional Materials

Building on successful strategies in our previous research [27,29,30], materials and strategies tested in Phase 1 of the present study included flyers with tear-offs, posters, table-tent cards (for cafeteria tables and tabling events), business-sized cards (for tabling events, college orientation, and college health centers), and variations on these *passive recruitment* hard-copy materials which were easy to produce and ship to campus champions.

#### Engagement With Community College Champions

To determine which materials, electronic strategies, or other student-engagement strategies were available and accessible, at least one campus champion from each study location was engaged and contacted regularly. Typically, champions were in the offices of the President, Student/Academic Affairs, Student Activities, or Student Health. It was determined that despite previous commitments of support for the present study from the institution (eg, letters of support at the time of funding applications), there was little if any *institutional memory* of the nature of the study, which resulted in newly beginning the engagement process with most campuses. Engaged champions assisted with mass emails, placement of recruitment ads in electronic media, coordination of hard-copy recruitment materials, and assistance with site-specific requirements (materials approvals, IRB approvals, and administrative approvals). Ongoing engagement consisted of phone calls,

emails, and regular newsletters with information on recruitment success and study goals. Support from officials at higher levels was also solicited, such as those from multicampus networks (eg, State University of New York, New York Community College Trustees, Illinois Council of Community College Administrators, Kentucky Community and Technical College System).

### Face-to-Face

Investigators periodically engaged in face-to-face events such as student meetings, classes, and tabling events (eg, health fairs) on campus. Given that only 16 campuses were readily accessible by the research team in the study's immediate geographic region, these more time- and resource-intensive activities were primarily limited to nearby campuses.

### Electronic Media

This category includes at least two instances of radio Public Service Announcement advertisements and fewer than 10 earned media events on local or statewide radio and television (eg, interviews regarding the study, or related tobacco control stories with opportunities to broadcast the study's contact information). However, this broad category primarily consists of electronic bulletin boards, computer screens on campus (eg, wallpaper and computer time-out messages), mass emails (eg, *email blasts*, *global emails*) sent to a college's entire student body, and placement of a recruitment ad on a college website or specific *courseware*, also known as *learning management systems* (LMSs) such as BlackBoard or Genesis.

### *Enhanced Recruitment Strategies*

In addition to the more traditional recruitment strategies described above, additional strategies were employed to enhance specific channel success (eg, adding multiple contact options, expanded use of digital strategies) and to provide the project with additional data sources (specifically, multiple REDCap datasets) for both recruitment and retention in the WATI trial. Additionally, a specific aim of the WATI study was to investigate successful recruitment strategies that could inform future research (not just smoking cessation trials). Therefore, protocols and channels were implemented to provide multiple opportunities for capitalizing on digitally-provided contact information.

### Posters With Quick Response Codes

Posters and flyers with QR codes were made available to community college campuses. Potential research subjects could scan the QR codes with a smartphone to access the study. Students using this channel entered their contact information into a specific REDCap database, and were offered a link to the baseline and consent processes to input their email address into an online registry (another REDCap database; see below). The research team accessed these registries to send additional direct emails with a link to the baseline enrollment survey.

### Online Registry

Potential participants who were not eligible at the time of initial online screening were offered the option of consenting to enroll in a wait-list registry, for the purposes of being contacted for the present study as well as future studies. To serve both the present trial and future trials, this protocol was separately approved by the principal investigator's IRB, and separate online informed consent was obtained from all participants. Regular monitoring of the data in this registry allowed project staff to identify persons who, depending on the reasons they were deemed ineligible at the time of initial screening, were likely to now be eligible. These instances include individuals who were 17 years of age at the time, or who were not ready to quit smoking within a three-month time frame. Such registry participants were recontacted periodically and offered new screening for the WATI trial. Other reasons for student ineligibility into the WATI study, but valid for potential inclusion in this broader registry for potential research participants, were that individuals were not currently smokers, smoked too infrequently, or were not community college students.

### Enrollment Completion Reminders

To complete enrollment, eligible individuals had to register with the intervention website and then log into the website at least one time within 72 hours of registration. These two vendor requirements became barriers to enrollment. The study's research team used phone calls and emails to remind potential enrollees to complete their enrollment by registering and logging in.

### Contacting Community Colleges

Contacts were attempted with numerous administrators at numerous community colleges around the country. A targeted strategy was used to maximize efficiency. First, an online search was conducted, focusing on community colleges located in states with a high prevalence of smoking and those with tobacco and/or smoke-free policies. Once a list of community colleges was generated, relevant contact information was obtained for the appropriate administrators (eg, Dean of Students, Vice President of Student Affairs, Administrator on the Smoking Policy Committee). When contacted, the details of the study were discussed and these contacts were followed up with appropriately to provide recruitment materials and to assist with any necessary IRB approvals.

### Re-engaging Noncompleters

A participant was fully engaged as a research participant after completing all enrollment tasks and logging into the intervention website for the first time. Dropouts were defined as persons who stopped engagement with the enrollment process prior to this initial log-in. Such persons dropped out (1) during the online consent and baseline process, or (2) at some point during the website vendor's multi-step process. Such participants were identified as noncompleters, and were recontacted by email and phone and, depending on when the drop out occurred (did not complete baseline, did not initially register with vendor, did not receive or retrieve email from vendor with log-in instructions, did not complete log-in with correct log-in credentials, or did not have correct log-in credentials), project staff would re-engage the participant to again initiate enrollment.

Each of the above strategies was considered a flexible and adaptive component of an overall proactive recruitment strategy. Changes were considered responsive to formative evaluation

results (Phase 1 findings), as well as process evaluation findings (relative success in the context of expected results, such as how well a recruitment channel is working). This adaptableness was purposefully built into the 5-year study design to accommodate the need to improve or refine recruitment strategies based on observed barriers and recruitment rates. Specifically, an initial small number of recruitment sites (four community colleges) allowed the project team to more intensively assess effective strategies and refine procedures. Early feedback from these four campuses that yielded poor recruitment led to a relaxation of participant inclusion criteria: from 10 cigarettes per day in the first few months of the study, to the inclusion of intermittent smokers. By carefully monitoring recruitment rates, two other key changes to methods were made to reach recruitment goals: (1) establishing a longer recruitment timeline (a full year was needed to reach the target sample size), and (2) expanding the targeted geographic regions to ensure adequate reach within the target population. The study expanded from 16 targeted community colleges to all community colleges in the State of New York, and then to all community colleges in the United States where the state quitline and quitsite were not managed by the study's intervention vendor (resulting in 27 eligible states).

## Results

### Phase 1: Qualitative Research

Cohen κ was run to determine if there was agreement between the two independent raters on whether 138 individual comments from FGs and KIIs were identified as *electronic recruitment* channels (eg, mass emails, website banner ads, LMS/courseware, QR codes, electronic bulletin boards), *passive recruitment* channels (eg, flyers, posters, table-top displays); or *personal recruitment* channels (eg, word of mouth, referral to the study). There was strong agreement between the two raters' judgments across all three categories: electronic recruitment, κ=.734 (95% CI 0.616-0.852, *P*<.001); passive recruitment, κ=.944 (95% CI 0.882-1.000, *P*<.001); and personal recruitment, κ=.708 (95% CI 0.532-0.885, *P*<.001).

No response differences or inconsistences were observed by interviewers or coders based on campus location (rural, urban, and suburban). As can be seen in Multimedia Appendix 7, illustrative quotes capture the nature of perceptions in each of the three overall domains (electronic, passive, and personal), and some key specific recruitment channels, particularly the use of global (mass or blanket) emails to students, the use of LMS, websites, and the more traditional channels of flyers, tabling, and personal referrals. Interestingly, some administrators' skepticism in students' regular use of campus mail (which contrasts with students' endorsements of this channel) helps to provide context for subsequent administrative barriers to allow for mass emails, vis-à-vis the relative success in recruitment of students (see below).

### Phase 2: Randomized Trial

#### Channel Reach

Placement of hard-copy materials (eg, flyers, posters, table-top tent cards) ranged greatly between campuses, from as few as one initiative with only one strategy at the beginning of one semester to high levels of engaged placement every semester across four consecutive semesters or more. Similarly, digital strategies ranged from as few as one website placement or one mass email to high levels of engaged recruitment efforts, including sustained placement of website and LMSs and mass emails multiple times per semester across four consecutive semesters or more. Precise numbers of exposures were only available from those campuses with supportive champions, while overall exposures to channels were primarily assessed by self-report from campus contacts and observable increases in recruitment activity, as measured by the various REDCap databases, consents, and enrollments.

Students responded from a total of 82 community colleges; 38 from the State of New York, and 44 from additional states when recruitment was expanded nation-wide, including Alabama, Arizona, California, Illinois, Indiana, Kentucky, Maine, Michigan, Minnesota, Nevada, New Jersey, Pennsylvania, South Carolina, Tennessee, Washington, and West Virginia. Across all study recruitment channels, a total of 10,914 potential participants were initially reached. This initial *reach* is defined by the total number of independent first-time communications with the study (emails and phone calls to the study coordinator, or completion of the online screener). These communications were facilitated by the study's recruitment channels, which directed subjects to one or more of these contact methods (email address, phone number, link to online screener). Of these, 2696 individuals (2696/10,914, 24.70%) completed the online consent process, and 1452 (1452/10,914, 13.30% of those reached; and 1452/2696, 53.86% of those consented) were successfully enrolled to the WATI study. Measures of the success of the recruitment channels were defined as percentage of those reached who qualified and consented to the study (2696/10914, 24.70%) and, from these, the percentage who completed all steps for full enrollment (1452/2696, 53.86%).

As described earlier, channel efficiency was defined as the percentage of those reached who ultimately enrolled for each channel. Individual channel reach and efficiency are reported including all channel exposures, as self-reported by participants (Table 1) and including only the single most influential channel per self-report (Table 2). Specifically, participants were asked two survey questions, each with drop-down choices of all recruitment channels. The first question, in which participants could select *all that apply* read, "How did you find out about this research study?" The second question read, "Of these, which one was most effective in getting YOU to join?"

**Table 1.** Channel reach (multiple channels reported).

| Channel | Initially Reached (n=10,914) | Completed Consent (n=2696) | Enrolled and Randomized (n=1452) | % Reached Who Then Consented | Channel Efficiency (%) | % of Total Enrollees |
|---|---|---|---|---|---|---|
| Email | 6139 | 1927 | 973 | 31.39 | 15.85 | 67.01 |
| Courseware message (Blackboard, Angel, Genesis, etc) | 769 | 309 | 176 | 40.18 | 22.89 | 12.12 |
| Faculty or staff member | 355 | 157 | 100 | 44.23 | 28.17 | 6.89 |
| Poster with tear-offs | 252 | 125 | 84 | 49.60 | 33.33 | 5.79 |
| Website | 399 | 128 | 74 | 32.08 | 18.55 | 5.10 |
| Electronic bulletin board | 258 | 92 | 57 | 35.66 | 22.09 | 3.93 |
| Friend/fellow student | 187 | 72 | 43 | 38.50 | 22.99 | 2.96 |
| Poster with QR code | 98 | 55 | 41 | 56.12 | 41.84 | 2.82 |
| Banner ad | 219 | 68 | 36 | 31.05 | 16.44 | 2.48 |
| Table-top advertisement (eg, flyer in napkin holder or in student services office) | 100 | 44 | 31 | 44.00 | 31.00 | 2.13 |
| Table or booth on campus with project staff | 85 | 38 | 28 | 44.70 | 32.94 | 1.93 |
| Health or Wellness Fair | 83 | 36 | 27 | 43.37 | 32.53 | 1.86 |
| Social media (eg, Facebook, Twitter, etc) | 169 | 48 | 26 | 28.40 | 15.38 | 1.79 |
| Student club meeting | 55 | 26 | 18 | 47.27 | 32.73 | 1.24 |
| Newspaper advertisement | 45 | 19 | 12 | 42.22 | 26.67 | 0.83 |
| Other | 76 | 23 | 12 | 30.26 | 15.79 | 0.83 |
| Participating friend/family | 39 | 14 | 9 | 35.90 | 23.08 | 0.62 |
| Campus radio advertisement | 39 | 9 | 4 | 23.08 | 10.26 | 0.28 |

Of those who did not report a most effective channel (at the *reach* level), 2961 left both survey items (channel reach and channel efficiency) blank. An additional 31 participants selected multiple channels for recruitment but did not identify one channel as most effective.

### Channel Efficiency

The top eight channels (allowing for self-report of multiple channel exposures) included email (reported by 67.01% of the enrolled sample, 973/1452), followed distantly by courseware (LMSs; reported by 176/1452, 12.12%), faculty/staff referrals (100/1452, 6.89%), posters with tear-offs (84/1452, 5.79%), websites (74/1452, 5.10%), electronic bulletin boards (57/1452, 3.93%), friends (43/1452, 2.96%), and QR codes (41/1452, 2.82%).

A similar but different profile is observed when assessing only the self-reported *most influential* recruitment channel. In this case, the top eight channels (1292/1452, accounting for 88.98% of randomized enrolled participants) again showed email to be cited most often (with 60.54% of the sample reporting this to be the most influential, 879/1452), and again this was followed (with a substantial drop off in percentage of enrolled participant endorsement) by courseware/LMS (123/1452, 8.47%), websites

(67/1452, 4.61%), faculty/staff referrals (53/1452, 3.65%), posters with tear-offs (54/1452, 3.72%), friends/family (43/1452, 2.96%), electronic bulletin boards (39/1452, 2.69%), and friends/fellow students (34/1452, 2.34%).

## Discussion

Findings from the qualitative phase of the study provided an examination of attitudes, perceived barriers, and perceived facilitators to the recruitment of community college students into an online randomized controlled trial. Common themes indicated support for the proposed electronic and online strategies, and little enthusiasm for traditional hard-copy materials such as flyers and posters. Findings support the supposition that research study recruitment at community colleges could benefit from maximizing available eHealth technology strategies [38] and strategies that include direct mass emails and links on websites and LMSs. By using these existing resources and infrastructure, community colleges could further increase recruitment opportunities within the context of community college students' ability to privately and conveniently access interactive information from their own homes or mobile devices [24].

**Table 2.** Channel efficiency (most influential channel reported).

| | Initially Reached (n=10,914) | Completed Consent (n=2696) | Enrolled and Randomized (n=1452) | % Reached Who Then Consented | Channel Efficiency (%) | % of Total Enrollees |
|---|---|---|---|---|---|---|
| Email | 5531 | 1721 | 879 | 31.11 | 15.89 | 60.54 |
| Courseware message (Blackboard, Angel, Genesis, etc) | 570 | 237 | 123 | 41.57 | 21.58 | 8.47 |
| Website | 333 | 118 | 67 | 35.43 | 20.12 | 4.61 |
| Faculty or staff member | 177 | 83 | 53 | 46.89 | 29.94 | 3.65 |
| Poster with tear-offs | 146 | 77 | 54 | 52.74 | 36.99 | 3.72 |
| Participating friend/family | 214 | 80 | 43 | 37.38 | 20.09 | 2.96 |
| Electronic bulletin board | 173 | 60 | 39 | 34.68 | 22.54 | 2.69 |
| Friend/fellow student | 157 | 59 | 34 | 37.57 | 21.66 | 2.34 |
| Other | 253 | 76 | 34 | 30.04 | 13.44 | 2.34 |
| Table or booth on campus with project staff | 54 | 31 | 25 | 57.41 | 46.30 | 1.72 |
| Social media (eg, Facebook, Twitter, etc) | 139 | 39 | 21 | 28.06 | 15.11 | 1.45 |
| Poster with QR code | 36 | 23 | 18 | 63.89 | 50.00 | 1.24 |
| Unreported | 2954 | 29 | 18 | 0.98 | 0.61 | 1.24 |
| Health or Wellness Fair | 73 | 23 | 17 | 31.51 | 23.29 | 1.17 |
| Student club meeting | 19 | 12 | 10 | 63.16 | 52.63 | 0.69 |
| Table-top advertisement (eg, flyer in napkin holder or in student services office) | 28 | 16 | 9 | 57.14 | 32.14 | 0.62 |
| Campus newspaper advertisement | 28 | 9 | 5 | 32.14 | 17.86 | 0.34 |
| Campus radio advertisement | 10 | 3 | 3 | 30.00 | 30.00 | 0.21 |

Findings from the quantitative phase of the study were consistent with these themes. Results indicated that one primary channel in particular was responsible for recruiting approximately two-thirds of the final enrolled sample of 1,452 subjects: mass emails. A number of secondary channels were also influential, including the online strategies using colleges' public websites and student-accessible LMS/courseware platforms. These results provide information that is useful for both ongoing process evaluation (maximizing successful channels and minimizing those with little yield) and outcome evaluation of recruitment channel success (channels that were successful for the final sample of enrolled subjects). By observing fluctuations in recruitment success through analysis of the self-reported influence of various channels, it is possible to make data-driven conclusions that can then influence the management of recruitment strategies, staff and resource allocation, and even costs [27]. As technology advances with increasing interactivity (data going to and coming from individuals) such as smartphone apps and wearable hardware (eg, glasses, watches, and biomedical attachments), so too will the potential to successfully and economically reach targeted special populations for recruitment purposes, including gathering specific individualized relevant statistics for various channels. Future research should continue to examine overall reach and specificity of reach to desired target populations in a variety of institutional contexts.

## Barriers to Recruitment

A number of factors have been identified as significant barriers to successful final enrollment, including high subject demands, staff turnover, champion turnover, lack of champion commitment, and a wide variance in resources and capabilities between college settings.

The demands on the subject (time and effort) from recruitment to intervention were atypically high, consisting of several time-consuming steps that involved a total of six online *stop points* (first page descriptions, study consent, baseline questionnaire assessment, study website registration, personal email access to credentials, and finally the study website). Dropouts were observed at each of these stages. This finding could mean that the study description and the outline of demands on the subjects were enough to dissuade certain types of otherwise eligible participants who simply didn't want to *work that hard*. Conversely, the increasing participant demands and collection of inclusion criteria (consent form process, baseline questionnaire, and vendor-specific log-in procedures involving the retrieval of log-in credentials via a separate email) worked to effectively *weed out* participants who may not have truly met study inclusion criteria.

Another possibility, especially given some of the challenges of low SES populations, could be that some potential subjects had

low *digital literacy*, which is defined as the total cognitive and technical abilities needed to use digital technologies for finding, evaluating, creating, and communicating information [39]. Such a skillset requires cognitive flexibility, as digital technologies and the literacies needed to navigate them constantly evolve [40]. Digitally literacy is key to functioning and adapting at home, at work, and when seeking health care.

A significant barrier that was identified was staff turnover (among project staff and among identified champions at community colleges). From semester to semester, the inconsistency in personnel necessitated repeated explanations of study details to new champions, and starting from the beginning in terms of enlisting these individuals for high-level cooperation and follow-up.

Relatedly, there was differential cooperation within individual community colleges. Despite local IRB approvals in many campuses, and approvals from college presidents and previous decision makers, a single midlevel administrator could (and often would) independently decide that our recommended recruitment channels would not be utilized. This problem was commonly the case for mass emails. As can be seen in our results, mass emails accounted for the majority of successfully reached (and recruited) study participants, but if a campus determined that they would not allow (or not frequently allow) a mass email to the student body, then that channel was limited or closed. This issue was problematic because this determination was often based on just one individual's interpretation of their campus' *policy*, despite the presence of evidence that their college had already agreed to assist in the proposed research strategies.

The reluctance or refusal to promote study recruitment via mass emails was the most significant barrier to recruitment, especially since (1) this channel produced the most number of recruits, and (2) there was such surprisingly little success in any of the other strategies. Strategies that at least showed steady (if not substantial) ongoing recruitment success in previous smoking cessation studies (eg, tear-off flyers, posters, face-to-face interactions, tabling), were relatively ineffective in the current study. This is an interesting finding, as the target population of mostly lower SES young adults is both understudied and underserved. What researchers and interventionists think of as *tried and true* strategies with other populations may result in a similar lack of success. In addition, newer high-technology approaches (eg, electronic bulletin boards, QR codes) were fully anticipated to have a steady and predictable recruitment rate, but these too did not result in substantive recruitment success.

Inconsistent infrastructures across campuses posed challenges to a standardized recruitment process. One campus might have mass email capabilities in an information technology department, while at another campus this might be housed in the office of the Dean or Vice President of Student Affairs, within a Health and Wellness Center, or even under the direct control of the office of the President. As discussed above, even with appropriate approvals *higher up*, a single person in charge of the mass email domain often decided whether or not to cooperate with recruitment requests. Staff turnover also made the sustainability of high-level cooperation challenging,

especially from one semester to the next, when communication frequency dropped off.

## Facilitators

An important facilitator was the *adaptive design* planned flexibility [41] built into the 5-year study design to accommodate the need to improve recruitment strategies based on observed barriers and recruitment rates. As described earlier, this flexibility included refining study procedures such as the inclusion criteria, the number of targeted recruitment sites, and the length of the recruitment period.

As the data show, and as discussed above, the use of mass emails (which included the cooperation of key college campus decision-makers) was the greatest facilitator of successful recruitment. Although relatively low in yield (estimated anecdotally in the present study to typically reflect approximately 1% response from the entire student body receiving emails), the effect was predictable. A mass email to a large campus could yield up to 60 participants engaging with the study's online process. Although low, this predictability allowed the investigators to maximize efforts towards encouraging this channel at every cooperating campus.

## Limitations

The Phase 1 qualitative work was conducted with only four campuses, all of which were in a single geographical area in Western New York. In Phase 2, community colleges (initially in Western New York, and eventually in multiple states) varied in their level of commitment to, and resources provided for, recruitment efforts. This issue resulted in wide variability in the types (and frequency) of channels used across campuses. Future research should examine standardized recruitment protocols with community colleges that are equally committed.

The lengthy subject demand process contributes to less generalization of study findings, but arguably may conversely contribute to the generalizability of findings in terms of (1) exclusion of *fake* study participants (eg, those only looking to earn the incentives), and (2) the *real-life* experience of registration and log-in credential retrieval in many popular Web-assisted tobacco interventions (and many other online experiences involving registration and log-in credentials). It is also noted that variances in *health literacy* or *computer literacy* may have accounted for differential success with online versus offline recruitment channels.

Finally, the inclusion criteria included a self-reported intention of quitting smoking within the next three months, to capture those who were in contemplation, preparation, and action phases of the Transtheoretical Model of Behavior change. Future studies are needed to assess recruitment and retention efforts for community college students who smoke and who are still in the precontemplation, maintenance, and relapse/recycle phases.

## Conclusion

This study explored details of the process and success of a variety of recruitment channels for study enrollment in a Web-assisted tobacco intervention study. Thoughtful planning and maximum flexibility are often needed to successfully meet projected study sample sizes. Analysis of relative channel

efficiency across a wide variety of channels indicated a strong effect for digital recruitment promotion, consistent with the strengths of eHealth technology. One primary channel (mass emails) and a small number of secondary channels (including websites and LMSs) accounted for most of the recruitment success. Future and ongoing research is needed with such eHealth technology strategies, emerging strategies, and other electronic channels not typically leveraged by researchers (eg, text messaging, Instagram, Facebook, LinkedIn) to further maximize the yield from study recruitment efforts.

## Conflicts of Interest

None declared.

## Multimedia Appendix 1

Email template.

[PNG File, 24KB - resprot_v6i5e79_app1.png ]

## Multimedia Appendix 2

Facebook.

[PNG File, 5KB - resprot_v6i5e79_app2.png ]

## Multimedia Appendix 3

Electronic bulletin board.

[PNG File, 296KB - resprot_v6i5e79_app3.png ]

## Multimedia Appendix 4

Flyer.

[PNG File, 137KB - resprot_v6i5e79_app4.png ]

## Multimedia Appendix 5

Key informant interview guide.

[PDF File (Adobe PDF File), 24KB - resprot_v6i5e79_app5.pdf ]

## Multimedia Appendix 6

Focus group guide.

[PDF File (Adobe PDF File), 21KB - resprot_v6i5e79_app6.pdf ]

## Multimedia Appendix 7

Recruitment domains, channels, and sample quotes.

[PDF File (Adobe PDF File), 33KB - resprot_v6i5e79_app7.pdf ]

## Multimedia Appendix 8

CONSORT-EHEALTH v1-6.

[PDF File (Adobe PDF File), 988KB - resprot_v6i5e79_app8.pdf ]

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## Abbreviations

**FG:** focus group
**IRB:** institutional review board
**KII:** key informant interview
**LMS:** Learning Management Systems
**SES:** socioeconomic status

XSL•FO
RenderX

**QR:** Quick Response
**REDCap:** Research Electronic Data Capture
**WATI:** Web-Assisted Tobacco Intervention