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Contents

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Protocol

A Digital Health App to Assess Decisional Capacity to Provide Informed Consent: Protocol for a Randomized Controlled Trial

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Abstract

Background: Any study with human subjects must have a robust consent process to ensure that participants understand the study and can decide whether they want to be involved. Investigators must determine whether a potential study participant is able to make an informed decision and what modifications or supports are needed to maximize participation in decision making. A variety of approaches have been used to modify consent forms and the consent process to increase the research participants' decisional capacity. This protocol describes a randomized controlled trial (RCT) of a digital health app to support decision making among individuals contemplating providing consent to participate in a clinical trial.

Objective: The objective of this RCT will be to determine if the use of a tablet-based app facilitates greater participation in and satisfaction with the consent process compared with standard practice and identify which individual factors are associated with better response to the decision aid. We hypothesize that the tablet-based version of the consent process will promote more informed decision making, including decisions that are more consistent with individual preferences and values expressed during qualitative data collection.

Methods: A two-arm RCT will be conducted in a sample of approximately 100 individuals with fragile X syndrome in their homes across the United States.

Results: Data analysis will be completed by late 2018.

Conclusions: By developing and testing a novel consent decision aid, we will have a better understanding of whether and how technological support can optimize the fit between the decisional capacity and the decisional process.

Trial Registration: ClinicalTrials.gov NCT02465931; https://clinicaltrials.gov/ct2/show/NCT02465931 (Archived by WebCite at http://www.webcitation.org/72Q3xJQAw)

International Registered Report Identifier (IRRID): PRR1-10.2196/10360

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KEYWORDS

clinical trial; decision support techniques; digital health; ethics; informed consent; fragile X syndrome

Introduction

Background

Any study with human subjects must have a robust consent process to ensure that participants understand the study and can decide whether they want to be involved. The Belmont Report [1] identified the following 3 ethical principles that should guide human subjects research: respect for persons, beneficence, and justice. However, investigators who study individuals with intellectual disability (ID) face a special challenge; they must determine whether a potential study participant is able to make an informed decision and what modifications or supports are needed to maximize participation in decision making. Fulfilling this obligation responsibly requires an understanding of the necessary components of consent, knowledge of common features of the cause of the person's ID, and evidence-based adaptations to maximize informed decision making. Ultimately, ID researchers must acknowledge the delicate balance between respect for autonomy and the responsibility to protect vulnerable individuals [2]. Unfortunately, there is limited research on the decisional capacity of people with ID and the supports they need to consent to participate in research studies. This study will expand this knowledge base through an assessment of a digital health intervention for adolescents and adults with fragile X syndrome (FXS). FXS is an excellent prototype because of the wide range of cognitive abilities in affected individuals and the recent increase in clinical trials for new medications targeted at the core biology of FXS.

Fragile X Syndrome

FXS is the most common known inherited cause of ID. Males typically have moderate ID, although impairment can range from mild to severe; females typically have mild ID, ranging from normal cognition to moderate impairment [3-5]. FXS is highly associated with a range of cooccurring conditions, the most common of which are attention problems and anxiety [6]. Longitudinal studies of FXS have shown deficits in areas such as sustained attention, response inhibition, working memory, and other executive functions likely to be associated with the capacity to consent [7-10]. Reading is challenging for males [11]. A large national survey found that although 44% of adult males with FXS could read basic picture books or simple stories, only 19% could read books that contain new words or concepts [12]. In contrast, 91% of adult females with FXS could read basic picture books or simple stories, and 76% could read books that contain new words or concepts. Further complicating these findings is the high coassociation between FXS and autism and consistent findings that individuals with both FXS and autism exhibit more severe deficits [9,11].

Recent advances in understanding the molecular basis of FXS have led to a new generation of targeted treatments [13,14], and clinical trials are under way using a variety of novel compounds. Owing to the possibility of side effects and the potential for significant changes in behavior or ability as a result of taking these medications, the importance of obtaining meaningful consent, not only from parents but also from individuals with FXS, has been elevated to a new level. Researchers and Institutional Review Board (IRB) members need data to guide decisions about involving individuals with FXS in the consent process. Unfortunately, little is known about the extent to which individuals with FXS can be or are involved in decisions about research participation.

Decisional Capacity and Informed Consent

A variety of approaches have been used to modify consent forms and the consent process to increase the research participants' decisional capacity. Early research focused on simplifying language (eg, shorter sentences and less technical vocabulary) and modifying the presentation (eg, bulleted or bolded text) [15-17]. Multimedia formats, such as slides, videos, or touchscreen computer programs, have also been tested [18-20]. Other approaches have sought to include a third party, such as a nurse or counselor, in the consent process [21,22]. Another alternative has focused on testing the participant on information contained in the consent form and providing feedback on incorrect answers [23,24].

However, most of these studies have not focused on individuals with ID. In a recent review, Goldsmith et al [25] summarized 22 studies of interventions designed specifically for individuals with ID. A primary finding was that life experiences—residence, history of decision making, and previous health experiences—contributed to the ability to provide consent [26-29]. Another key finding is that the method of presentation is important, especially for individuals with poor communication skills or lower memory ability [19,30]. Many studies have shown that general intelligence, verbal ability, and memory are correlated with the ability to consent [26-31].

Despite these conclusions, we still do not have a validated digital health app to enhance the decisional capacity in individuals with ID, and there is no consensus on the best approach to use [32]. A variety of techniques may be needed depending on the skill level of participants [33]. For example, although individuals with FXS have some weaknesses in visual-spatial processing [34], they have a relative strength in visual contextual memory [35], suggesting visual cues may help increase understanding. Recent papers suggested that the use of new technologies, primarily apps designed for tablets such as the iPad, have great potential for enhancing communication with people with ID [36,37]. Tablets are designed to be engaging and relatively intuitive to use. Our belief is that an appropriately designed tablet-based informed consent app has great potential for enhancing the decisional capacity.

This study will be the first systematic investigation of the decisional capacity in FXS in which we will develop and evaluate a decision aid (DA) with the intent of enhancing participation in the informed consent processes. The content of the digital informed consent app is based on an existing gold standard measure of the decisional capacity, the MacArthur Competence Assessment Tool for Clinical Research (MacCAT-CR) [38]. The MacCAT-CR is a structured clinical interview used to assess the capacity to consent in individuals with known or suspected deficits in cognitive ability. The interview covers the following 4 areas of the capacity to consent: understanding of the information presented about the nature of the research project; appreciation of the effects of research participation (or nonparticipation) on the potential participant's

own situation; reasoning about the decision to participate (or not); and expressing a choice about participation. The MacCAT-CR has been used in research settings with individuals with Alzheimer's disease or schizophrenia [39,40]. Although the MacCAT-CR has been adapted for use in individuals with general ID [41], it has never been used to examine the capacity in a specific subpopulation, such as FXS, or been modified for use in a digital health app. Below we briefly describe the development of a tablet-based app.

Description of the Digital Health App

Design and development of the intervention material and the principles that informed our approach are described elsewhere [42]. The FXS DA is a tablet-optimized, responsive Web app that delivers content through 3 major components as follows: scenario-based vignettes to present key concepts on clinical trials, informed consent, and other IRB-required material; quiz items to assess the decisional capacity based on the MacCAT-CR; and a tile sorting activity to provide a values clarification exercise at the conclusion of each session (Figures 1 and 2). Material for the DA was developed using input from a multidisciplinary committee of experienced developmental or clinical psychologists, clinicians, and communication scientists, based on data from qualitative interviews conducted with caregivers and individuals with FXS. Technical activities were informed by an agile, user-centered design approach, existing literature on the principles of universal design, and best practices for developing DA. The DA was implemented in Hypertext Markup Language 5 using CreateJS libraries for integration of animated multimedia, audio narration, and active tasks. The user interface and user experience were optimized for iOS tablet-based deployment and support interaction through standard touchscreen gestural controls (eg, swipe, tap, drag, and pinch).

A custom case management system enables event logging for each study participant, including case identifier, interaction specifics, and session time stamps. Built-in app analytics report events via JavaScript Object Notation packets sent over Secure Hypertext Transfer Protocol to a data management service that logs events, storing data in an encrypted relational database. Data extraction and reporting are performed by analysts using Structured Query Language queries and scripted transformations to prepare session data for the statistical analysis. FXS DA sessions lasted approximately 25 minutes and were intended to be deployed under supervised, experimental conditions in a study participant's home or clinical setting by field staff. Devices used for field deployment were configured and conditioned throughout data collection in a manner consistent with the recommendations for tablet-based digital health intervention research by Furberg et al [43]. A video demonstration of the FXS DA is available in Multimedia Appendix 1.

Figure 1. FXSDA screenshot.

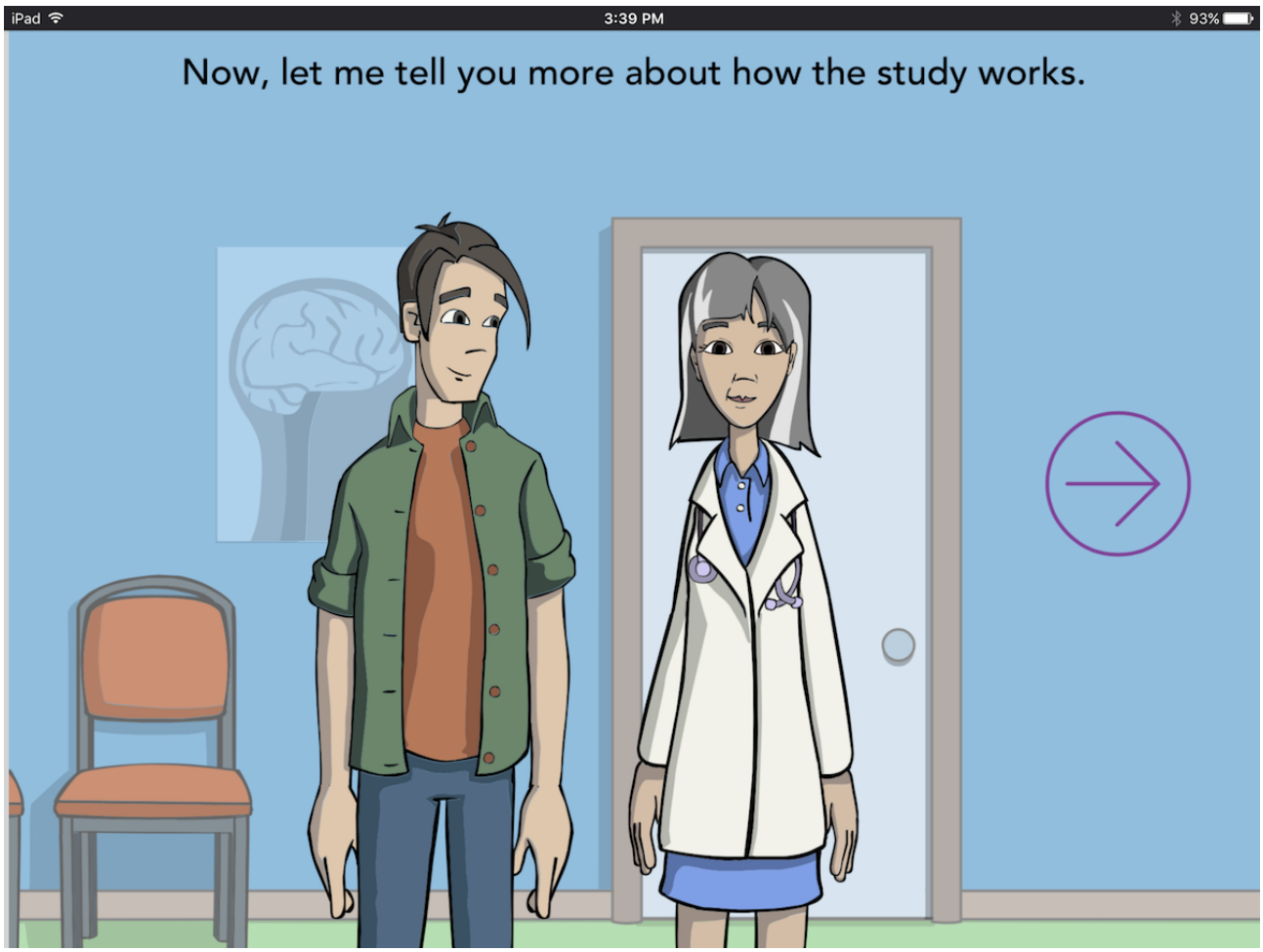
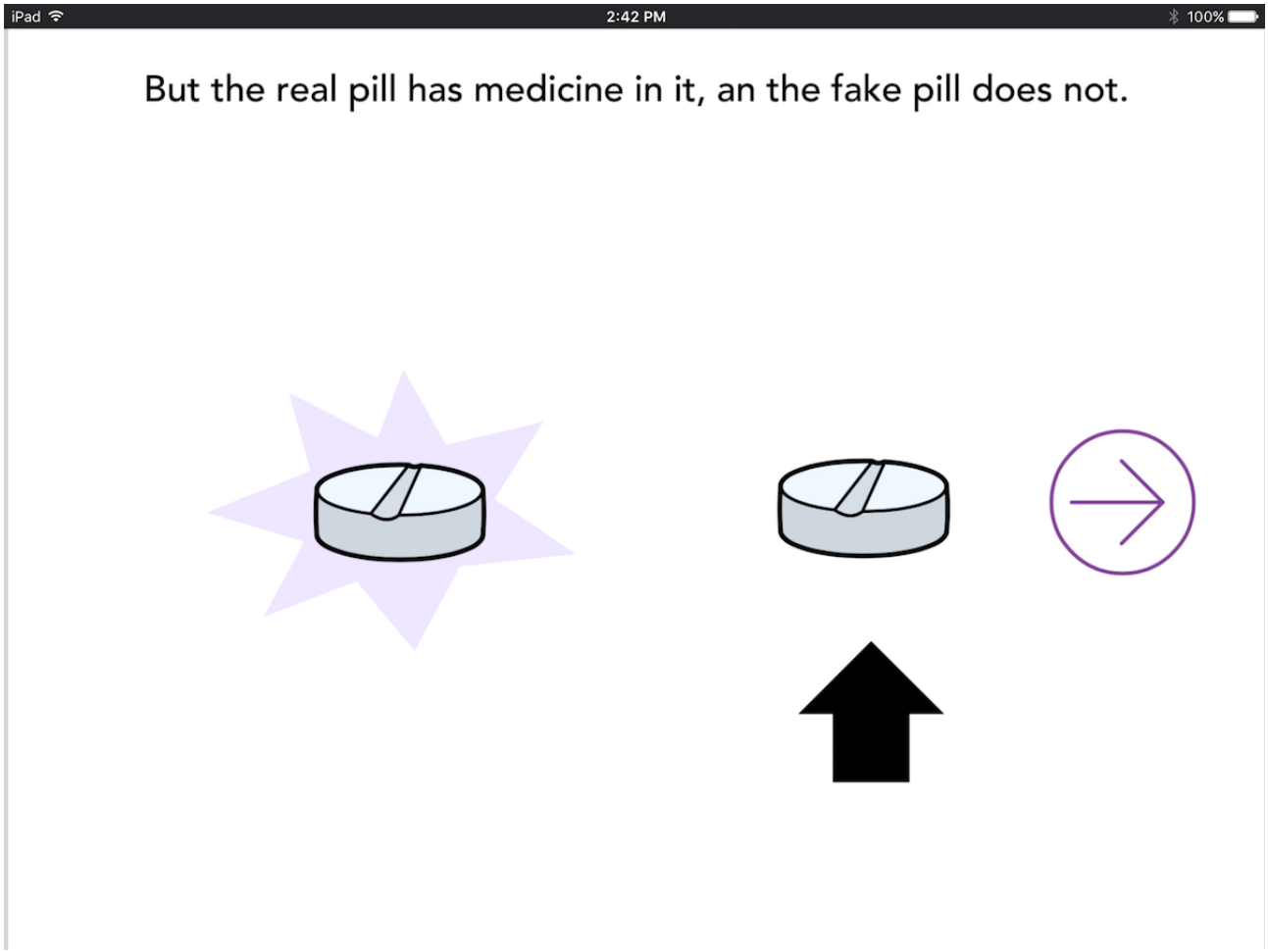


Figure 2. FXSDA screenshot.



Research Questions and Hypotheses

The primary research question was, "Does a tablet-based app facilitate greater participation in and satisfaction with the consent process compared with standard practice?" We hypothesize that the tablet-based version of the consent process will promote more informed decision making, including decisions that are more consistent with individual preferences and values expressed during qualitative data collection. The secondary research question was, "What individual factors, such as IQ, autism status, or executive function, are associated with better response to the decision aid?" We hypothesize that all individuals with FXS will benefit from the tablet-based version, but those with higher functioning levels may benefit the most. Potential advantages of a tablet-based approach to patient education include consistent content and delivery, active learning, privacy, potentially greater access than a human health educator, and potential cost-effectiveness [44]. We expect that the interactive nature of the app will foster greater involvement in the decision making, a sense of empowerment, greater self-efficacy, and more satisfaction.

Methods

Trial Design

We will use a two-arm, parallel-design, randomized control trial (RCT) with a 1:1 allocation ratio. Participants will be randomized into either the control or experimental group. As shown in Table 1, both groups will be exposed to the same informed consent content but delivered through different channels—a digital informed consent app (experimental) or paper informed consent or usual practice (control). The content of both versions of the informed consent describes the requirements for participating in a hypothetical clinical trial for a fake prescription drug for FXS. Both versions include IRB-required information (eg, study procedures, study duration, and compensation). The digital informed consent app does not meet all of the regulated technical requirements for electronic informed consent (ie, the signature component). Additional details regarding trial design and conduct can be found in the CONSORT-EHEALTH checklist (Multimedia Appendix 2).

Participants

Up to 50 pairs of adolescents or adults (aged ≥14 years) with FXS, a subset of 250 individuals who completed a battery of neurocognitive assessments (including intelligence quotient, reading abilities, autism, and anxiety comorbidities) between 2013 and 2016, will participate in this study.

Table 1. An overview of the study design, with details regarding how the variables differ across conditions.

Component	Control	Experimental
Delivery of information	• Paper informed consent form paired with verbal overview of key points	• Paper informed consent form paired with tablet-based tool which contains visual and audio components
Language	• Complex (paper) and simplified (verbal overview)	• Complex (paper) and simplified (tablet-based tool)
Exposure to information	• Paper informed consent form will be sent to participant and family before data collection visit. They will be able to review as many times as they wish before visit • During visits, simplified overview of informed consent form will be provided in person just once	• Paper informed consent form will be sent to participant and family before data collection visit. They will be able to review as many times as they wish before visit • During visit, the participant can go through the tablet-based tool up to 3 times
MacCAT questions	• All questions will be asked after the disclosure information has been presented • Questions will have the same wording as experimental condition • Procedures will mimic MacCAT or flipchart (incorrect or partial credit will be given opportunity to answer question again after disclosure information is repeated) • Multiple choice options rather than open-ended • Paper and pencil data collection	• All questions will be embedded within the vignettes or presentation of disclosure information • Use simplified wording for questions- similar to flipchart • Procedures will mimic MacCAT or flipchart (incorrect or partial credit will be given opportunity to answer question again after disclosure information is repeated) • Multiple choice options rather than open-ended. • Response data stored within tool and exported to dataset for analysis

Recruitment

In this study, the following 3 primary methods will be used for recruitment: recontacting families who have participated in prior longitudinal assessment studies conducted by the research team; recruiting through the fragile X research registry maintained by the University of North Carolina at Chapel Hill; and announcing the research on the National Fragile X Foundation website. We have been highly successful in recruiting fragile X study participants, including a large national survey of >1000 families [45] so anticipate few problems in recruiting an adequate sample.

Inclusion or Exclusion Criteria

Eligibility will be determined by a person's scores on an initial assessment, which includes a standardized IQ and autism measure. Participants will be excluded if they receive a score of ≤30 on the IQ measure; receive a score between 31 and 40 on the IQ measure and have a diagnosis of autism with severe autism symptoms as noted on a standardized autism measure; or are determined to have other behavioral challenges that would preclude their inclusion (eg, mutism and severe aggression). These exclusion criteria cutoffs were established to ensure a minimal level of comprehension and adaptive behavior for the study; IQs of ≤35 are indicative of severe ID.

Intervention

Control Group

Participants randomized to the control group will be exposed to a paper consent form that covers the same informed consent information presented in the tablet-based app and mimics informed consent forms used for real clinical trials. The complex language that is typically used in current standard practice (ie, *participation* vs *take part*) will be retained in the paper version. The control group will be designed to mimic typical informed consent procedures, that is, the verbal transmission of study information from a clinician to the individual and caregivers. To standardize this practice, we will develop a script that is verbally reviewed with control group participants, including a simplified overview of the key information in the paper consent form.

Experimental Group

Participants randomized to the experimental group will receive the paper consent form (the same form the control group participants received) and will also be exposed to the tablet-based app. Given that the digital app does not meet the requirements of electronic consent, the paper consent form will still be needed for documenting that informed consent was obtained.

Randomization

We will use a stratified, block randomization method to assign participants to the control or experimental group. Two stratification variables will be used—verbal IQ score (3 levels) and age (2 levels). Age was selected as a randomizing variable because children and adolescents under 18 are not able to provide informed consent, only assent, as their parents are their legal guardians. Verbal IQ was selected as a second variable because we had a small sample size and wanted to control for any possible effects on the outcome variables. However, we could have also chosen to account for any possible group differences based on IQ through statistical analyses. Given that enrollment for the RCT will be done on a rolling basis, a 10-block, 2-group design will be used. Thus, we will randomize 10 participants at a time into either the control or experimental group. Furthermore, we will utilize a random number generator (www.randomizer.com) to make the assignments.

Blinding

Owing to the nature of the study, participants and data collectors were not blinded to the group assignment.

Study Setting and Data Collection Procedures

Each study session will occur in the individual's home and will be videotaped to allow subsequent coding of individual engagement in the decisional process. Approximately 10 days prior to the visit, the participant or their primary caregiver will be sent the standard paper consent form for a hypothetical clinical trial. All participants, including parents and caregivers, will be informed that the clinical trial is hypothetical. Participants will be asked to review the consent form as they would any research consent form.

On the day of the visit, parents and individuals with FXS who are their own legal guardian will be asked to complete a 5- to 10-minute pretest to assess their or their child's belief and attitudes about participating in clinical trials. Pretest items included questions such as participants' possible reasons for participating in clinical trials, the likelihood of participating, and whom they think should make the decision about enrolling in a trial (full list of domains in "Study Outcomes" section below). Participants will then complete either the experimental or control group informed consent procedure. Both the control and experimental groups will be asked the modified MacCAT examination items throughout the informed consent process to assess the decisional capacity. The questions are identical for each group. After the informed consent procedure, all participants will again be asked to complete the posttest questions about their beliefs and attitudes about clinical trials.

Study Outcomes

The following measures will be collected as part of the study protocol: time spent with DA or in discussion with research assistant; perceptions about reasons to participate in trials (eg, altruism; pre- and posttest item); likelihood of enrolling in a clinical trial (pre- and posttest item); the preferred level of involvement in the decision (pre- and posttest item); self-efficacy related to decision-making ability (pre- and posttest item); level of engagement in the decision-making process (pre- and posttest item); satisfaction with the decision (posttest only); the perceived value of the educational information provided (posttest only); and session analytics, including time on page and session duration.

Participant Timeline

Pretest measures, the intervention or control condition, and posttest measures will all be conducted on the same day during an approximately 1-hour study session. The pre- and posttest measures will take approximately 15 minutes to complete, and the control and intervention condition will last approximately 30 minutes. No additional follow-up is planned.

Statistical Methods

In the analyses, we will examine the effect of the app on the decisional capacity, controlling for sociodemographic characteristics and severity of delay. We will first conduct bivariate analyses comparing the decisional capacity, decision-making preferences, and the likelihood of trial participation across the 2 study groups (tablet vs standard procedure), using chi-square tests for categorical outcomes and *t* tests for continuous outcomes. In addition, we will conduct multiple regression models to compare study outcomes by the study group after controlling for demographics and severity of developmental delay. Linear regression models will be conducted for continuous outcomes (eg, decisional capacity scores and preferences) and logistic regression models for categorical outcomes (eg, the likelihood of participating in a hypothetical trial). Within these models, we will test for interactions between study group and demographic characteristics to identify the differential impact of the intervention on particular subgroups. For example, testing an interaction between study group and severity of delay would allow us to determine whether the tablet-based intervention is more or less successful among more impaired participants.

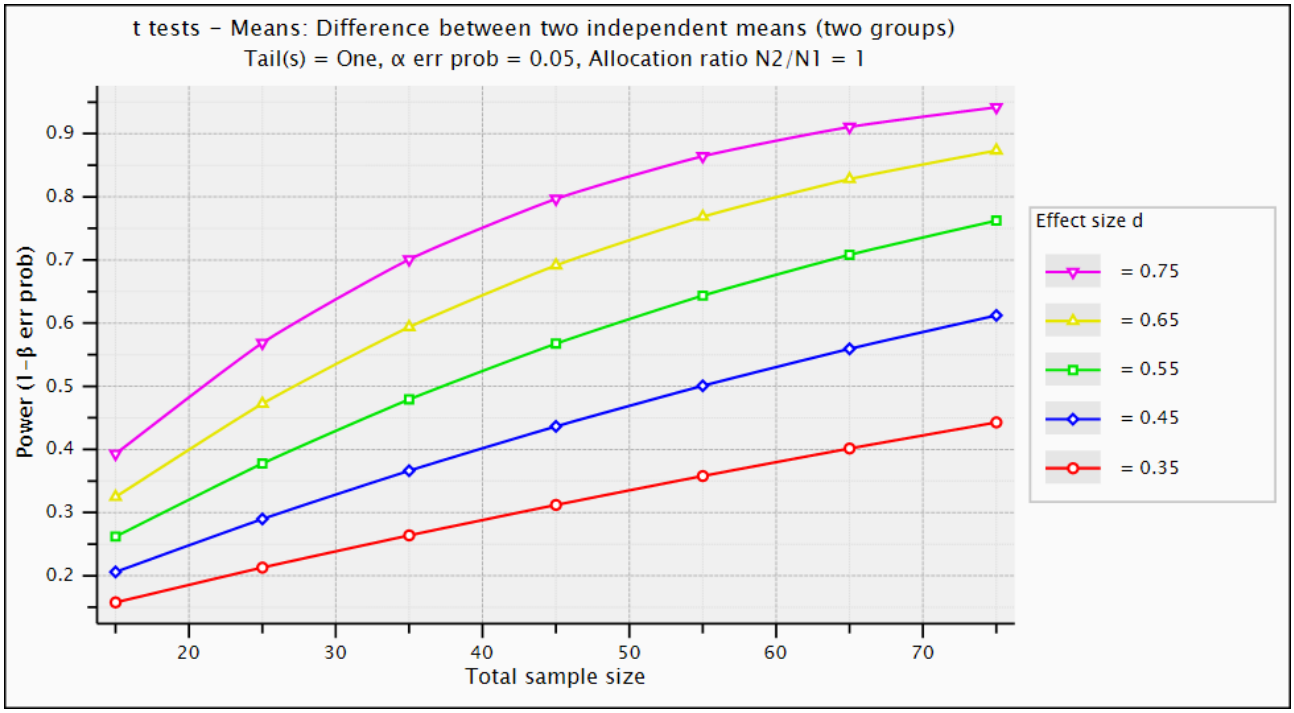
Power Analyses

We have conducted a power analysis using a between-subjects design (ie, participants are randomized to the control or experimental group) to determine the recommended sample size (Figure 3). With a sample size of 70 (35 participants per group), we will have 90% power to detect an effect size of 0.75.

Ethics and Confidentiality

This research protocol was reviewed and approved by 2 Independent Review Boards from the University of North Carolina Office of Human Research Ethics (IRB Number: 13-1128) and RTI International Office of Research Protection (0281200.276). This study has been registered with ClinicalTrials.gov (NCT02465931).

Figure 3. FXSDA screenshot.



Results

Data collection began in January 2016 and concluded in January 2017. Data analysis began in mid-2017 and will be completed by late 2018.

Discussion

Principal Findings

Discoveries about the underlying mechanisms of conditions such as FXS inevitably will lead to a new generation of targeted pharmaceuticals to be tested in clinical trials. Consenting individuals with ID to participate in clinical trials will always require an individualized approach. But in-depth knowledge about the nature and range of the decisional capacity, cognitive and experiential factors influencing the decisional capacity, and the use of various DAs can make the individualization process more efficient and effective. We chose FXS as the condition of interest for this app because recent advances in treatment potential have led to a rapid growth in clinical trials testing new medications and the extraordinary range in cognitive ability and emotional problems in FXS, both within and across genders, makes it virtually impossible to characterize the decisional capacity of the population as a group. By describing and explaining the range of the decisional capacity in individuals with FXS, we will have a better estimate of both how many and how well individuals with FXS can participate in the consent process. By developing and testing a novel consent DA, we will have a better understanding of whether and how technological support can optimize the fit between the decisional capacity and the decisional process.

Study Strengths

This protocol provides an overview of the design and implementation of a distributed, RCT to evaluate the use of a digital health app to support individual decision making for participation in clinical trials. Relatively few studies have been published on the use of digital resources to support this type of decision making given the ethical challenges of conducting such research without compromising the ethical or legal credibility and protections for human subjects.

Limitations

Despite the strength of the evaluation design and scalability, the major limitation of this study is the focus on assessing decision making to participate in a hypothetical clinical trial.

Acknowledgments

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Conflicts of Interest

None declared.

Multimedia Appendix 1

FXSDA Parent Demo

[MP4 File (MP4 Video), 71MB - resprot_v7i11e10360_app1.mp4]

Multimedia Appendix 2

CONSORT-EHEALTH checklist (V 1.6.1).

[PDF File (Adobe PDF File), 2MB - resprot_v7i11e10360_app2.pdf]

References

1. Department of Health, Education,Welfare, National Commission for the Protection of Human Subjects of BiomedicalBehavioral Research. The Belmont Report. Ethical principles and guidelines for the protection of human subjects of research. J Am Coll Dent 2014;81(3):4-13. [Medline: 25951677]
2. Freedman R. Ethical challenges in the conduct of research involving persons with mental retardation. Ment Retard 2001 Apr;39(2):130-141. [doi: 10.1352/0047-6765(2001)039<0130:ECITCO>2.0.CO;2] [Medline: 11340962]
3. Hall S, Burns DD, Lightbody AA, Reiss AL. Longitudinal changes in intellectual development in children with Fragile X syndrome. J Abnorm Child Psychol 2008 Aug;36(6):927-939 [FREE Full text] [doi: 10.1007/s10802-008-9223-y] [Medline: 18347972]
4. Loesch D, Huggins RM, Hagerman RJ. Phenotypic variation and FMRP levels in fragile X. Ment Retard Dev Disabil Res Rev 2004;10(1):31-41. [doi: 10.1002/mrdd.20006] [Medline: 14994286]
5. Raspa M, Wheeler AC, Riley C. Public Health Literature Review of Fragile X Syndrome. Pediatrics 2017 Jun;139(Suppl 3):S153-S171 [FREE Full text] [doi: 10.1542/peds.2016-1159C] [Medline: 28814537]
6. Bailey D, Raspa M, Olmsted M, Holiday DB. Co-occurring conditions associated with FMR1 gene variations: findings from a national parent survey. Am J Med Genet A 2008 Aug 15;146A(16):2060-2069. [doi: 10.1002/ajmg.a.32439] [Medline: 18570292]
7. Baker S, Hooper S, Skinner M, Hatton D, Schaaf J, Ornstein P, et al. Working memory subsystems and task complexity in young boys with Fragile X syndrome. J Intellect Disabil Res 2011 Jan;55(1):19-29 [FREE Full text] [doi: 10.1111/j.1365-2788.2010.01343.x] [Medline: 21121991]
8. Hooper S, Hatton D, Sideris J, Sullivan K, Hammer J, Schaaf J, et al. Executive functions in young males with fragile X syndrome in comparison to mental age-matched controls: baseline findings from a longitudinal study. Neuropsychology 2008 Jan;22(1):36-47. [doi: 10.1037/0894-4105.22.1.36] [Medline: 18211154]
9. Ornstein P, Schaaf JM, Hooper SR, Hatton DD, Mirrett P, Bailey DB. Memory skills of boys with fragile X syndrome. Am J Ment Retard 2008 Nov;113(6):453-465. [doi: 10.1352/2008.113:453-465] [Medline: 19127656]
10. Sullivan K, Hatton DD, Hammer J, Sideris J, Hooper S, Ornstein PA, et al. Sustained attention and response inhibition in boys with fragile X syndrome: measures of continuous performance. Am J Med Genet B Neuropsychiatr Genet 2007 Jun 05;144B(4):517-532. [doi: 10.1002/ajmg.b.30504] [Medline: 17427192]
11. Roberts J, Schaaf JM, Skinner M, Wheeler A, Hooper S, Hatton DD, et al. Academic skills of boys with fragile X syndrome: profiles and predictors. Am J Ment Retard 2005 Mar;110(2):107-120. [doi: 10.1352/0895-8017(2005)110<107:ASOBWF>2.0.CO;2] [Medline: 15762821]
12. Bailey D, Raspa M, Holiday D, Bishop E, Olmsted M. Functional skills of individuals with fragile x syndrome: a lifespan cross-sectional analysis. Am J Intellect Dev Disabil 2009 Jul;114(4):289-303. [doi: 10.1352/1944-7558-114.4.289-303] [Medline: 19642710]
13. Dölen G, Carpenter RL, Ocain TD, Bear MF. Mechanism-based approaches to treating fragile X. Pharmacol Ther 2010 Jul;127(1):78-93. [doi: 10.1016/j.pharmthera.2010.02.008] [Medline: 20303363]
14. Hagerman R, Berry-Kravis E, Kaufmann WE, Ono MY, Tartaglia N, Lachiewicz A, et al. Advances in the treatment of fragile X syndrome. Pediatrics 2009 Jan;123(1):378-390 [FREE Full text] [doi: 10.1542/peds.2008-0317] [Medline: 19117905]
15. Bjorn E, Rossel P, Holm S. Can the written information to research subjects be improved?--an empirical study. Journal of Medical Ethics 1999 Jun 01;25(3):263-267. [doi: 10.1136/jme.25.3.263]
16. Dresden G, Levitt MA. Modifying a standard industry clinical trial consent form improves patient information retention as part of the informed consent process. Acad Emerg Med 2001 Mar;8(3):246-252 [FREE Full text] [Medline: 11229946]
17. Murphy D, O'Keefe ZH, Kaufman AH. Improving comprehension and recall of information for an HIV vaccine trial among women at risk for HIV: reading level simplification and inclusion of pictures to illustrate key concepts. AIDS Educ Prev 1999 Oct;11(5):389-399. [Medline: 10555623]
18. Agre P, Campbell FA, Goldman BD, Boccia ML, Kass N, McCullough LB, et al. Improving informed consent: the medium is not the message. IRB 2003;Suppl 25(5):S11-S19. [Medline: 14870732]

19. Dunn L, Lindamer LA, Palmer BW, Golshan S, Schneiderman LJ, Jeste DV. Improving understanding of research consent in middle-aged and elderly patients with psychotic disorders. Am J Geriatr Psychiatry 2002;10(2):142-150. [Medline: 11925275]
20. Fureman I, Meyers K, McLellan AT, Metzger D, Woody G. Evaluation of a video-supplement to informed consent: injection drug users and preventive HIV vaccine efficacy trials. AIDS Educ Prev 1997 Aug;9(4):330-341. [Medline: 9376207]
21. Aaronson N, Visser-Pol E, Leenhouts GH, Muller MJ, van DSAC, van DFS, et al. Telephone-based nursing intervention improves the effectiveness of the informed consent process in cancer clinical trials. J Clin Oncol 1996 Mar;14(3):984-996. [doi: 10.1200/JCO.1996.14.3.984] [Medline: 8622050]
22. Fitzgerald D, Marotte C, Verdier RI, Johnson WD, Pape JW. Comprehension during informed consent in a less-developed country. Lancet 2002 Oct 26;360(9342):1301-1302. [doi: 10.1016/S0140-6736(02)11338-9] [Medline: 12414207]
23. Stiles P, Poythress NG, Hall A, Falkenbach D, Williams R. Improving understanding of research consent disclosures among persons with mental illness. Psychiatr Serv 2001 Jun;52(6):780-785. [doi: 10.1176/appi.ps.52.6.780] [Medline: 11376225]
24. Wirshing D, Wirshing WC, Marder SR, Liberman RP, Mintz J. Informed consent: assessment of comprehension. Am J Psychiatry 1998 Nov;155(11):1508-1511. [doi: 10.1176/ajp.155.11.1508] [Medline: 9812110]
25. Goldsmith L, Skirton H, Webb C. Informed consent to healthcare interventions in people with learning disabilities--an integrative review. J Adv Nurs 2008 Dec;64(6):549-563. [doi: 10.1111/j.1365-2648.2008.04829.x] [Medline: 19120568]
26. Arscott K, Dagnan D, Kroese BS. Assessing the ability of people with a learning disability to give informed consent to treatment. Psychol Med 1999 Nov;29(6):1367-1375. [Medline: 10616942]
27. Cea CD, Fisher CB. Health care decision-making by adults with mental retardation. Ment Retard 2003 Apr;41(2):78-87. [doi: 10.1352/0047-6765(2003)041<0078:HCDMBA>2.0.CO;2] [Medline: 12622524]
28. Dye L, Hare DJ, Hendy S. Capacity of People with Intellectual Disabilities to Consent to Take Part in a Research Study. J Appl Res Int Dis 2007 Mar;20(2):168-174. [doi: 10.1111/j.1468-3148.2006.00310.x]
29. Fisher C, Cea CD, Davidson PW, Fried AL. Capacity of persons with mental retardation to consent to participate in randomized clinical trials. Am J Psychiatry 2006 Oct;163(10):1813-1820. [doi: 10.1176/ajp.2006.163.10.1813] [Medline: 17012694]
30. Wong J, Clare CH, Holland AJ, Watson PC, Gunn M. The capacity of people with a 'mental disability' to make a health care decision. Psychol Med 2000 Mar;30(2):295-306. [Medline: 10824650]
31. Morris C, Niederbuhl JM, Mahr JM. Determining the capability of individuals with mental retardation to give informed consent. Am J Ment Retard 1993 Sep;98(2):263-272. [Medline: 8398085]
32. Cleaver S, Ouellette-Kuntz H, Sakar A. Participation in intellectual disability research: a review of 20 years of studies. J Intellect Disabil Res 2010 Mar;54(3):187-193. [doi: 10.1111/j.1365-2788.2010.01256.x] [Medline: 20146739]
33. Swaine J, Parish SL, Luken K, Atkins L. Recruitment and consent of women with intellectual disabilities in a randomised control trial of a health promotion intervention. J Intellect Disabil Res 2011 May;55(5):474-483. [doi: 10.1111/j.1365-2788.2011.01399.x] [Medline: 21385259]
34. Mazzocco M. Math learning disability and math LD subtypes: evidence from studies of Turner syndrome, fragile X syndrome, and neurofibromatosis type 1. J Learn Disabil 2001;34(6):520-533. [doi: 10.1177/002221940103400605] [Medline: 15503567]
35. Cornish K, Munir F, Cross G. Differential impact of the FMR-1 full mutation on memory and attention functioning : a neuropsychological perspective. J Cogn Neurosci 2001 Jan 01;13(1):144-150. [Medline: 11224914]
36. Palmer SB, Wehmeyer ML, Davies DK, Stock SE. Family members' reports of the technology use of family members with intellectual and developmental disabilities. J Intellect Disabil Res 2012 Apr;56(4):402-414. [doi: 10.1111/j.1365-2788.2011.01489.x] [Medline: 21988242]
37. Hirsch IB, Martinez J, Dorsey ER, Finken G, Fleming A, Gropp C, et al. Incorporating Site-less Clinical Trials Into Drug Development: A Framework for Action. Clin Ther 2017 May;39(5):1064-1076 [FREE Full text] [doi: 10.1016/j.clinthera.2017.03.018] [Medline: 28413148]
38. Appelbaum PS, Grisso T. MacArthur competence assessment tool for clinical research. Sarasota, FL: Professional Resource Press; 2001.
39. Carpenter W, Gold JM, Lahti AC, Queern CA, Conley RR, Bartko JJ, et al. Decisional capacity for informed consent in schizophrenia research. Arch Gen Psychiatry 2000 Jun;57(6):533-538. [Medline: 10839330]
40. Karlawish JHT, Casarett DJ, James BD, Xie SX, Kim SYH. The ability of persons with Alzheimer disease (AD) to make a decision about taking an AD treatment. Neurology 2005 May 10;64(9):1514-1519. [doi: 10.1212/01.WNL.0000160000.01742.9D] [Medline: 15883310]
41. Fisher CB, Cea CD, Davidson PW, Fried AL. Capacity of persons with mental retardation to consent to participate in randomized clinical trials. Am J Psychiatry 2006 Oct;163(10):1813-1820. [doi: 10.1176/ajp.2006.163.10.1813] [Medline: 17012694]
42. Furberg RD, Ortiz AM, Moultrie RR, Raspa M, Wheeler AC, McCormack LA, et al. A Digital Decision Support Tool to Enhance Decisional Capacity for Clinical Trial Consent: Design and Development. JMIR Res Protoc 2018 Jun 06;7(6):e10525 [FREE Full text] [doi: 10.2196/10525] [Medline: 29875084]

43. Furberg RD, Ortiz AM, Zulkiewicz BA, Hudson JP, Taylor OM, Lewis MA. Supporting Tablet Configuration, Tracking, and Infection Control Practices in Digital Health Interventions: Study Protocol. JMIR Res Protoc 2016 Jun 27;5(2):e136 [FREE Full text] [doi: 10.2196/resprot.5400] [Medline: 27350013]
44. Jimison HB, Sher P. Advances in presenting health information to patients. In: Chapman GB, Sonnenberg FA, editors. Decision making in health care: Theory, psychology, and application. Cambridge: Cambridge University Press; 2000:334-361.
45. Bailey JD, Raspa M, Holiday D, Bishop E, Olmsted M. Functional skills of individuals with fragile x syndrome: a lifespan cross-sectional analysis. Am J Intellect Dev Disabil 2009 Jul;114(4):289-303. [doi: 10.1352/1944-7558-114.4.289-303] [Medline: 19642710]

Abbreviations

DA: Decision Aid
FXS: fragile X syndrome
ID: intellectual disability
IRB: Institutional Review Board
MacCAT: MacArthur Competence Assessment Tool for Clinical Research
RCT: randomized controlled trial

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Protocol

Monitoring the Control of Sexually Transmissible Infections and Blood-Borne Viruses: Protocol for the Australian Collaboration for Coordinated Enhanced Sentinel Surveillance (ACCESS)

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Abstract

Background: New biomedical prevention interventions make the control or elimination of some blood-borne viruses (BBVs) and sexually transmissible infections (STIs) increasingly feasible. In response, the World Health Organization and governments around the world have established elimination targets and associated timelines. To monitor progress toward such targets, enhanced systems of data collection are required. This paper describes the Australian Collaboration for Coordinated Enhanced Sentinel Surveillance (ACCESS).

Objective: This study aims to establish a national surveillance network designed to monitor public health outcomes and evaluate the impact of strategies aimed at controlling BBVs and STIs.

Methods: ACCESS is a sentinel surveillance system comprising health services (sexual health clinics, general practice clinics, drug and alcohol services, community-led testing services, and hospital outpatient clinics) and pathology laboratories in each of Australia's 8 states and territories. Scoping was undertaken in each jurisdiction to identify sites that provide a significant volume of testing or management of BBVs or STIs or to see populations with particular risks for these infections ("priority populations"). Nationally, we identified 115 health services and 24 pathology laboratories as relevant to BBVs or STIs; purposive sampling was undertaken. As of March 2018, we had recruited 92.0% (104/113) of health services and 71% (17/24) of laboratories among those identified as relevant to ACCESS. ACCESS is based on the regular and automated extraction of deidentified patient data using specialized software called GRHANITE, which creates an anonymous unique identifier from patient details. This identifier allows anonymous linkage between and within participating sites, creating a national cohort to facilitate epidemiological monitoring and the evaluation of clinical and public health interventions.

Results: Between 2009 and 2017, 1,171,658 individual patients attended a health service participating in ACCESS network comprising 7,992,241 consultations. Regarding those with unique BBV and STI-related health needs, ACCESS captured data on 366,441 young heterosexuals, 96,985 gay and bisexual men, and 21,598 people living with HIV.

Conclusions: ACCESS is a unique system with the ability to track efforts to control STIs and BBVs—including through the calculation of powerful epidemiological indicators—by identifying response gaps and facilitating the evaluation of programs and interventions. By anonymously linking patients between and within services and over time, ACCESS has exciting potential as a research and evaluation platform. Establishing a national health surveillance system requires close partnerships across the research, government, community, health, and technology sectors.

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Australia; blood-borne viruses; public health; sentinel surveillance; sexually transmissible infections

Introduction

Globally, sexually transmissible infections (STIs) and blood-borne viruses (BBVs) are associated with significant morbidity, mortality, health costs, and social stigma. Indeed, these infections represent a major public health burden. There are, for example, nearly 37 million people currently infected with HIV and >1 million associated deaths per year [1], while an estimated 70 million people live with hepatitis C, from which nearly half a million die each year [2]. Regarding hepatitis B, >250 million people live with this infection, which causes >800,000 deaths annually [3,4]. Around the world, there are >350 million new cases of curable STIs every year—chlamydia, gonorrhea, syphilis, and trichomoniasis [5]—and human papillomavirus (HPV) is responsible for nearly all cases of cervical cancer, the fourth most common malignancy worldwide [6].

In Australia, the control and elimination of some BBVs and STIs are increasingly feasible through combinations of new and existing strategies of prevention, treatment, and management. For HIV, elimination is a tantalizing possibility through regular testing in combination with pre-exposure prophylaxis among uninfected individuals and antiretroviral treatment among those living with the virus [7-9]. Achieving something as lofty as HIV elimination will, naturally, be a major challenge [10] and certainly one that requires close monitoring of biomedical prevention coverage and impact to guide the refinement of implementation strategies [11]. Similarly, curative therapy with direct-acting antivirals for hepatitis C has been made available to all infected people in Australia, representing a major advance for both individual and public health [12] but one that also requires monitoring, evaluation, and adaptation if there is any hope of reducing infection rates [13].

For some other infections—notably hepatitis B and HPV—vaccinations have proved highly effective in reducing population incidence and prevalence. There remain, however, cohorts of people not included in vaccination schedules because of their age or who have migrated to Australia from countries where prevalence is high and vaccination programs limited. For these infections, ongoing clinical screening is required to identify unvaccinated individuals, and in the case of HPV, intervene early as a precursor to cancer. In addition, for curative STIs, frequent testing and timely treatment are fundamental components of interrupting incubation and preventing unintended onward transmission [14]. For STIs and BBVs, it is clear that ongoing efforts are required to track progress against targets, monitor population health, assess the impact of interventions, and plan into the future.

Surveillance and monitoring of BBVs and STIs are often complicated by the fact that they disproportionately affect populations defined by sexual identity, sex practice, drug use, and ethnicity [11,13,14]. Thus, their management requires a holistic and comprehensive approach to care, which in Australia and many other countries, involves sexual health clinics, targeted general practice clinics, drug and alcohol services, and hospitals. Health services like these play a vital role not only in diagnosing and managing BBVs and STIs but also in their prevention by encouraging uptake of diagnostic testing, treatment, and vaccines where available. Calculating the uptake of these initiatives, however, requires knowing the number of total attending patients—the denominator—and such information can only be sourced directly from health services. When linked between individuals' episodes of care, these data can also be used to calculate other powerful impact indicators such as incidence or the time between diagnosis and treatment.

Here, we describe ACCESS—the Australian Collaboration for Coordinated Enhanced Sentinel Surveillance—a national system of sentinel surveillance that draws upon data from several different types of health services and pathology laboratories to inform and evaluate Australia's BBV and STI control efforts.

Methods

Overview and Aims

ACCESS is a system that routinely extracts and collates line-listed, deidentified data from health services and pathology laboratories across Australia. Through anonymous patient linkage between and within services and laboratories, ACCESS produces a retrospective and prospective cohort of patients attending participating sites. Established in 2008, ACCESS began as a sentinel system for chlamydia surveillance [15] that was expanded in 2013 to include BBVs and other STIs in some Australian jurisdictions. Through funding from the Australian Department of Health in 2016, ACCESS expanded further to encompass a greater number and a more diverse selection of sites relevant to these infections in all 8 Australian states and territories.

The overall aim of ACCESS is to support the Australian response to STIs and BBVs by monitoring the testing, diagnosis, and management of these infections. In addition, ACCESS aims to operate as an evaluative platform to measure the impact and

outcomes of relevant programs and interventions. This includes attention to Australian priority populations (gay and bisexual men and other men who have sex with men, people who use drugs, Aboriginal and Torres Strait Islander people, young heterosexuals, sex workers, and people from culturally and linguistically diverse backgrounds) and to "cascades of care" (eg, HIV) [16].

Infections

ACCESS focuses on specific infections, including HIV, hepatitis B, hepatitis C, HPV, chlamydia, gonorrhea, syphilis, and trichomoniasis. The design of ACCESS, however, allows for the addition of other infections or conditions as required into the future. Already, for example, steps have been taken to begin collecting data on *Mycoplasma genitalium*, a newly identified STI.

Sites and Recruitment

The ACCESS network seeks to include health services and pathology labs that best represent the prevention and management of BBVs and STIs nationally and in each state and territory. To be eligible, health services are required to use an electronic patient management system (ie, not based solely on paper files) and be willing to participate for a minimum of 2 years. Of note, we have encountered no health services still exclusively using paper files. In addition, health services have to see at least 50 individuals per year categorized as ≥1 of Australia's priority populations for BBVs and STIs or they have to represent a service designed specifically for the care and management of these infections (eg, sexual health clinics and HIV testing sites). Given differences in the overall population size between each state and territory—the largest contains >7.5 million people, while the smallest has just >200,000—we are flexible in our assessment of caseloads to allow for recruitment in smaller jurisdictions. For example, while a caseload of 50 patients with HIV might be considered small or medium in New South Wales, it would be considered large, if not the largest, in Tasmania.

Within these parameters, per jurisdiction, we have sought to include a minimum of 2 sites with large caseloads of people living with or at risk of HIV, 2 with large caseloads of people living with or at risk of hepatitis and 2 with a large amount of STI-related testing and care. In addition, we sought to recruit 2 pathology laboratories per jurisdiction (one public and one private) that conducted testing for BBVs and STIs. While in larger states (New South Wales, Queensland, and Victoria), it was necessary to exceed these targets and recruit larger number of sites, the opposite was true in some smaller jurisdictions. In the Australian Capital Territory, for example, the vast majority of BBV-related and STI-related tests were conducted by a single pathology laboratory, making it unnecessary to recruit a second site of this kind. Details like this one highlight the need and strength for a tailored approach to recruitment, given the significant differences between each state and territory.

As noted, ACCESS has been in operation since 2008 with recruitment taking place over many years and in different iterations. Most recently, recruitment was undertaken from 2016 through 2018 to expand the network's coverage in jurisdictions beyond New South Wales and Victoria. Over time, however, methods of identifying and recruiting sites have remained consistent; to gain jurisdictionally specific information on potential sites, we consult with local stakeholders in government, health, community organizations, and research institutes. We ask them to nominate sites that either conduct a large amount of testing for or care of BBVs and STIs, or sites that provide care for concentrations of Australia's priority populations. Where available, we also review public health data on locations of BBV and STI diagnoses (by general geographic areas) to identify health services located nearby, and we review publicly available lists of doctors licensed to prescribe treatments for HIV and hepatitis C.

When this process was undertaken in 2016 and 2017, we identified 115 health services and 24 pathology laboratories across Australia that met our eligibility criteria. Three-quarters of these sites were already involved with ACCESS, noting that since its inception in 2008, no site has ever withdrawn participation in the network. Of the remaining "new" sites identified through our scoping process, we undertook purposive sampling that deferred to sites with large caseloads and those that introduced diversity either through their location, patients' characteristics, or service model.

Table 1. Health services and pathology laboratories participating in the Australian Collaboration for Coordinated Enhanced Sentinel Surveillance network as of March 2018, by site type and jurisdiction.

Site type	Total	Jurisdiction							
		Australian Capital Territory	New South Wales	Northern Territory	Queensland	South Australia	Tasmania	Victoria	Western Australia
Sexual health clinic	58	1	38	3	8	1	3	2	2
General practice clinic	29	1	10	0	2	1	0	13	2
Hospital outpatient clinic	7	0	2	0	1	0	1	2	1
Community-led services	9	0	4	0	2	1	0	1	1
Drug and alcohol service	1	0	0	0	0	0	0	1	0
Private pathology laboratory	6	1	3	0	0	0	1	1	0
Public pathology laboratory	11	0	5	0	1	0	1	4	0

A total of 31 new sites were recruited to ACCESS, resulting in 92% (104/113) of health service identified nationally and 71% (17/24) of laboratories identified nationally participating in ACCESS. Participation is being negotiated with further 11 sites, 3 refused participation altogether, and 4 were not pursued because of small patient caseloads compared with other similar services in their jurisdiction. Table 1 provides an overview of sites contributing data to ACCESS as of March 2018, noting that these numbers will continue to change over time. Figure 1 depicts participating sites on a map of Australia.

Figure 1. Health services participating in the Australian Collaboration for Coordinated Enhanced Sentinel Surveillance network as of March 2018.

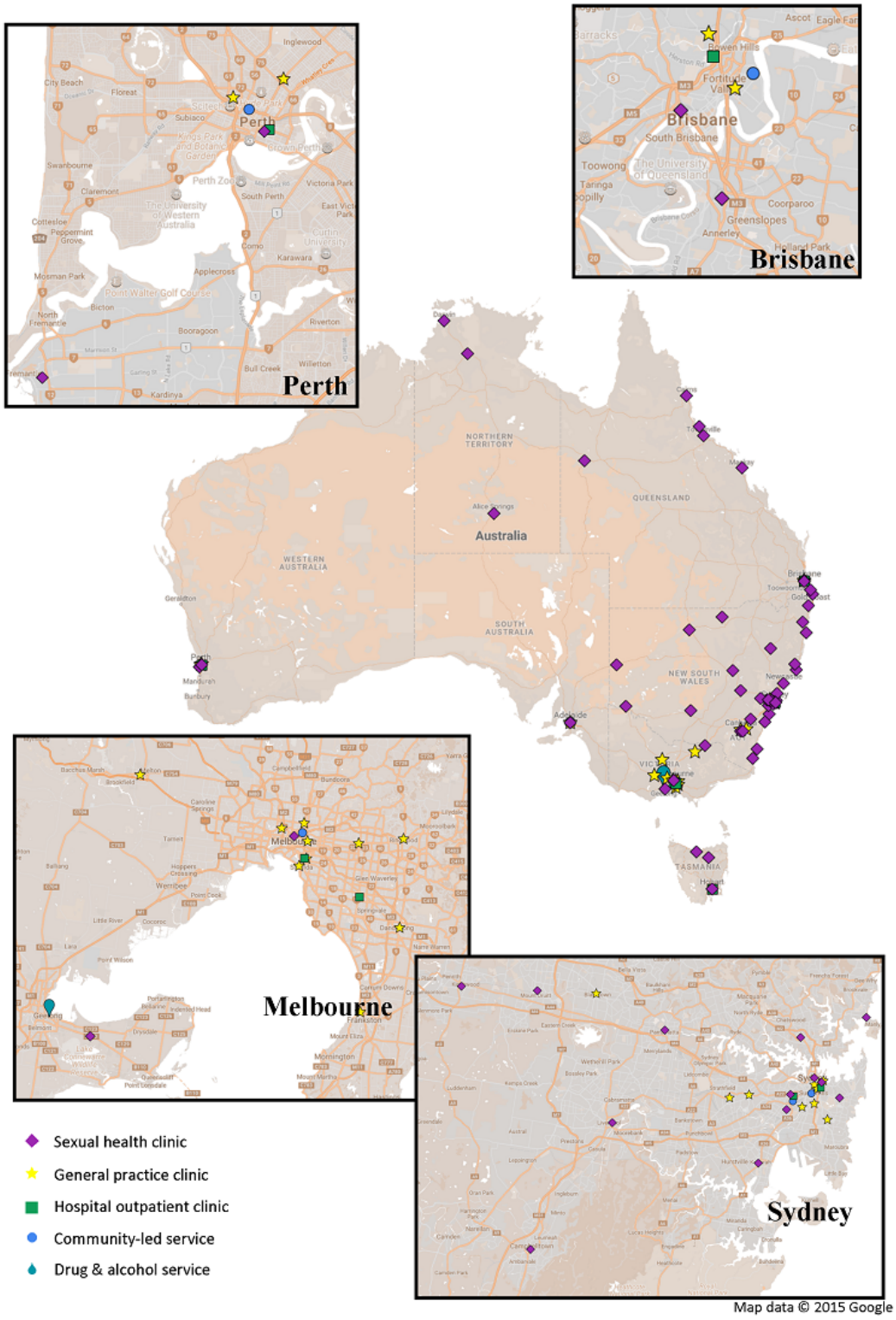

Table 2. Variables extracted (where available) from participating health services via Australian Collaboration for Coordinated Enhanced Sentinel Surveillance.

Domain	Variables
Patient information	• Age • Gender • Home postcode • Indigenous status • Country of birth • Preferred Language • Year of arrival in Australia • Sexual behavior
Consultation details	• Date • Type • Reason for attendance • Clinical diagnosis
Laboratory testing	• Tests requested • Results • Specimen type • Anatomical site
Treatment	• Drug name • Start or stop dates • Dose • Frequency • Route
Vaccination details	• Vaccination history • Vaccines administered • Type • Dose number
Behavioral: sexual practices	• Sexual partner gender(s) • Sexual partner numbers • Condom use • Sex work • Sex work location
Behavioral: drug use	• Use of injecting drugs • Shared injecting equipment • Drugs injected

Data Extraction and Management

Data are extracted from participating sites using software known as GRHANITE, which was designed specifically for the secure collection of deidentified health data. GRHANITE works by being installed on a local system at each participating site. Technical and financial costs associated with calibrating and installing GRHANITE are borne by ACCESS, making it a cost-neutral enterprise for sites. On an at least monthly basis, querying the site's database or accessing files already extracted from the database is performed. The nature of these queries is guided by schemas customized to meet the requirements and structures of each database. Because of their flexibility, GRHANITE's schemas can be deployed for use with almost any database structure to work across diverse systems ranging from established commercial platforms to unique systems built-for-purpose by individual services. Details of GRHANITE have been published previously [17,18]. Table 2 lists variables extracted for ACCESS, where available. Some sites routinely collect behavioral information from patients, and where available, these data are also extracted.

As part of the extraction process, GRHANITE removes any data that could potentially identify a patient. While still working within a participating site, GRHANITE generates probabilistic record linkage keys (or signatures) called "hashes." These signatures are derived from, but do not contain, personal information, which means that probabilistic linkage can be safely conducted between and within participating ACCESS sites. This process makes it possible to monitor patient movement between services in a way that is anonymous and ensures that no identifiable patient details are ever transmitted beyond participating sites. Following extraction, GRHANITE encrypts the data and transmits it to a central, secure server.

Data are extracted for all patients and consultations, but pathology and treatment data are only extracted when there is evidence of testing or treatment for an STI or BBV. This approach helps limit the size of the ACCESS database by focusing on the most relevant pathology testing. In general

practice clinics, notably, the majority of testing would be unrelated to these infections, which would place an unnecessarily high technical burden on systems to fully extract all data. Thus, filters are used and regularly reviewed to ensure accuracy and completeness.

ACCESS data are processed using code that organizes pathology testing, treatment, and patient details into standardized formats. This step also involves unifying the structure of data received from different systems. Notably, because many patient management systems store pathology results as free text, computational parsing is used to identify test names, dates, and results to organize that information into consistent categories. This code is regularly reviewed for accuracy and adapted over time, as required. A similar process is used to identify patients that form part of Australia's priority populations, which involves drawing upon numerous pieces of information (eg, demographics, behavioral details, and pathology tests) to properly categorize patient files. For example, previous research has found that sexual orientation is not well recorded among men attending Australian general practice clinics [19]. To address this issue, we use history of rectal swabs for STI testing as a proximal marker indicating anal sex, which has previously been found to be effective for identifying gay and bisexual men and other men who have sex with men [20]. Definitions for organizing pathology tests and categorizing patients into priority populations were constructed in close consultation with relevant clinical and laboratory experts, as well as community representatives.

Data Quality

The quality of ACCESS data is ensured through a number of processes. Data extracted from new services are validated through a consultative process with site investigators, which includes sharing preliminary outputs to gauge the degree to which they converge (or diverge) from clinical experience. This feedback is then used to improve data processing and address gaps or errors in the extraction process. For example, to ensure data completeness, we might ask clinic staff to estimate the number of HIV-positive patients they see each year or the number of chlamydia tests they conduct in an average week, which can then be compared against extracted and processed data. This process has previously identified components missing from extracts, including pathology test names, drugs types, and demographic variables, and then used to adapt and correct extraction processes.

Beyond completeness, we also carefully attend to the accuracy of ACCESS data. This involves what is extracted as well as how we process extracted data, which is to say how variables are organized into distinct and consistent categories. Wherever possible, ACCESS data are triangulated with other sources to improve accuracy. This process includes comparing extracted health service data to that from pathology laboratories; because some participating laboratories serve participating health services, we can assess the degree to which the number of tests and results align. Comparing data in this way has allowed us to refine pathology filters and our processes for organizing results. In the past, ACCESS data have also been assessed for accuracy against passive surveillance information. For example, we previously requested information on HIV and STI notifications among sexual health clinic attendees in New South Wales to calibrate our systems for processing diagnoses in these clinics [21].

Routine data quality checks are also conducted on a quarterly basis, which focus on assessing if there are significant changes in test frequencies over time to generate alerts for significant deviations. For example, if the number of tests extracted for chlamydia doubled from one period to the next, this would be used as a point of investigation. Investigations include reviewing data processing, checking raw data, and consulting with site investigators. This kind of quality assurance is done on the dataset as a whole, by health service type and to the level of individual sites.

Dissemination and Use

ACCESS data are used for diverse purposes. Data extracted via ACCESS can be used to generate a number of powerful indicators relevant to BBVs and STIs, most commonly those related to diagnostic testing (test uptake, test frequency, test comprehensiveness, and retesting), treatment (treatment uptake and treatment success), infections (test yield, test positivity, incidence, and reinfection), and vaccinations (coverage of vaccine-acquired immunity). Indeed, indicators like these form part of ACCESS's contributions to the national surveillance of BBVs and STIs [22] and their surveillance by individual states and territories, including as stand-alone reports or as part of existing reporting mechanisms [23]. In reports such as these, ACCESS has been used to improve estimates of treatment uptake and success, which supports more accurate "cascades of care" for HIV and other infections. The automated nature of data extraction and processing facilitates timely production of reports, which in some cases are published as early as 4 weeks from the end of a reporting period. Furthermore, site-specific ACCESS data are routinely reported back to participating sites, which can include analyses of testing uptake, test positivity, and diagnosis frequency.

In addition to routine surveillance reporting, ACCESS data are used for a number of other related projects. Notably, ACCESS data have been used in stand-alone analyses of population health, for example, in studies of HIV and STIs among sex workers in Australia [24,25] and an analysis of hepatitis C testing and diagnoses among people living with HIV [26]. Moreover, ACCESS data have been used to assess the impact of syphilis testing interventions [27]. Beyond this work, ACCESS is being used increasingly to support other forms of research and evaluation. In some projects, ACCESS provides line-listed and deidentified datasets, which are and have been used to conduct a large-scale study of HIV treatment-as-prevention [28], evaluate pre-exposure prophylaxis implementation trials [29,30], and study Victoria's hepatitis C elimination response [31]. In other cases, as in the evaluation of HIV control in New South Wales [32], ACCESS has routinely provided specifically designed indicators (eg, HIV testing uptake and rates of viral suppression) to monitor and evaluate various aspects of BBV prevention and management. In many of these examples, ACCESS fills an important role by providing the kinds of data and indicators that are required for research of this kind to be conducted. Through

these projects, ACCESS demonstrates its capacity to support diverse research on STIs and BBVs, which extends beyond the realms of surveillance and monitoring.

Ethics and Governance

Ethical approval was granted by the lead human research ethics committee of Alfred Hospital in Melbourne (248/17), University of Tasmania (H0010220), and the Menzies School of Health Research (08/047). All ethics committees waived the need for consent to be collected from individual patients. Furthermore, ethical reviews were provided by organizations representing key populations, notably gay and bisexual men, people living with HIV, sex workers, and Aboriginal and Torres Strait Islander people.

To protect the identities of individual patients, access to the line-listed database is restricted to a small and select group of researchers. Where data are shared with others, potentially identifying details (eg, patient postcode) are replaced with broad categories (eg, urban/nonurban), which is a similar approach taken in any reporting of ACCESS data. Furthermore, analyses that produce cell counts of <5 individuals are suppressed.

An advisory committee was established comprising representatives from government organizations, community groups, health services and laboratories, and research institutes. This committee provides advice on the project's development and conduct; promotes its aims and objectives; and contributes to analysis, interpretation, and dissemination.

Results

Although some sites were able to provide electronic data going back as far as the 1980s, data quality and completeness tends to diminish further back in time when health services were less familiar with technologies of electronic health that dominate today. To examine a more recent period, we note that ACCESS captured data from a total of 1,171,658 individual patients who attended a participating health service at least once in the recent past between 1 January 2009 and 31 December 2017. These patients attended for a total of 7,992,241 clinical consultations or an average of 0.8 consultations per patient per year. Patient gender was evenly represented between men (597,545/1,171,658, 51%) and women (574,112/1,171,658, 49%), and records were extracted from a total of 1116 transgender patients (380/1116, 34% transgender men; 356/1116, 32% transgender women, and 380/1116, 34% unspecified gender).

Specific to Australia's priority populations, from 2009 to 2017, ACCESS captured data of 366,441 young heterosexuals aged 16-29 years. In addition, the network includes data from 96,985 gay and bisexual men and other men who have sex with men. Data were also captured from 21,598 people living with HIV, drawing upon recorded HIV diagnoses, confirmed HIV pathology results, viral load testing, and clinical attendance for "HIV management." In total, 22,089 Aboriginal and Torres Strait Islander patients attended an ACCESS health service during this period, noting that this variable was incomplete for 74% (576,219/778,674) of patients attending general practice clinics and 50% (196,490/392,984) of patients attending other services. Even though Australian guidelines recommend collecting indigenous status from all patients [33], it seems that this indicator is still not routinely collected.

As noted, sexual health clinics in Australia routinely collect enhanced behavioral data on factors associated with BBVs and STIs. This information is used by ACCESS to further identify members of priority populations. From 2009 to 2017, for example, it is possible to identify 12,111 people who attended an ACCESS site and reported injecting drug use at least once in the 12 months prior to consultation, as it is possible to identify 21,205 men and women who reported sex work in the previous 12 months. As noted, identifying members of these priority populations is not possible in settings other than sexual health and community-lead clinics, which is attributed to a lack of standardized methods for collecting and recording behavioral data. Work is ongoing to support the implementation of behavioral surveys in some general practice clinics and to develop algorithms for recognizing these populations through other means, such as through certain types and patterns of pathology tests and testing.

Discussion

In this paper, we described the methods used to establish a national sentinel surveillance system for BBVs and STIs. ACCESS seeks to complement the existing passive surveillance by tracking the uptake and impact of strategies aimed at controlling these infections. The system is highly flexible and can be adapted for use in a multitude of health contexts and evolve over time to address emerging surveillance needs. In addition, it is a project deeply rooted in collaboration, involving government, researchers, community, and clinicians from every corner of Australia. ACCESS is a unique national resource and a model with potential relevance for other countries.

A key strength of ACCESS is its ability to anonymously link patients between services and over time. In some ways, this feature makes ACCESS akin to a national retrospective and prospective cohort, which has exciting possibilities in a number of areas. ACCESS allows scrutiny of the ways that individuals move through different pathways of care, including the overall trajectory and the time it takes to move from diagnosis to viral suppression or cure. Furthermore, this linkage facilitates the calculation of powerful epidemiological markers, like incidence and test frequency and also allows for examinations of compliance with clinical guidelines associated with testing (eg, chlamydia testing among young people presenting to clinics or following past positive tests). ACCESS also makes possible detailed, individual, and large-scale evaluations of public health policy, interventions, and other strategies aimed at controlling BBVs and STIs.

Another key strength of ACCESS relates to its coverage. Specifically, the network of health services in every state and territory enables comparison between not only Australian jurisdictions but also different types of service models, such as community-based testing services, sexual health clinics, and hospitals. These comparisons are important for identifying gaps, comparing the utility of different ways for providing care and nuanced information on how BBVs and STIs are diagnosed and managed. Furthermore, by attending to the geographic

concentrations of Australia's priority populations and working with community groups and health experts, ACCESS has collated some of the largest samples of "high-risk" priority populations seen anywhere in the world.

The automated nature of ACCESS significantly reduces the resources and time required to report surveillance data, benefits that are already being realized through quarterly reporting to state health departments. Although initial enrollment of new sites to ACCESS requires some time, maintenance is minimal once established, which helps ensure the system's ongoing sustainability. Moreover, participating sites realize benefits through the publication of scientific research and the ability to more readily access their own data, including through tailored site reports that can include comparisons with aggregated data from similar sites. These strengths are reflected in the observation that in a decade of operation, no site has yet chosen to withdraw from ACCESS.

There are some limitations of the system that warrant consideration. As a surveillance network, ACCESS does not capture all new diagnoses and is, therefore, not a replacement for passive surveillance. Although we have described the process for anonymously linking patients between ACCESS sites, gaps arise when patients attend health services outside of the network. These gaps can be partly overcome through data from participating laboratories but they are inherent in the network's "sentinel" nature. Another limitation is ACCESS's inability to collect all clinical information, in particular, the free text detail contained within patient notes. Patient notes contain a wealth of details that would likely be relevant to BBVs and STIs but are not accessed by this system because they can potentially contain identifying information. Options for identifying and extracting relevant details through the use of text-recognition software are currently being assessed as a potential means of using this information confidentially. Finally, ACCESS is entirely reliant on routinely recorded health information; the quality and completeness of these details can vary between and within sites. This limitation, however, can be overcome in some cases with ACCESS's capacity for anonymous patient linkage by pooling information from multiple services and laboratories to construct a more complete picture.

ACCESS represents a new way of conducting sentinel surveillance, which adds value for government, research, clinical, and community partners. With data extraction under way across the country, over the coming years, the project will focus on new ways of providing regular feedback to health service and laboratory sites as a way to improve service delivery, sustain interest, and capitalize on the network's potential. In the future, it is imagined that ACCESS will continue to develop as a readily accessible resource for diverse stakeholders that seek to make use of it as a unique, national database.

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Conflicts of Interest

None declared.

References

1. UNAIDS. 2015 World AIDS Day report: Fact Sheet 2015 URL: http://www.unaids.org/en/resources/fact-sheet [accessed 2018-05-10] [WebCite Cache ID 6zIbRRapQ]
2. Stanaway JD, Flaxman AD, Naghavi M, Fitzmaurice C, Vos T, Abubakar I, et al. The global burden of viral hepatitis from 1990 to 2013: findings from the Global Burden of Disease Study 2013. Lancet 2016 Sep 10;388(10049):1081-1088 [FREE Full text] [doi: 10.1016/S0140-6736(16)30579-7] [Medline: 27394647]

3. Ott JJ, Stevens GA, Groeger J, Wiersma ST. Global epidemiology of hepatitis B virus infection: new estimates of age-specific HBsAg seroprevalence and endemicity. Vaccine 2012 Mar 09;30(12):2212-2219 [FREE Full text] [doi: 10.1016/j.vaccine.2011.12.116] [Medline: 22273662]
4. Goldstein ST, Zhou F, Hadler SC, Bell BP, Mast EE, Margolis HS. A mathematical model to estimate global hepatitis B disease burden and vaccination impact. Int J Epidemiol 2005 Dec;34(6):1329-1339. [doi: 10.1093/ije/dyi206] [Medline: 16249217]
5. Newman L, Rowley J, Vander HS, Wijesooriya NS, Unemo M, Low N, et al. Global Estimates of the Prevalence and Incidence of Four Curable Sexually Transmitted Infections in 2012 Based on Systematic Review and Global Reporting. PLoS One 2015;10(12):e0143304 [FREE Full text] [doi: 10.1371/journal.pone.0143304] [Medline: 26646541]
6. World Health Organization. Cervical cancer estimated incidence, mortality and prevalence worldwide in 2012 URL: http://globocan.iarc.fr/old/FactSheets/cancers/cervix-new.asp [accessed 2018-05-10] [WebCite Cache ID 6zIbaJC1q]
7. World Health Organization. Consolidated Guidelines on the Use of Antiretroviral Drugs for Treating and Preventing HIV Infection: Recommendations for a public health approach. 2nd edition. Geneva, Switzerland: World Health Organization; 2016.
8. Cohen MS, Chen YQ, McCauley M, Gamble T, Hosseinipour MC, Kumarasamy N, et al. Prevention of HIV-1 infection with early antiretroviral therapy. N Engl J Med 2011 Aug 11;365(6):493-505 [FREE Full text] [doi: 10.1056/NEJMoa1105243] [Medline: 21767103]
9. UNAIDS. 90-90-90 An ambitious treatment target to help end the AIDS epidemic. 2014. URL: http://www.unaids.org/sites/default/files/media_asset/90-90-90_en.pdf [accessed 2018-05-10] [WebCite Cache ID 6zIbpaaJS]
10. Scott N, Stoové M, Kelly SL, Wilson DP, Hellard ME. Achieving 90-90-90 Human Immunodeficiency Virus (HIV) Targets Will Not Be Enough to Achieve the HIV Incidence Reduction Target in Australia. Clin Infect Dis 2018 Mar 19;66(7):1019-1023. [doi: 10.1093/cid/cix939] [Medline: 29099920]
11. Australian Government Department of Health. Seventh National HIV Strategy 2014-2017. Canberra, ACT, Australia: Commonwealth of Australia; 2014. URL: http://www.health.gov.au/internet/main/publishing.nsf/content/ohp-bbvs-hiv [accessed 2018-05-10] [WebCite Cache ID 711SZUe0c]
12. Dore GJ, Feld JJ. Hepatitis C virus therapeutic development: in pursuit of “perfectovir”. Clin Infect Dis 2015 Jun 15;60(12):1829-1836. [doi: 10.1093/cid/civ197] [Medline: 25761867]
13. Australian Government Department of Health. Fourth National Heptatits C Strategy 2014-2017. Canberra, ACT, Australia: Commonwealth of Australia; 2014. URL: http://www.health.gov.au/internet/main/publishing.nsf/content/ohp-bbvs-hepc [accessed 2018-05-10] [WebCite Cache ID 711SgrY6l]
14. Australian Government Department of Health. Third National Sexually Transmissible Infections Strategy 2014-2017. Canberra, ACT, Australia: Commonwealth of Australia; 2014. URL: http://www.health.gov.au/internet/main/publishing.nsf/content/ohp-bbvs-sti [accessed 2018-05-10] [WebCite Cache ID 6zIbkDhK6]
15. Guy RJ, Kong F, Goller J, Franklin N, Bergeri I, Dimech W, et al. A new national Chlamydia Sentinel Surveillance System in Australia: evaluation of the first stage of implementation. Commun Dis Intell Q Rep 2010 Sep;34(3):319-328. [Medline: 21090187]
16. Medland NA, McMahon JH, Chow EPF, Elliott JH, Hoy JF, Fairley CK. The HIV care cascade: a systematic review of data sources, methodology and comparability. J Int AIDS Soc 2015;18:20634 [FREE Full text] [Medline: 26626715]
17. Boyle DIR. Middleware Supporting Next Generation Data Analytics in Australia. Stud Health Technol Inform 2015;216:1019. [Medline: 26262320]
18. Boyle D, Kong F. A Systematic mechanism for the collectioninterpretation of display format pathology test results from Australian primary care records. Electronic Journal of Health Informatics 2011;6(2):7.
19. Callander D, Bourne C, Pell C, Finlayson R, Forssman B, Baker D, et al. Recording the sexual orientation of male patients attending general practice. Fam Pract 2015 Feb;32(1):35-40. [doi: 10.1093/fampra/cmu061] [Medline: 25236604]
20. Ampt FH, El-Hayek C, Agius PA, Bowring AL, Bartnik N, Fairley CK, et al. Anorectal swabs as a marker of male-to-male sexual exposure in STI surveillance systems. Epidemiol Infect 2017 Dec;145(12):2530-2535. [doi: 10.1017/S095026881700098X] [Medline: 28528588]
21. Bourne C, Lam M, Selvey C, Guy R, Callander D. Changing pattern of sexually transmissible infections and HIV diagnosed in public sexual health services compared with other locations in New South Wales, 2010-14. Sex Health 2018 Jul 16. [doi: 10.1071/SH17183] [Medline: 30008288]
22. The Kirby Institute. HIV, Viral Hepatitis and Sexually Transmissible Infections in Australia: Annual Surveillance Report. Sydney, NSW: The Kirby Institute, UNSW; 2017. URL: https://kirby.unsw.edu.au/report/annual-surveillance-report-hiv-viral-hepatitis-stis-2016 [accessed 2018-10-22] [WebCite Cache ID 73N9fJh1i]
23. The NSW Ministry of Health. NSW HIV Strategy 2016-2020: April-June 2017 Data Report. 2017. URL: http://www.health.nsw.gov.au/endinghiv/Publications/q2-2017-nsw-hiv-data-report.pdf [accessed 2018-10-10] [WebCite Cache ID 6zIc6Sweg]
24. Callander D, McManus H, Guy R, Hellard M, O'Connor CC, Fairley CK, et al. Rising Chlamydia and Gonorrhoea Incidence and Associated Risk Factors Among Female Sex Workers in Australia: A Retrospective Cohort Study. Sex Transm Dis 2018 Mar;45(3):199-206. [doi: 10.1097/OLQ.0000000000000714] [Medline: 29420449]

25. Callander D, Read P, Prestage G, Minichiello V, Chow EPF, Lewis DA, et al. A cross-sectional study of HIV and STIs among male sex workers attending Australian sexual health clinics. Sex Transm Infect 2017 Jun;93(4):299-302. [doi: 10.1136/sextrans-2016-052578] [Medline: 27591189]
26. Boettiger DC, Law MG, Dore GJ, Guy R, Callander D, Donovan B, et al. Hepatitis C testing and re-testing among people attending sexual health services in Australia, and hepatitis C incidence among people with human immunodeficiency virus: analysis of national sentinel surveillance data. BMC Infect Dis 2017 Dec 01;17(1):740 [FREE Full text] [doi: 10.1186/s12879-017-2848-0] [Medline: 29191154]
27. Chow EPF, Callander D, Fairley CK, Zhang L, Donovan B, Guy R, ACCESS collaboration. Increased Syphilis Testing of Men Who Have Sex With Men: Greater Detection of Asymptomatic Early Syphilis and Relative Reduction in Secondary Syphilis. Clin Infect Dis 2017 Aug 01;65(3):389-395. [doi: 10.1093/cid/cix326] [Medline: 28419198]
28. Callander D, Stoové M, Carr A, Hoy JF, Petoumenos K, Hellard M, et al. A longitudinal cohort study of HIV 'treatment as prevention' in gay, bisexual and other men who have sex with men: the Treatment with Antiretrovirals and their Impact on Positive And Negative men (TAIPAN) study protocol. BMC Infect Dis 2016 Dec 12;16(1):752 [FREE Full text] [doi: 10.1186/s12879-016-2073-2] [Medline: 27955627]
29. Ryan K, Lockwood J, Asselin J, Mak A, Price B, Murphy D, et al. Health systems and study design features permitting rapid enrolment of individuals at high-risk of HIV acquisition into a pre-exposure prophylaxis study in Melbourne, Victoria, Australia. 2017 Presented at: International AIDS Conference on HIV Science; 2017; Paris, France.
30. Zablotska IB, Selvey C, Guy R, Price K, Holden J, Schmidt H, EPIC-NSW study group. Expanded HIV pre-exposure prophylaxis (PrEP) implementation in communities in New South Wales, Australia (EPIC-NSW): design of an open label, single arm implementation trial. BMC Public Health 2018 Dec 02;18(1):210 [FREE Full text] [doi: 10.1186/s12889-017-5018-9] [Medline: 29394918]
31. Pedrana A. Implementing an Elimination program for Hepatitis C: A partnership approach in Australia. Implementing an Elimination program for Hepatitis C: A partnership approach in Australia. International Symposium on Hepatitis Care in Substance Users. New Jersey. USA; 2017 Presented at: International Symposium on Hepatitis Care in Substance Users; 2017; New Jersey, USA.
32. Keen P, Selvey C, Grulich A. The HIV prevention revolution: measuring outcomesmaximising effectiveness in NSW. HIV Australia 2016;14(2):35-37 [FREE Full text]
33. Australian Institute of Health and Welfare. National best practice guidelines for collecting Indigenous status in health data sets. Canberra, Australia; 2010 Apr 08. URL: https://www.aihw.gov.au/reports/indigenous-australians/national-guidelines-collecting-health-data-sets/contents/table-of-contents [accessed 2018-10-10] [WebCite Cache ID 6zIcHKdOP]

Abbreviations

ACCESS: Australian Collaboration for Coordinated Enhanced Sentinel Surveillance
BBV: blood-borne virus
HPV: human papillomavirus
STI: sexually transmissible infection

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Protocol

Negative-Pressure Wound Therapy Versus Standard Treatment of Adult Patients With Conflict-Related Extremity Wounds: Protocol for a Randomized Controlled Trial

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Abstract

Background: In armed conflict, injuries commonly affect the extremities and contamination with foreign material often increases the risk of infection. The use of negative-pressure wound therapy has been described in the treatment of acute conflict-related wounds, but reports are retrospective and with limited follow-up.

Objective: The objective of this study is to investigate the effectiveness and safety of negative-pressure wound therapy use in the treatment of patients with conflict-related extremity wounds.

Methods: This is a multisite, superiority, pragmatic randomized controlled trial. We are considering for inclusion patients 18 years of age and older who are presenting with a conflict-related extremity wound within 72 hours after injury. Patients are block randomly assigned to either negative-pressure wound therapy or standard treatment in a 1:1 ratio. The primary end point is wound closure by day 5. Secondary end points include length of stay, wound infection, sepsis, wound complications, death, and health-related quality of life. We will explore economic outcomes, including direct health care costs and cost effectiveness, in a substudy. Data are collected at baseline and at each dressing change, and participants are followed for up to 3 months. We will base the primary statistical analysis on intention-to-treat.

Results: The trial is ongoing. Patient enrollment started in June 2015. We expect to publish findings from the trial by the end of 2019.

Conclusions: To the best of our knowledge, there has been no randomized trial of negative-pressure wound therapy in this context. We expect that our findings will increase the knowledge to establish best-treatment strategies.

Trial Registration: ClinicalTrials.gov NCT02444598; http://clinicaltrials.gov/ct2/show/NCT02444598 (Archived by WebCite at http://www.webcitation.org/72hjI2XNX)

International Registered Report Identifier (IRRID): DERR1-10.2196/12334

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KEYWORDS

war-related injuries; negative-pressure wound therapy; extremity wounds; resource-limited settings

Introduction

Background

During armed conflict, injuries commonly affect the extremities, among both civilians [1] and combatants [2]. These injuries are often contaminated with foreign material, increasing the risk of infection [3,4]. Traditionally, conflict-related wounds are surgically treated with debridement of devitalized or contaminated tissue and then covered with a nonadhesive dressing. After 3 to 5 days, the wound is generally examined a second time in the operating room [5].

Negative-pressure wound therapy (NPWT) is widely used in the treatment of wounds and is claimed to promote wound healing and prevent infectious complications. The technique involves covering the wound with a solid foam followed by a plastic film through which a negative pressure is applied. Any wound and tissue fluid is drawn away from the area and collected into a canister. NPWT is suggested by expert consensus for use in a range of surgical applications, including after or in between debridements, as a bridge to definite closure of soft tissue wounds [6]. The technique has previously been used in the treatment of acute conflict-related wounds, but existing reports are retrospective and with limited follow-up [7-10]. Two independent Cochrane reviews of NPWT for the treatment of surgical wounds [11] and traumatic wounds [12] were inconclusive due to the lack of suitably powered, high-quality trials.

Summary of Potential Risks and Benefits

Both treatment methods (NPWT and conventional dressings) are well established and used in the treatment of acute and chronic wounds. As it is unknown whether there is any difference in outcome between the two treatment modalities, neither patient group may be regarded as receiving preferential treatment. In this study, we will allocate treatment at the end of the first surgery so there is no difference between the groups in terms of surgical risks.

NPWT has not regularly been used at the study sites prior to this study. The introduction of NPWT is not associated with any serious risks compared with standard treatment. Potential benefits of NPWT are shortened healing time and fewer infectious complications. The occlusive dressing may, on the other hand, cause more infections or delay the identification of infection. Other potential risks include pain, mainly associated with dressing changes [13], and bleeding, predominantly minor bleeding from granulation tissue [14]. Conventional wound dressing has the potential benefit of being a safe treatment method used for many years. Since this method permits air into the wound, the risk of health care–associated infections is potentially higher.

Objective

The objective of this study is to evaluate the effectiveness and safety of NPWT in the treatment of traumatic extremity wounds in a context associated with a high level of contamination and infection.

Methods

Study Design

This is a multisite, superiority, pragmatic randomized controlled trial comparing NPWT versus conventional dressing methods in the treatment of patients with conflict-related extremity wounds (ClinicalTrials.gov NCT02444598).

End Points

The primary end point is wound closure by day 5, by suture, flap, or split-thickness skin graft.

The coprimary end point is net clinical benefit, defined as a composite of wound closure by day 5 and freedom from any bleeding, infection, sepsis, or loss of index limb.

The secondary end points are (1) rate of wound healing, defined as days to wound closure by suture, flap, or split-thickness skin graft; (2) wound infection, defined as purulent discharge [15]; (3) wound size ratio at day 14 (wound size day 14 compared with size day 0, ie, wound healing rate after 14 days); (4) time until wound is deemed no longer requiring professional care; (5) number of surgeries; (6) time to hospital discharge; (7) quality-of-life aspects; (8) wound healing at follow-up days 14 and 30, and at 3 months; (9) bleeding leading to blood transfusion; (10) sepsis; (11) limb amputation (limb with wound included in the study); (12) death; (13) direct health care costs (substudy); and (14) cost effectiveness (substudy).

Participants

Patients 18 years of age and older presenting at the hospital within 72 hours of sustaining a conflict-related extremity wound are included as they present at the emergency department. In case of multiple wounds, we are selecting the extremity wound with the estimated largest area. Patients are included if they are transferred from another hospital within 72 hours of initial trauma. Patients who present with wounds considered ready for primary closure by suture, flap, or split-thickness skin graft are excluded. Local or systemic infections are treated according to local standard protocols. Wounds in need of debridement are debrided according to International Committee of the Red Cross war surgery protocols [5].

Setting

Jordan is an upper-middle-income country [16], currently hosting 655,000 Syrian refugees [17]. Médecins Sans Frontières/Doctors Without Borders (MSF), an international nongovernmental organization, runs an emergency trauma project at the Jordan Ministry of Health hospital in Ar Ramtha, 5 km from the Syrian border. Patients within the project receive treatment for blast and gunshot wounds sustained in the Syrian armed conflict. Discharged patients are sometimes continuously treated by MSF in Zaatari refugee camp. The wound infection rate among patients receiving acute surgical treatment at the project has been found to be 11%, with 3 out of 4 patients infected by multidrug-resistant bacteria [18]. Physicians within the project have found wound management to be a major challenge [19]. Patient enrollment in Ar Ramtha, Jordan started in June 2015.

Iraq is an upper-middle-income country [16]. Emergency Hospital is a trauma center in Erbil, Iraqi Kurdistan that is run by a local nongovernmental organization called Emergency Management Center. Most patients receive treatment for conflict-related injuries, and the hospital was one of the key medical institutions receiving the injured from Mosul during the Iraqi offensive against the so-called Islamic State of Iraq and Syria during October 2016 to July 2017 [20]. Patient enrollment in Erbil is ongoing since May 2017.

Randomization and Blinding

We use a computer-generated randomization code with random variation of 2 fixed block sizes to achieve balance in the allocation of participants to the 2 treatment arms and reduce the opportunity for bias and confounding. Each site has its own dedicated randomization list respecting the 1:1 ratio. The sealed randomization envelopes are opened by the operating room nurse at the end of the first surgery, but before the wound dressing is applied. By randomizing after the operation, we eliminate the risk of treatment allocation influencing the surgeon's choice of debridement technique. Wound photographs will be evaluated by 2 independent trained evaluators who are blinded to the treatment allocation. Due to the nature of the treatment methods, blinding of the patients or staff involved in the treatment would not be possible.

Interventions

Patients in the NPWT group receive treatment using a Conformité Européenne–marked professional device with continuous negative pressure of 125 mm Hg. Patients in the control group are treated with conventional wound therapy according to International Committee of the Red Cross war surgery protocols: a nonadhesive dressing covered with a bandage [5]. The exact details of the dressing technique are left to the discretion of the treating surgeon. Dressing details are recorded. All patients receive prophylactic narrow-spectrum antibiotic agents. Fractures are generally immobilized with external fixation. Dressing change frequencies are determined by the treating physician, generally every 3 to 5 days. Any further wound dressing will follow the allocated treatment. Wounds are treated until wound closure. Estimated median duration of treatment (control group) is 5 days.

Follow-Up Procedures

Follow up is done at each dressing change, at hospital discharge, at days 14 and 30 and at 3 months following the day of randomization (Table 1). Full wound healing or size of wound at the treatment location is noted. Discharged patients either return to the hospital for follow-up or are contacted by phone. If possible, wounds are photo documented and evaluated as described below.

Quality of Life

We use the 20-item Self Reporting Questionnaire (SRQ-20) to screen for psychological distress [21]. In addition, wound-specific quality-of-life details are recorded, including noise generated by the NPWT pump, movement impairment, skin irritation, odor, sleep quality, discomfort during dressing changes, and pain. SRQ-20 scores and wound-specific quality-of-life details are recorded at baseline and before hospital discharge.

Sample Size and Power Calculation

The sample size calculation was based on detection of a difference of 25% between treatment groups in the proportion of patients for the primary outcome. We estimated the expected rate of patients reaching the primary outcome at day 5 to be 75% in the NPWT group and 50% in the control group. Based on a power of 80% and a significance level of 5%, we calculated that we would need a minimum sample size of 116 patients (58 per group) to detect a significant difference in the proportions. To adjust for dropouts, we aim to include 200 patients (100 per group).

Data Collection

Dedicated research nurses collect and enter data into paper-based case report forms during the study period. For all enrolled patients, contact details including mobile phone number are collected. Wounds are photo documented at day 0, at every dressing change, at day 14, and, if possible, at 1 and 3 months' follow-up. Photo documentation is done in a standardized way with a single-colored background and an adhesive paper ruler attached to the edge of the wound.

Table 1. Timeline of trial activities.

Time point	Activity
Baseline	Patient inclusion (consent within 5 days of randomization), patient details, injury details, wound details, photograph of wound, SRQ-20[a] scores, and quality-of-life details
End of first surgery	Randomization, allocation of treatment, wound details, treatment details, photograph of wound
Dressing change	Treatment details, wound details, photograph of wound
Hospital discharge	Treatment details, wound details, SRQ-20 scores, and quality-of-life details
Day 14	Treatment details, wound details, photograph of wound
Day 30	Treatment details, wound details, photograph of wound
3 months	Treatment details, wound details, photograph of wound

[a]SRQ-20: 20-item Self Reporting Questionnaire.

Data Management

We will use the EpiData entry software, version 4.4.3.1 (The EpiData Association) to build a database. All data will remain anonymous throughout the data entry and analysis process. Only the research team will know the participants' names. Identification codes will be safeguarded at the research facilities for the duration of the study.

Statistical Analysis

We will perform analyses on an intention-to-treat basis with a 2-sided significance level of .05. The primary end point (wound closure by day 5) will be presented as proportions with a 95% confidence interval for the difference in proportions. We will analyze the coprimary end point with standard survival analysis using proportional hazards for comparison of the treatment arms. For the primary end point, we will also perform a per-protocol analysis, excluding patients who did not receive the planned treatment or did not survive to day 5. We will report baseline characteristics as means and standard deviations or numbers and percentages, as appropriate. Subgroup analyses will include age, injury mechanism, initial injury severity, associated fracture versus no fracture, and initial wound size.

Ethics and Oversight

This study is performed in accordance with the Declaration of Helsinki and the specifications of the International Conference on Harmonisation of Good Clinical Practice. We will report on the trial in line with the Consolidated Standards of Reporting Trials (CONSORT) statement. Ethical approval was given by the Ethics Review Committee of Jordan Ministry of Health (MOH REC 150037) and the Ethics Review Board of MSF (ID 1520) before study initiation in Jordan. We obtained approval from the Research Ethics Committee, Kurdistan Regional Government (2:10 6/3/2017) before study initiation in Iraq. An external monitor regularly inspect the trial master file, monitoring the processes of consent taking, randomization, registration, provision of information, and provision of treatment.

Informed Consent

Written and oral information in English and Arabic is given to eligible participants. Participants are informed regarding their right to withdraw from the study and issues concerning confidentiality. No incentives or inducements are provided to any participant. Written informed consent before randomization or delayed consent within 5 days of randomization is collected from each patient who agrees to be included.

The principle of delayed consent is an established principle in trials that include critically ill patients and has been considered acceptable from research participants' perspectives [16]. Due to the nature of the study setting, patients will be transported from the emergency room to the operating room for emergency surgery, often without full consciousness. The emergency circumstances require prompt action and generally provide insufficient time and opportunity to locate and obtain consent from each patient's legally authorized representative. Therefore we cannot practically carry out the research without the use of delayed consent. Patients who have acute surgery enter the study under presumed consent. Patients are then informed and written consent for continuation in the trial is collected at the fist appropriate time in the postoperative period.

Results

The trial is ongoing. Patient enrollment started in June 2015. We expect to obtain the results of this trial in 2019.

Discussion

We present a study protocol for a randomized controlled trial to assess the effectiveness and safety of NPWT use in the treatment of patients with conflict-related extremity wounds. To the best of our knowledge, there has been no randomized trial of NPWT of wounds in this context. We will disseminate the results through peer-reviewed publications. We expect that the findings will increase the knowledge to establish best-treatment strategies.

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Authors' Contributions

AÄ and JM take primary responsibility for the design of the analysis plan. All authors made substantial contributions to the conception and design of the research and to the revision of the manuscript, and have read and approved the final manuscript.

Conflicts of Interest

None declared.

References

1. Brennan RJ, Burkle FM, Burkholder BT, Lillibridge SR. Wartime civilian injuries: epidemiology and intervention strategies. J Trauma 1998 Jul;45(1):175-176. [Medline: 9680037]

2. Schoenfeld AJ, Dunn JC, Bader JO, Belmont PJ. The nature and extent of war injuries sustained by combat specialty personnel killed and wounded in Afghanistan and Iraq, 2003-2011. J Trauma Acute Care Surg 2013 Aug;75(2):287-291. [doi: 10.1097/TA.0b013e31829a0970] [Medline: 23887561]
3. Covey DC, Lurate RB, Hatton CT. Field hospital treatment of blast wounds of the musculoskeletal system during the Yugoslav civil war. J Orthop Trauma 2000 May;14(4):278-86; discussion 277. [Medline: 10898201]
4. Fares Y, El-Zaatari M, Fares J, Bedrosian N, Yared N. Trauma-related infections due to cluster munitions. J Infect Public Health 2013 Dec;6(6):482-486 [FREE Full text] [doi: 10.1016/j.jiph.2013.05.006] [Medline: 23999350]
5. Giannou C, Baldan M. War Surgery: Working With Limited Resources in Armed Conflict and Other Situations of Violence. Volume 1. Geneva, Switzerland: International Committee of the Red Cross; 2010 May. URL: https://www.icrc.org/en/doc/assets/files/other/icrc-002-0973.pdf
6. Krug E, Berg L, Lee C, Hudson D, Birke-Sorensen H, Depoorter M, International Expert Panel on Negative Pressure Wound Therapy [NPWT-EP]. Evidence-based recommendations for the use of negative pressure wound therapy in traumatic wounds and reconstructive surgery: steps towards an international consensus. Injury 2011 Feb;42 Suppl 1:S1-12. [doi: 10.1016/S0020-1383(11)00041-6] [Medline: 21316515]
7. Machen S. Management of traumatic war wounds using vacuum-assisted closure dressings in an austere environment. US Army Med Dep J 2007:17-23. [Medline: 20084702]
8. Peck MA, Clouse WD, Cox MW, Bowser AN, Eliason JL, Jenkins DH, et al. The complete management of extremity vascular injury in a local population: a wartime report from the 332nd Expeditionary Medical Group/Air Force Theater Hospital, Balad Air Base, Iraq. J Vasc Surg 2007 Jun;45(6):1197-204; discussion 1204 [FREE Full text] [doi: 10.1016/j.jvs.2007.02.003] [Medline: 17543685]
9. Leininger BE, Rasmussen TE, Smith DL, Jenkins DH, Coppola C. Experience with wound VAC and delayed primary closure of contaminated soft tissue injuries in Iraq. J Trauma 2006 Nov;61(5):1207-1211. [doi: 10.1097/01.ta.0000241150.15342.da] [Medline: 17099530]
10. Hinck D, Franke A, Gatzka F. Use of vacuum-assisted closure negative pressure wound therapy in combat-related injuries--literature review. Mil Med 2010 Mar;175(3):173-181. [Medline: 20358706]
11. Webster J, Scuffham P, Stankiewicz M, Chaboyer WP. Negative pressure wound therapy for skin grafts and surgical wounds healing by primary intention. Cochrane Database Syst Rev 2014 Oct 07(10):CD009261. [doi: 10.1002/14651858.CD009261.pub3] [Medline: 25287701]
12. Iheozor-Ejiofor Z, Newton K, Dumville JC, Costa ML, Norman G, Bruce J. Negative pressure wound therapy for open traumatic wounds. Cochrane Database Syst Rev 2018 Dec 03;7:CD012522. [doi: 10.1002/14651858.CD012522.pub2] [Medline: 29969521]
13. Krasner DL. Managing wound pain in patients with vacuum-assisted closure devices. Ostomy Wound Manage 2002 May;48(5):38-43. [Medline: 12046489]
14. Argenta LC, Morykwas MJ. Vacuum-assisted closure: a new method for wound control and treatment: clinical experience. Ann Plast Surg 1997 Jun;38(6):563-76; discussion 577. [Medline: 9188971]
15. Horan TC, Andrus M, Dudeck MA. CDC/NHSN surveillance definition of health care-associated infection and criteria for specific types of infections in the acute care setting. Am J Infect Control 2008 Jun;36(5):309-332. [doi: 10.1016/j.ajic.2008.03.002] [Medline: 18538699]
16. World Bank country and lending groups. Washington, DC: World Bank Group; 2018. URL: http://data.worldbank.org/about/country-classifications [WebCite Cache ID 72hjXunI0]
17. Syria emergency. Geneva, Switzerland: UNHCR; 2018. URL: http://www.unhcr.org/syria-emergency.html [accessed 2018-11-22] [WebCite Cache ID 747ywUReA]
18. Älgå A, Wong S, Shoaib M, Lundgren K, Giske CG, von Schreeb J, et al. Infection with high proportion of multidrug-resistant bacteria in conflict-related injuries is associated with poor outcomes and excess resource consumption: a cohort study of Syrian patients treated in Jordan. BMC Infect Dis 2018 May 22;18(1):233 [FREE Full text] [doi: 10.1186/s12879-018-3149-y] [Medline: 29788910]
19. Älgå A, Karlow HK, Alrawashdeh M, Wong S, Khankeh H, Stålsby LC. “Reality rarely looks like the guidelines”: a qualitative study of the challenges hospital-based physicians encounter in war wound management. Scand J Trauma Resusc Emerg Med 2018 Jun 27;26(1):52 [FREE Full text] [doi: 10.1186/s13049-018-0517-y] [Medline: 29945644]
20. Nerlander MP, Haweizy RM, Wahab MA, Älgå A, von Schreeb J. Epidemiology of trauma patients from the Mosul Offensive, 2016–2017: results from a dedicated trauma center in Erbil, Iraqi Kurdistan. World J Surg 2018 Oct 24. [doi: 10.1007/s00268-018-4817-1] [Medline: 30357467]
21. Beusenberg M, Orley J. A user's guide to the Self Reporting Questionnaire (SRQ). Geneva, Switzerland: World Health Organization; 1994. URL: http://apps.who.int/iris/bitstream/handle/10665/61113/WHO_MNH_PSF_94.8.pdf

Abbreviations

CONSORT: Consolidated Standards of Reporting Trials
MSF: Médecins Sans Frontières/Doctors Without Borders

NPWT: negative-pressure wound therapy
SRQ-20: 20-item Self Reporting Questionnaire

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Protocol

Efficacy of an Online Self-Help Treatment for Comorbid Alcohol Misuse and Emotional Problems in Young Adults: Protocol for a Randomized Controlled Trial

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Abstract

Background: Alcohol misuse and emotional problems (ie, depression and anxiety) are highly comorbid among Canadian young adults. However, there is a lack of integrated, accessible, and evidence-based treatment options for these young adults.

Objective: The main goal of this study is to develop and test the efficacy of an integrated, online self-help program designed to target both alcohol misuse and emotional problems.

Methods: A two-arm randomized controlled trial design will be used to compare the efficacy of the online integrated treatment to a psychoeducational control group. A target sample of 214 participants will be recruited and randomly assigned to either condition. The integrated treatment will last 8 weeks, and participants will work through 12 modules. Modules will incorporate content based on principles of cognitive behavioral therapy and motivational interviewing. Participants in the control group will receive links to psychoeducational resources and will have access to the full treatment after follow-up. The primary outcome will be the number of Canadian standard drinks consumed in the week leading up the assessment. Secondary outcomes of interest include symptoms of depression, anxiety, alcohol-related problems, quality of life, and use of other drugs. Assessments will be completed at 3 time-points: at baseline, at the end of treatment (ie, 8 weeks), and at follow-up (ie, 24 weeks). Upon completion, data will be analyzed using generalized linear mixed models.

Results: Data collection began in June 2018 and will continue until January 2020. Final study results will be submitted for publication by July 2020.

Conclusions: Currently, there are no integrated treatments designed to target alcohol misuse and the range of emotional problems experienced by young adults. This research stands to provide an effective, accessible (ie, Web-based), and feasible option to treat the many struggling young adults in this country.

Trial Registration: ClinicalTrials.gov ID NCT03406039; https://clinicaltrials.gov/ct2/show/NCT03406039 (Archived by WebCite at http://www.webcitation.org/72fDefnrh)

Registered Report Identifier: PRR1-10.2196/11298

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KEYWORDS

alcohol misuse; anxiety; cognitive behavioral therapy; depression; integrated treatment; mobile phone; motivational interviewing; online; self-help

Introduction

Background

Many young adult Canadians struggle with comorbid alcohol misuse and emotional problems (ie, depression and anxiety). According to national statistics, 3.1 million Canadians consume enough alcohol to place themselves at risk of harm or injury [1]. Existing reports show that 50%-60% of adults with an alcohol use disorder also meet clinical criteria for a depressive or anxiety disorder [2-5]. Prevalence rates of these mental health concerns vary based on the geographic location, with the highest rates of alcohol abuse and emotional problems being reported by people living in rural and Northern communities [1]. In addition, data show that the combinations of alcohol misuse and depression or anxiety are the most frequent mental health comorbidities in general populations [6,7]. We know that this comorbidity results in high disease burden—much more than each disorder separately [6,7]. At the individual level, comorbid alcohol misuse and depression or anxiety are linked to chronic poor health, increased suicidality, marital dysfunction, physical injury, and early mortality [2,8,9]. At a societal level, this comorbidity contributes to overburden on the health care system, high rates of absenteeism and unemployment, and increased legal problems [10]. There is currently a need for effective integrated treatments designed to treat alcohol misuse and co-occurring emotional problems.

This study will design and deliver an online self-help intervention for comorbid alcohol misuse and emotional problems in young adults (aged 18-35 years). This intervention will contain strategies drawn from cognitive behavioral therapy (CBT) and motivational interviewing (MI)—both evidence-based psychotherapies for alcohol misuse and depression or anxiety [11,12]. The main strength is that this intervention will be integrated—meaning that it will target symptoms of both alcohol misuse and depression or anxiety within the same treatment. In addition, the Web-based platform is advantageous relative to face-to-face approaches. We will be able to better reach individuals in rural and Northern communities—where we know that some of the highest rates of alcohol misuse and emotional issues exist. These individuals often have difficulty accessing in-person treatments because of community remoteness. Thus, they may be left to struggle with major mental health concerns and associated harms. Furthermore, young adults may feel less stigma associated with accessing support online. Thus, the proposed treatment has the potential to improve the health and well-being of young adult Canadians and their families.

Current State of Knowledge

Research on integrated treatment is relatively new. This is surprising, given that it has been long understood that alcohol misuse and comorbid emotional problems are associated with a complex clinical presentation [5,8]. Specifically, the presence of an emotional disorder (relative to its absence) contributes to high rates of relapse, greater functional impairment, and poorer responses to treatment among individuals with substantial alcohol problems [5]. Traditional approaches to treating comorbid alcohol misuse and depression or anxiety include sequential or parallel intervention [13,14]. During a sequential approach, clinicians treat the disorder viewed as “primary” first, followed by the treatment of the comorbid condition. Often times, this means that symptoms of emotional problems are not addressed in treatment until an individual achieves some notable period of abstinence from drinking. Thus, in the sequential model, treatment is provided for one disorder at a time—with the more acute disorder (ie, alcohol misuse) taking first priority. The sequential model of intervention remains the most widely used approach to treating alcohol misuse-depression or anxiety comorbidities [14]. In contrast, the parallel model involves treating alcohol misuse and emotional problems separately by two distinct professionals or clinical teams [13,14]. A notable example of this approach would be a person seeing a family doctor for management of antidepressant medications while working with a psychologist to reduce drinking. Therefore, in the parallel model, an individual receives support for alcohol misuse and depression or anxiety simultaneously, but from distinct professionals.

Although still widely used, sequential and parallel approaches are limited as intervention models for comorbid disorders [14]. A sequential approach may be necessary for crisis situations, such as when a person needs hospitalization for alcohol-related seizures or acute suicidality. However, in the absence of an emergency warranting the immediate stabilization of one disorder over the other, sequential treatment may impede the treatment of both disorders [13]. Specifically, sequential treatment does not consider the interconnectedness of alcohol misuse and emotional problems. Moreover, in a parallel treatment model, there is often little communication between professionals independently treating each disorder [14]; this is problematic because professionals often have different case conceptualizations and treatment recommendations. Hence, it is very common for a person to receive conflicting advice and feedback in a parallel treatment approach [14]. Furthermore, it is up to patients to integrate distinct treatment approaches, which is likely difficult because of high rates of cognitive impairment among those with alcohol problems [14]. The limitations of a

parallel approach may lead to adverse patient outcomes, such as frustration, continued mental health challenges, and, in the most extreme case, discontinuation of treatment of both disorders. Overall, attesting to the above limitations, the literature shows that sequential and parallel approaches result in poor treatment outcomes in those struggling with alcohol misuse and comorbid emotional problems [15-17].

Integrated psychological treatments are designed to target symptoms of comorbid disorders within the same intervention [14]. There is a growing interest in combining CBT and MI to treat alcohol misuse and comorbid emotional problems [6,18]. CBT is an evidence-based therapy where the goal is for patients to develop better coping skills for alcohol and mood or anxiety issues [11]. These skills become important when patients have to navigate challenging internal (eg, negative thoughts) and external (eg, stressors) triggers in their daily lives. Meta-analyses show that CBT leads to marked reductions in depression and anxiety symptoms, with effect sizes being moderate-to-large relative to other treatments [11,19]. In addition, relapse rates for depression after CBT tend to be half those of medication treatments [20]. Besides, CBT has been shown to be effective in reducing substance and alcohol use, though effect sizes tend to be smaller relative to the effects found for depression and anxiety [21]. Moreover, MI is an evidence-based psychological intervention, often described as a patient-centered, collaborative approach to help elicit and strengthen motivation for change [22]. The emphasis in MI is to help patients resolve ambivalence about change and, hence, move in a positive direction that is consistent with personal values. Several meta-analyses support the use of MI as a front-line intervention for alcohol misuse, with typical effect sizes being in the moderate-to-large range relative to no treatment [23]. Furthermore, MI has been used to treat depression and anxiety, though the evidence base is comparably smaller than for alcohol misuse [24,25].

Emerging work suggests that combined CBT and MI have synergistic, beneficial effects on both alcohol misuse and comorbid emotional problems within an integrated framework [6]. MI aims to improve patients' motivation for changing problem behaviors. Motivational deficits are common in both alcohol misuse and emotional disorders, and the data show that low motivation for change predicts poor treatment engagement and poor outcomes [22]. By increasing motivation for change using MI, clients may be more willing to engage in the effortful activities of CBT (eg, homework and behavioral activation)—which are essential for building better coping skills. In addition, concurrent MI may help to clarify patients' core values in CBT by developing a discrepancy between current and desired behavior. Thus, from a theoretical perspective, MI and CBT naturally complement each other in the treatment of comorbid alcohol and emotional problems. While this is a relatively new treatment approach, emerging data are promising. Much of the work has focused on testing the usefulness of CBT or MI for alcohol misuse and comorbid depression [6]. Comparatively, there has been much less focus on targeting co-occurring anxiety symptoms in this literature. A recent meta-analysis of 12 RCTs showed that combined integrated CBT or MI (relative to control conditions) reduces alcohol misuse and depressive symptoms [6]. Effect sizes were comparable for subclinical (relative to clinically elevated) symptoms, suggesting that integrated CBT or MI may be beneficial in earlier stages of risk as well. Furthermore, combined CBT or MI has the potential to alleviate co-occurring anxiety symptoms in those with alcohol misuse. However, the usefulness of integrated treatments for the alcohol misuse-anxiety comorbidity remains unexamined.

Rationale and Objectives of the Proposed Study

Current integrated psychological treatments use a traditional face-to-face modality [6]. However, there are distinct advantages of online delivery of integrated treatment among Canadian young adults. First, online interventions would be able to reach young adults from rural and Northern communities. We know from most recent health statistics that the highest rates of alcohol misuse and emotional issues exist in these communities [1]. Second, young adults may be more willing to engage in an online self-help intervention (relative to in-person); this is because an online modality may be associated with reduced shame and stigma—which are known, persistent barriers to seeking treatment among substance abusers [26]. Third, online treatments offer the potential for early intervention [27,28]. Self-guided online interventions may be helpful during a period earlier in the risk pathway when young adults are experiencing moderate (but still subclinical) problems. This may serve to prevent an escalation of clinical disorders later in adulthood. Finally, online interventions could markedly reduce the burden on the mental health care system in Canada. More young people with alcohol misuse and co-occurring emotional problems would be helped for much less cost relative to inpatient treatments. Data show that cost-effective, online interventions reduce alcohol misuse [29], depression [30], and anxiety [31] separately, with effect sizes being comparable to those of in-person treatments.

The goal of the proposed study will be to adapt, implement, and test an integrated, online treatment for alcohol misuse and comorbid emotional problems in young adult Canadians. The intervention will be adapted from a new online integrated treatment developed by collaborators Schaub et al at the Swiss Research Institute for Public Health and Addiction [27] called *Take Care of You*; this intervention is in German and Dutch, and it is the first online integrated treatment for alcohol misuse and depression in young adults. *Take Care of Me* (ie, the current intervention) is an internet-based, self-help program designed to reduce symptoms of alcohol use and emotional problems (ie, depression and anxiety). The treatment combines elements of CBT and MI and is designed to target young adults at risk for developing more severe alcohol misuse, depression, and anxiety should they not receive care. This intervention will be translated into English, and new treatment modules will be added to target anxiety symptoms as well. This is an important and novel expansion of the German-Dutch intervention, given the high co-occurrence of alcohol misuse and anxiety symptoms in clinical and general populations [7,8]. In addition, depression and anxiety symptoms tend to co-occur at high rates in young adults [6]. Accordingly, the proposed study will be a randomized controlled trial (RCT) examining the efficacy of an online, self-help intervention for alcohol misuse and comorbid

emotional problems relative to a psychoeducational control group. We have proposed the following hypotheses:

1. Participants in the integrated treatment condition will show larger reductions in weekly alcohol use (primary outcome) relative to participants in the psychoeducational control group over the 8-week *Take Care of Me* program.
2. Participants in the integrated treatment condition will show larger reductions on measures of alcohol misuse, depression, anxiety, as well as increases in a measure of the quality of life (secondary outcomes) over the 8-week *Take Care of Me* program.
3. Symptom improvements during integrated treatment will be maintained at 6-month follow-up.

Methods

Study Design

A two-arm RCT will be used. Eligible participants will be randomized to either the online integrated treatment condition or the psychoeducational control condition. Assessments will occur before randomization (T0; baseline), at 8 weeks (T1; treatment end), and at 24 weeks (T2; follow-up). The study will not be blinded. Participants will be made aware of which condition they have been assigned to as soon as they complete baseline measures and are deemed eligible. Blinding of researchers is not necessary as they will not be providing treatment to participants.

Recruitment

Recruitment of study participants began in June 2018 and will continue until January 2020. Participants will be recruited through a number of means across the country (Textbox 1). Our main recruitment objective is to recruit across Canada using Web-based advertisements (eg, Google Ads, Kijiji, and Craigslist), contacting student services at major Canadian universities, and through social media (eg, Facebook). The goal is that utilizing Web-based means will ensure that a large sample of Canadian young adults receives the link to the study website. In addition, prominent addiction community services in the province of Manitoba have agreed to assist with recruitment, which will provide access to many individuals struggling with alcohol use problems. Study posters will also be put up at community organizations, hospitals, local university campuses, and popular drinking locations (eg, bars and restaurants). Recruitment rates will be monitored on an ongoing basis (eg, % completing screening relative to % meeting criteria to participate). With regard to our recruitment strategies, one potential drawback is that participants may come primarily from the same place (eg, the same university), creating a homogenous sample. However, our plan is to utilize many different avenues, with the goal of creating as heterogenous a sample as possible. Similarly, it is possible that those recruited through social media may share characteristics that interact with their experience in the program. Utilizing multiple recruitment strategies simultaneously, as well as examining potential moderators upon data analysis, will help mitigate this potential challenge.

Inclusion and Exclusion Criteria

There has been a shift to include heterogeneous samples in RCTs to improve the generalizability of findings to other samples [32]. Therefore, inclusion or exclusion criteria will be kept to a minimum. Our main participant demographic will be young adult Canadians with, at least, moderate alcohol misuse and emotional symptoms. Young adults will be targeted as the highest national rates of drinking are observed among individuals in this age group [33]. Furthermore, we know young adults are at an increased risk of both alcohol-related problems and emotional challenges [6]. Inclusion criteria for participation will be as follows: (1) individuals aged 18-35 years; (2) scores >3 for women and >4 for men on a brief version of the Alcohol Use Disorders Identification Test (AUDIT-C) [33]; (3) self-reporting, at least, moderate depression or anxiety symptoms, or both, indicated by a score >16 on the Center for Epidemiological Studies Depression Scale (CES-D) [34], and a score of >10 on the Generalized Anxiety Disorder Scale (GAD-7) [35]; (4) fluency in English; and (5) having weekly internet access. Individuals will be ineligible to participate if they (1) self-report engaging in other psychological or pharmacological treatments for alcohol misuse or depression or anxiety; (2) report elevated suicidality, defined as scoring greater than “minimal risk” on the P4 Suicidality Screener [36], a widely used measure in RCTs, as well as in primary care settings worldwide; and (3) report current psychosis or mania.

Informed Consent Procedure

Interested participants will be invited to contact the primary investigators for a link to the study website (Figure 1). They will have seen this contact information from any of the recruitment materials that informed them about the study. The website link will include all pertinent information about the study; it will also direct them to the page where they will be able to provide informed consent on the treatment website. Prior to consenting, participants will be informed about the following: the inclusion or exclusion criteria of the study, the potential risks or benefits of completing the intervention, safety arrangements during and after the study, and that participation is voluntary. In addition, they will be told the circumstances under which they should contact their family doctor or another professional from an emergency list that will be accessible at all times via the menu item “Help Me” on the intervention website. They will first be provided with detailed instructions on how to create a user account for the self-help program and be encouraged to contact the researchers should they have any trouble. Informed consent will be demonstrated by checking several boxes, stating that they have read and understood the terms of the research. After participants have provided informed consent, they will be able to register on the study website. They will need to create a username as well as verify their account via email before they can access the website. All data will be encrypted and stored on a Canadian host server. No other personal information will be required to register. After informed consent has been obtained and their account has been verified, they will immediately be asked to complete the baseline assessment measures to determine the eligibility.

Randomization and Trial Flow

Eligible participants will be randomly assigned to either the treatment or control condition using a 1:1 ratio (Figure 1); this will happen automatically on the study website.

Participants will immediately be provided with instructions on the study website once they have been assigned to either group. Participants assigned to the treatment condition will be told that they have been selected to participate in the program and will be provided with instructions on how to proceed. Individuals assigned to the control condition will be provided links to general psychoeducation websites about alcohol and mental illness but told that they would be given full access to the program in 6 months. Assessments will then take place at the end of treatment (ie, T1, 8 weeks) and at follow-up (ie, T2, 24 weeks or 16 weeks after the end of treatment). In addition, participants will be asked to provide brief feedback (eg, helpfulness and enjoyment) about their experience in the program at the follow-up assessment. Participants will be reminded of the assessments at each time-point via email. They will receive automatic reminders about the assessment every 2 days for 1 week until they have completed the assessment. Participants will be compensated with a Can $10 Amazon gift card for each assessment that they complete, for a total potential compensation of Can $30. Participants will be told about the compensation process during informed consent.

Textbox 1. Wording to be used in recruitment emails and advertisements.

Recruitment email

Dear Participant,

You are receiving this e-mail because you may be eligible to participate in an online study being offered to young adults in Canada between the ages of 18 to 35 struggling with alcohol use and anxiety or depression?

The purpose of this study is to test the effectiveness of an 8-week, self-directed online treatment program designed to help you cope with symptoms of alcohol use and anxiety or depression. Over the course of the 8-weeks, you will learn strategies and techniques from 12 different modules to help you cope with these challenges, while also receiving online support from our researchers. Our hope is that by the end of the program, you will experience a reduction in your alcohol use as well as your symptoms of anxiety or depression. During the study, all information you provide will be kept confidential. You will also receive a small honorarium for your participation.

If this sounds like something you would be interested in, please visit the study website at www.takecareofme.ca to sign up. You may also contact either Jona Frohlich or Dr. Matthew Keough at support@takecareofme.ca. This research has been approved by the University of Manitoba Psychology/Sociology Research Ethics Board.

Thank you for your consideration!

*NOTE: You must be fluent in English, have weekly access to the internet, and not currently be in treatment elsewhere in order to participate. You must also be prepared to commit approximately 3 hours/week to the program.

Advertisement

RESEARCH STUDY

Are you between the ages of 18-35 and currently struggling with alcohol use and anxiety or depression?

If so, you may benefit from joining our treatment study about alcohol misuse and emotional problems in young adult Canadians.

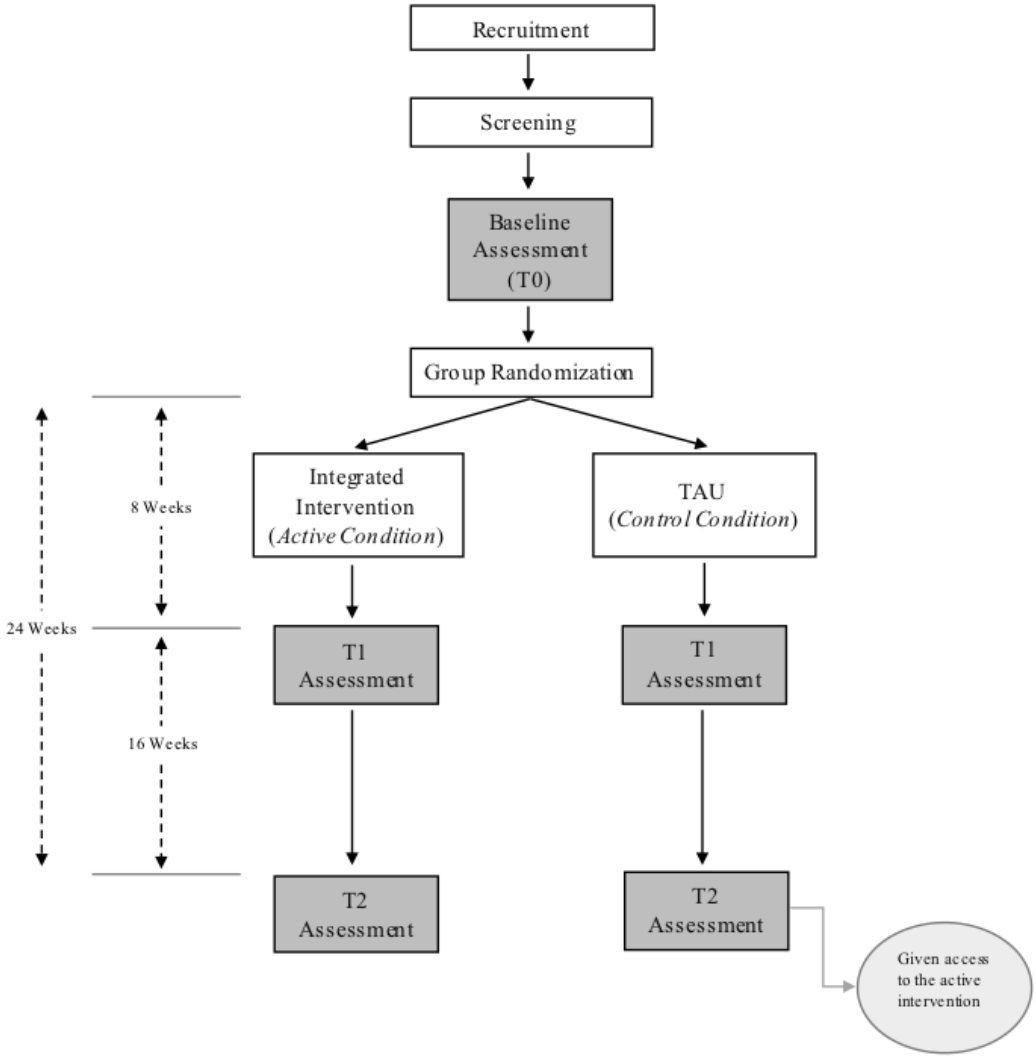
You will be invited to participate in an 8-week, self-directed online treatment program designed to help you cope with symptoms of alcohol use and anxiety or depression. The program consists of 12 modules.

While participating in the online program may be challenging at times, it may also help reduce your alcohol use, as well as improve your emotional well-being. All of the information you provide during your participation in this study will remain confidential. You will also receive a small honorarium for your participation. *NOTE: You must not currently be in treatment elsewhere and be prepared to commit approximately 3 hours/week.

If you have any questions about this research, or for more information, please contact: Dr. Matthew Keough OR Jona Frohlich. Email: support@takecareofme.ca

This research has been approved by the University of Manitoba Psychology/Sociology Research Ethics Board. Concerns can be directed to the Human Ethics Coordinator @ 204-474-8113 or email: humanethics@umanitoba.ca

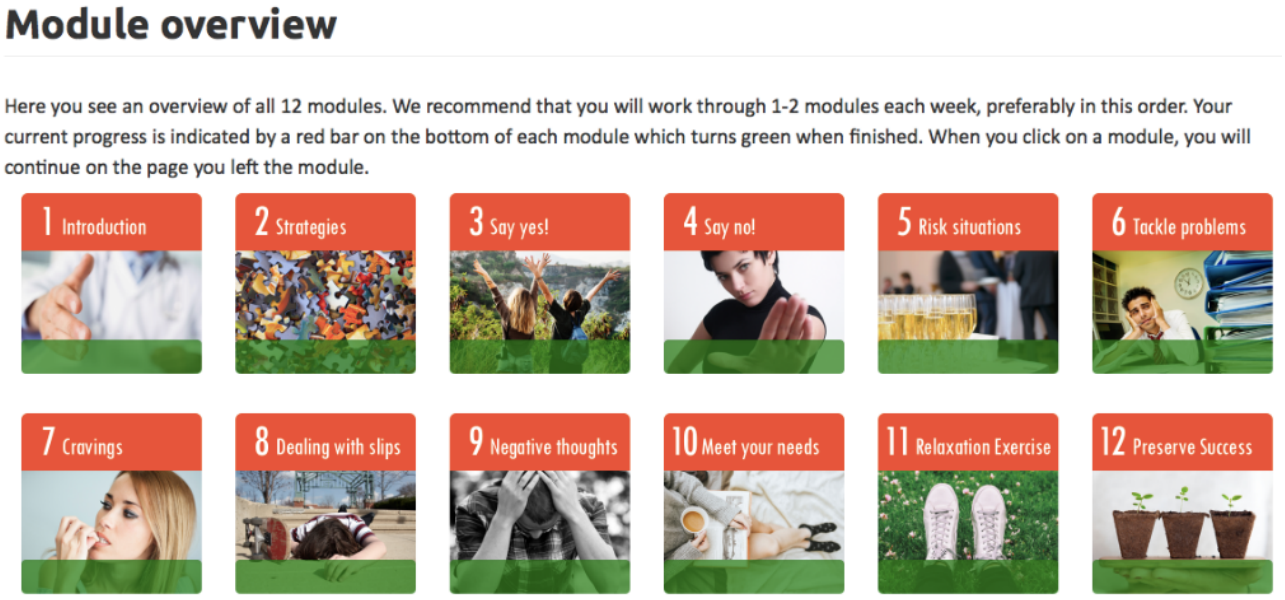
Figure 1. Randomization and trial flowchart. TAU: treatment as usual.



Integrated Treatment (Active Condition)

The website content is a further development of the *Take Care of You* intervention [27] designed for use in English, with added content specific to symptoms of both depression *and* anxiety. The study website includes a dashboard with user information, a diary for participants to track their alcohol use and mood, 12 treatment modules, and a "Help Me" page of additional resources in various Canadian communities. Participants in the treatment condition will have access to 12 treatment modules (Figure 2) and will have 8 weeks to complete the modules. The average amount of text in each module is roughly the same. The content of all modules will be derived from CBT and MI principles (Table 1). For example, through module engagement, young adults will identify goals related to alcohol use and mood; learn strategies to cope with alcohol cravings, triggers, and social pressures; and learn how to prevent relapse. In addition, there will be content to target anxiety and depression, focusing on strategies designed to help reduce negative thinking and worry, increase behavioral activation, and increase self-care (eg, sleep hygiene). While participants can technically access all modules at once, they will be encouraged to work through the modules in sequential order. More specifically, they will be encouraged to complete 1-2 modules per week over the course of 8 weeks. However, they will be able to return to modules more than once or move ahead to modules that may be more relevant in a given moment if they so choose. For example, a participant may jump ahead to the relaxation module if he or she is having strong anxiety symptoms in a given week. Participants will be encouraged to complete the modules as many times as needed, and their progress will be visible on a digital progress bar. Modules will keep the place of participants within a module should they exit the program but want to continue where they left off upon their return. Furthermore, participants will also be asked to track their alcohol use and depression or anxiety symptoms each week. On the "dashboard" intervention page, participants will be able to see a graph depicting treatment progress. The website will automatically adapt for use on smartphones and tablets.

Figure 2. Main menu of intervention modules. Source: takecareofme.ca. Author: Swiss Research Institute for Public Health and Addiction.



Intervention Support Person

The literature shows that adherence to treatment tends to be suboptimal in addiction intervention studies, including both in-person and online modalities [37]. In this study, comorbid emotional symptoms may compound potential issues with treatment adherence. For example, depression is associated with low motivation, and this, in turn, may contribute to difficulties with treatment engagement and homework completion. The support-accountability module [38] posits that these difficulties with adherence, particularly in online programs, may be mitigated by the support of an individual who is viewed as competent, trustworthy, and available. Therefore, an intervention support person (ie, a research assistant) will provide primarily automatic ongoing feedback about module progress, with reminders about completing sections of the intervention. This automatic feedback will also include motivational content that is personalized and signed off by the intervention support person. Textbox 2 shows the examples of this automated motivational content for the first few weeks. Emails of this nature will be sent for the duration of the active treatment condition. Moreover, a research assistant involved in this component of the project will provide support on demand—meaning that they will provide answers to questions when asked specifically by participants through email. Therefore, the use of a research assistant for this purpose will help to reduce the risk of attrition. Consistent with previous research, automatic and personal feedback should also improve adherence, as is commonly observed in self-guided behavior change interventions [38]. It is important to note that the purpose of the intervention support person (ie, research assistant) in this role is not to take the place of a therapist, but rather to answer any questions participants may have as they work their way through the modules, which will be largely administrative. Despite the anticipated benefits of incorporating support of this nature, it is overall not considered equivalent to receiving in-person therapy. However, we will obtain data on the number of emails exchanged for participants in each condition.

Dashboard

The purpose of this page is to provide a main menu where participants can access important information about the program and their progress in one place. On this page, they will be able to see the latest automated message from the research assistant, Deborah, the date on which they started the study, which assessments have been completed, their module progress, and their weekly mood and drinking diary. Furthermore, the dashboard will have an activity portal where participants can log an activity and corresponding mood if they wish.

Social Presence

Each module will begin with a brief introduction video to bring a small social presence to the treatment. Previous research suggests that adding this social factor will personalize the online program and may influence accountability [38], especially considering that it is self-guided. At the outset of treatment, participants will also be asked to select an animated personal companion whom they identify with in terms of sex, age, occupation, and family background. All companions will be fictional, yet relatable. The purpose of this companion is to provide advice and examples pertaining to the content throughout the intervention. The personal companion will appear in each module, at least, once.

Consumption and Mood Diary

Participants in the integrated treatment condition will be asked to track both their weekly alcohol use and mood as they progress through the program. These levels will be displayed on a graph that will be visible to participants at all times. Participants will be able to observe simultaneous changes in alcohol use and negative mood by consistently filling out their diary.

Table 1. Overview of the module content.

Module number and title	Module content
M1: Introduction	• Introduction to intervention • Motivational enhancement (ie, identifying reasons for change and pros and cons of drinking and not drinking) • Self-monitoring alcohol use and mood
M2: Strategies for meeting your goals	• Strategies to change drinking habits, including stimulus control (eg, ridding the home of cues) • Resisting alcohol in specific situations (eg, situations involving negative emotions) • Practicing refusal skills in high-risk situations • Developing personal strategies to reduce or abstain from harmful alcohol use
M3: Say yes!	• Learning about the relationship between mood and behavior • Increasing behavioral activation (ie, scheduling rewarding or pleasurable activities during the week) • Tips for dealing with motivational and implementation problems
M4: Learning to “say no” to alcohol	• Learning about the various ways to say no to alcohol • Ways to resist social pressures to drink • Trying out a few role-plays to practice drinking refusal skills
M5: Identifying risky situations	• Identifying personal high-risk situations for drinking • Learning about “seemingly unimportant decisions” that could lead to heavy drinking
M6: Linking negative emotions and drinking to life problems	• Relating issues with mood or alcohol to problems • The difference between controllable and uncontrollable problems • Formal problem solving (including problem identification, generating possible solutions, evaluating possible solutions, selecting a course of action, and evaluating the implementation of the action plan)
M7: Coping with craving	• Psychoeducation about craving (eg, different forms of craving [mental and physical]) • Introduce self-monitoring of craving • New ways to effectively cope with cravings (eg, distraction, talking, experiencing the craving, and recalling the negative outcomes of drinking)
M8: Dealing with slips	• Define a “slip” versus a full-blown relapse • Introduce ways to cope with slip in mood and drinking
M9: Challenging automatic negative thoughts	• Discuss think the link between thoughts, feelings, behaviors, and bodily sensations • Review common thinking errors (or cognitive distortions) • Introduce balanced thinking • Encourage participants to make links between negative thoughts and drinking • Encourage participants to complete at least one thought record for a problem situation • Identity ways to “test” negative thoughts in real life
M10: Meeting your needs	• Discussing “Sleep Hygiene” • Ruminating and worrying less • Increasing and improving social network
M11: Relaxation exercise	• Key relaxation exercise to reduce anxiety (ie, progressive muscle relaxation) • Deep breathing • Scheduling relaxation times during the week
M12: Preserve your success	• Identify “early warning signs” for slip or relapse • Create personalized relapse prevention plan • Discuss ways to cope with relapse • Identify top five coping strategies

Textbox 2. Examples of automated motivational emails sent to the intervention group by the support person (ie, research assistant).

After 1 week

Subject: First week is Over

Text:

Hi [Participant]!

You survived the first week! Congratulations! We hope you have been feeling well in the last few days.

Tomorrow starts your second week. Please log in today and fill out your diaries on . Fill in how much you drank in the past few days and how much you plan to drink in the upcoming week. Also, please enter your mood ratings for the previous week.

At this time, we would also like to encourage you to start another module if you haven't yet done so. The more modules you do, the more likely you are to make progress!

Have a good week,

Deborah

After 2 weeks

Subject: Two weeks so far

Text:

Hello [Participant]

Two weeks have passed. We hope you are doing well and are starting to become familiar with the layout of this treatment program.

Tomorrow starts your third week. Please log in today and fill out your alcohol use and mood diaries on

Fill in how much you drank in the past few days and how much you plan to drink for in upcoming week. Also, Also, please enter your mood ratings for the previous week.

Have a good week,

Deborah

After 3 weeks

Subject: Week 3

Text:

Hello [Participant]!

You've completed three weeks of this course now! You're doing great.

Maybe people in your life have noticed some changes in your behavior, (e.g. that you do not drink as much as you used to). If you encounter people trying to convince you to drink, we suggest you work through Module 4 (Say No).

And as always, don't forget to update your drinking diary with your consumption for last week, as well as your intentions for next week on: [study website]. Also, please enter your mood ratings for the previous week.. Also, please enter your mood ratings for the previous week.

Have a good week,

Deborah

Psychoeducation (Control Condition)

Consistent with similar RCTs conducted in the field [6,27], the control group will receive links to websites that provide general psychoeducation about alcohol and mental illness. Therefore, the control group will be defined as having access to the available Web-based psychoeducational material. Participants assigned to the control group will be told that they cannot utilize the 12 modules right away, but that they can access the said resources in the meantime if they wish, and that they will be provided access to the full intervention at the end of follow-up (ie, 6-months after the first assessment). At both the end of treatment and follow-up, participants assigned to the control condition will be asked which resources they utilized and how many hours they spent, on average, looking at the said resources. This will help support the notion that both knowledge acquisition and time were controlled for (ie, differed between the 2 study arms).

Measures

Table 2 provides a schedule of assessments. Demographic information will include age, biological sex, gender, ethnicity, history, and treatment for any physical or mental conditions, and family history of alcohol use. All self-report questionnaires will be administered through Web.

Table 2. Schedule of assessment measures.

Self-report measures	Baseline (T0)	8 weeks (T1)	24 weeks (T2)
Demographics (eg, age, sex, treatment history, psychiatric or medical history)	✓		
Suicidality (P4 Screener)	✓	✓	✓
Timeline Followback	✓	✓	✓
Center for Epidemiological Studies Depression Scale	✓	✓	✓
Generalized Anxiety Disorder Scale	✓	✓	✓
Alcohol Use Disorder Identification Test	✓	✓	✓
Quality of Life (World Health Organization Quality of Life brief version)	✓	✓	✓
Drug Use (National Institute on Drug Abuse Alcohol, Smoking, and Substance Involvement Screening Test)	✓	✓	✓
Motivation assessment	✓	✓	✓

Primary Outcome

Alcohol use will be assessed using the Timeline Followback (TLFB) procedure at all assessment points (T0-T2). The primary outcome measure will be the number of Canadian standard drinks consumed in the past 7 days prior to the assessment. Standard drinks are defined as a 12-oz can or a bottle of beer, a 5-oz glass of wine, or a 1.5-oz shot of hard liquor. The TLFB procedure has been shown to provide reliable and valid estimates of alcohol use and is widely used in basic [38] and treatment [27] studies.

Secondary Outcomes

Depression

Depression symptoms will be captured at all assessment points (T0-T2) using the CES-D, a 20-item self-report questionnaire. A sum score will be used. The CES-D is one of the most widely used, validated measures of depression severity [34].

Anxiety

Anxiety symptoms will be captured at all assessment points (T0-T2) using the GAD-7. The GAD-7 is a 7-item self-report instrument that measures the severity of anxiety symptoms. A sum score will be used. Studies in the extant literature support its reliability and validity [37].

Alcohol Misuse

The AUDIT is a 10-item self-report measure designed to assess alcohol misuse and will be included in this study as an additional secondary outcome. Overall, the measure provides an indication of both alcohol use and alcohol-related problems. The AUDIT is a widely used, reliable, and valid estimate of alcohol misuse [33] and will be administered at all assessment points (ie, T0, T1, and T2).

Combined Reduction of Alcohol Use and Comorbid Emotional Problems

We will also use a combined outcome to look at clinically significant reductions in alcohol misuse and depression or anxiety. Specifically, a short version of the AUDIT (first 3 items of the full AUDIT, referred to as AUDIT-C) will be used, where scores <3 for women and <4 for men would reflect that participants are no longer drinking hazardously. Similarly, falling below 16 on the CES-D or 10 on the GAD-7 would reflect that participants are no longer experiencing moderate emotional symptoms. A binary outcome will be created for participants scoring below the AUDIT-C cutoff and the cutoff for either depression or anxiety (coded as 1) versus those scoring above cutoffs (coded as 0). Furthermore, the AUDIT-C will be used to determine eligibility during the baseline assessment.

Quality of Life

An additional secondary outcome will be the quality of life. The World Health Organization Quality of Life Assessment (WHOQOL-BREF) is a 26-item self-report measure that assesses functionality in various life domains (eg, “How satisfied are you with your ability to perform your daily living activities?”). A sum score will be used to assess the overall quality of life at all assessments (T0-T2). The WHOQOL-BREF has become one of the most widely used quality of life measures in the literature [39].

Drug Use

Participants’ use of other drugs in addition to alcohol will also be included as a secondary outcome and assessed using the National Institute on Drug Abuse Alcohol, Smoking, and Substance Involvement Screening Test [40]. Examples of these additional substances include cannabis, cocaine, prescription medication, methamphetamine, and opioids. This information will be collected to examine potential transfer effects to other substances.

Motivation

Finally, given the large MI component, participants’ level of motivation will be assessed at all assessment points. The motivation for change will be assessed along 3 dimensions—importance, confidence, and readiness. Participants will be asked how important it is, how confident they are, and how ready they are to change their alcohol use and negative emotions. Each item will be assessed using a single item on a scale ranging from 0 *(Not Important or Confident or Ready)* to 10 *(Very Important or Confident or Ready)*.

Sample Size Calculation

A recent meta-analysis showed that combined CBT and MI resulted in statistically significant reductions in alcohol use and

depressive symptoms, with effect sizes being in the small range for both clinical and subclinical groups (g=0.17-0.27). Data show relatively comparable effect sizes for online and in-person interventions for alcohol misuse and emotional symptoms [29,30]. Therefore, a small effect size (g=0.25) is expected for group differences in alcohol use and emotional symptoms at the end of treatment. Using G*Power, the sample size required to detect a small effect with 80% power, alpha=.05, and a correlation of .50 between repeated measures was N=164. Based on the previous literature using online interventions to target alcohol use and depression [28], approximately 30% of participants are expected to be lost at follow-up. Therefore, to consider attrition, the sample size will be increased to N=214; this will allow for a buffer, should recruitment and attrition pose more of a challenge than anticipated.

Data Analysis Plan

Before hypothesis testing, we will run preliminary analyses (eg, baseline differences and missing data analyses). In addition, we will examine overall group differences in clinically meaningful variables (ie, % below moderate cutoffs on the AUDIT, CES-D, and GAD-7 after treatment and at follow-up). Next, generalized linear mixed models will be used under the framework of intent-to-treat to evaluate the main hypotheses that integrated treatment will result in the largest reductions in alcohol use, depression, and anxiety. The use of generalized linear mixed models is a multilevel modeling technique that is preferable to repeated-measures analysis of variance for pre- and postanalyses, as it will allow us to include all randomized participants in analyses [41]. This results in less bias due to missing follow-up data [41]. However, owing to potential attrition problems, we also plan to conduct a sensitivity analysis to ensure that data are missing at random. Furthermore, primary and secondary outcomes will be tested sequentially in a mixed within- (repeated assessments) and between-subjects (treatment condition) design.

Safety

We are aware of the increased risks associated with recruiting young adults with moderate (and distressing) alcohol misuse and emotional symptoms. We would expect higher base rates of suicidality and self-harming behaviors in these individuals relative to those without these mental health concerns. Accordingly, we will have safeguards to minimize the risk of harm. Young adults who report suicidal ideation and plans during screening will be recommended to visit their local medical professional or hospital for support. In addition, they will be given access to the integrated intervention, but their data will neither be analyzed nor included in the RCT. We will also be monitoring changes in suicidality at each assessment and will direct participants to emergency services if needed. Moreover, participants will have full-time access to a list of mental health services, including community resources, hospitals, and helplines. Supports will also be accessible to participants at all times via the menu item “Help Me” on the intervention website. Finally, participants in the control condition will be given access to the active treatment after the final assessment (6 months). They will receive all elements of the integrated intervention. To maintain transparency, updates will be made on ClinicalTrials.gov at each stage of the research process. Finally, the project has been funded by Research Manitoba, meaning that it has undergone a substantial peer-review process also considering safety aspects right from the beginning (Multimedia Appendices 1 and 2).

Results

The intervention will be designed to adhere to the ethical principles of the Declaration of Helsinki and the Consolidated Standards of Reporting Trials guidelines for internet-based interventions [42]. The study has been granted procedural ethics from the Psychology/Sociology Research Ethics Board at the University of Manitoba, P2017:128 HS21125. All study procedures will be conducted in accordance with this ethics board at the granting institution, who will receive updates of the study status and will immediately be notified when the study is complete. Finally, the intervention is currently registered on ClinicalTrials.gov for traceability (ID: NCT03406039). We will update the status of the intervention at each stage of the study process in accordance with website guidelines.

Primary trial findings will be published in open-access journals so that both the public and policy makers in Canada can learn about and use the intervention. Anonymized study data will be available on request, and interested participants will be provided with a summary of the results once the study is complete. Finally, dissemination will also include providing talks at various community locations, major hospitals and universities, and at public institutions (eg, libraries) to ensure that results are as far-reaching as possible.

Discussion

Principal Findings

High rates of substance use and emotional issues in Canada demonstrate a clear need for additional and more accessible mental health services in the country. In addition, many provinces have considerable rural spread, meaning that several communities are dispersed throughout the province with little access to major city centers; this poses a substantial challenge for providing equal access to mental health care services. Furthermore, young people living in remote communities are at a marked disadvantage, as they seem to be struggling most with substance use and related problems but have limited access to treatment facilities. Thus, the proposed study has the potential to substantially improve the health and well-being of young adults living across the country. Given that we will be targeting young adults (ie, those who are early in the risk pathway), our intervention may help individuals change their mental health trajectories. That is, an early evidence-based intervention may provide “at-risk” young adults effective coping strategies and, therefore, prevent the escalation of problems in the future, thus, resulting in fewer adults with alcohol use and emotional disorders. Furthermore, the intervention stands to provide a cost-effective method (relative to traditional in-person treatments) of improving mental health care delivery to Canadians. Online interventions have the potential to save the government millions of dollars via the reduced burden on the health care system.

Limitations and Mitigation Plan

Intervention studies show substantial variability in attrition rates, depending on the treatment orientation and clinical severity [43,44]. Generally, dropout rates are high in populations with alcohol and substance use disorders—ranging from 21% to 80% [45]. We are aware of this possible influence on attrition. However, regular contact with the intervention support person will likely provide personalized support that is not typical of online interventions; this may reduce dropout. In addition, we will offer participants the possibility to receive a summary report at the end of the study of overall findings. This report will contain information about the effects of the treatment, significant or not, based on aggregate-level data. The combined use of the strategies above will help reduce attrition. An additional limitation of this study is the use of self-report measures in a Web-based format, of which not all have been tested online. However, assessments of this nature remain widely used in clinical research and increasing reliability and validity evidence for these Web-based tools is accumulating in the clinical literature.

Conclusions

The proposed intervention is a potentially effective, cost-friendly means to enhance mental health care delivery to young adults in Canada. Currently, no such treatments exist for young adults in the country who struggle with addiction and comorbid emotional problems. Research wise, the proposed intervention is a novel expansion of the Swiss study. One major new feature will be the inclusion of content that specifically targets anxiety symptoms—which are currently missing from existing online integrated treatments. It is essential to provide young adults with the skills to cope with these emotional problems because both are known triggers for alcohol misuse and both often occur within the same individual. Therefore, by including new skills to target anxiety, we will enhance the therapeutic benefits of our intervention. Overall, the proposed intervention stands to have a substantial positive impact on the lives of young Canadians and on government expenditures related to mental health care.

Acknowledgments

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Conflicts of Interest

MK, MPS, and MB have been involved in the development of both the current and previous versions of the intervention. However, they do not have any financial interest in the outcome of these interventions.

Multimedia Appendix 1

Grant review 1.

[PDF File (Adobe PDF File), 38KB - resprot_v7i11e11298_app1.pdf]

Multimedia Appendix 2

Grant review 2.

[PDF File (Adobe PDF File), 40KB - resprot_v7i11e11298_app2.pdf]

References

1. Government of Canada. Ottawa, ON: Public Health Agency of Canada. The chief public health officer's report on the state of public health in Canada, 2015: Alcohol consumption in Canada URL: http://healthycanadians.gc.ca/publications/department-ministere/state-public-health-alcohol-2015-etat-sante-publique-alcool/alt/state-phac-alcohol-2015-etat-aspc-alcool-eng.pdf [accessed 2018-07-17] [WebCite Cache ID 70y7UbDOT]
2. Stinson FS, Grant BF, Dawson DA, Ruan WJ, Huang B, Saha T. Comorbidity between DSM-IV alcohol and specific drug use disorders in the United States: Results from the National Epidemiologic Survey on Alcohol and Related Conditions. Drug Alcohol Depend 2005 Oct 01;80(1):105-116. [doi: 10.1016/j.drugalcdep.2005.03.009] [Medline: 16157233]
3. Swendsen JD, Merikangas KR. The comorbidity of depression and substance use disorders. Clin Psychol Rev 2000 Mar;20(2):173-189. [Medline: 10721496]
4. Conway KP, Compton W, Stinson FS, Grant BF. Lifetime comorbidity of DSM-IV mood and anxiety disorders and specific drug use disorders: Results from the National Epidemiologic Survey on Alcohol and Related Conditions. J Clin Psychiatry 2006 Feb;67(2):247-257. [Medline: 16566620]
5. Lai HMX, Cleary M, Sitharthan T, Hunt GE. Prevalence of comorbid substance use, anxiety and mood disorders in epidemiological surveys, 1990–2014: A systematic review and meta-analysis. Drug and Alcohol Dependence 2015 Sep;154:1-13. [doi: 10.1016/j.drugalcdep.2015.05.031] [Medline: 26072219]

6. Riper H, Andersson G, Hunter SB, de Wit J, Berking M, Cuijpers P. Treatment of comorbid alcohol use disorders and depression with cognitive-behavioural therapy and motivational interviewing: A meta-analysis. Addiction 2014 Mar;109(3):394-406. [doi: 10.1111/add.12441] [Medline: 24304463]
7. Gadermann AM, Alonso J, Vilagut G, Zaslavsky AM, Kessler RC. Comorbidity and disease burden in the National Comorbidity Survey Replication (NCS-R). Depress Anxiety 2012 May 14;29(9):797-806. [doi: 10.1002/da.21924] [Medline: 22585578]
8. Beidel D, Frueh B, Hersen M, editors. Adult Psychopathology and Diagnosis (7th Edition). Hoboken, NJ: Wiley; 2014.
9. Keough MT, O'Connor RM, Sherry SB, Stewart SH. Context counts: Solitary drinking explains the association between depressive symptoms and alcohol-related problems in undergraduates. Addictive Behaviors 2015 Mar;42:216-221. [doi: 10.1016/j.addbeh.2014.11.031] [Medline: 25486616]
10. Whiteford HA, Ferrari AJ, Degenhardt L, Feigin V, Vos T. The global burden of mental, neurological and substance use disorders: an analysis from the Global Burden of Disease Study 2010. PLoS One 2015;10(2):e0116820 [FREE Full text] [doi: 10.1371/journal.pone.0116820] [Medline: 25658103]
11. Hofmann SG, Asnaani A, Vonk IJJ, Sawyer AT, Fang A. The efficacy of Cognitive Behavioral Therapy: A review of meta-analyses. Cognit Ther Res 2012 Oct 1;36(5):427-440 [FREE Full text] [doi: 10.1007/s10608-012-9476-1] [Medline: 23459093]
12. Vasilaki EI, Hosier SG, Cox WM. The efficacy of motivational interviewing as a brief intervention for excessive drinking: A meta-analytic review. Alcohol Alcohol 2006;41(3):328-335 [FREE Full text] [doi: 10.1093/alcalc/agl016] [Medline: 16547122]
13. DeVido JJ, Weiss RD. Treatment of the depressed alcoholic patient. Curr Psychiatry Rep 2012 Dec;14(6):610-618 [FREE Full text] [doi: 10.1007/s11920-012-0314-7] [Medline: 22907336]
14. Mueser KT, Noordsy DL, Drake RE, Smith LF. Integrated treatment for dual disorders: A guide to effective practice. New York, NY: Guilford Press; 2003.
15. Polcin DL. Issues in the treatment of dual diagnosis clients who have chronic mental illness. Professional Psychology: Research and Practice 1992;23(1):30-37. [doi: 10.1037//0735-7028.23.1.30]
16. Drake RE, Mueser KT, Brunette MF. Management of persons with co-occurring severe mental illness and substance use disorder: Program implications. World Psychiatry 2007 Oct;6(3):131-136 [FREE Full text] [Medline: 18188429]
17. Havassy BE, Shopshire MS, Quigley LA. Effects of substance dependence on outcomes of patients in a randomized trial of two case management models. Psychiatr Serv 2000 May;51(5):639-644. [doi: 10.1176/appi.ps.51.5.639] [Medline: 10783183]
18. Morley KC, Baillie A, Leung S, Sannibale C, Teesson M, Haber PS. Is specialized integrated treatment for comorbid anxiety, depression and alcohol dependence better than treatment as usual in a public hospital setting? Alcohol and Alcoholism 2016 Jul;51(4):402-409. [doi: 10.1093/alcalc/agv131] [Medline: 26672793]
19. Butler AC, Chapman JE, Forman EM, Beck AT. The empirical status of cognitive-behavioral therapy: A review of meta-analyses. Clin Psychol Rev 2006 Jan;26(1):17-31. [doi: 10.1016/j.cpr.2005.07.003] [Medline: 16199119]
20. Magill M, Ray LA. Cognitive-behavioral treatment with adult alcohol and illicit drug users: a meta-analysis of randomized controlled trials. J Stud Alcohol Drugs 2009 Jul;70(4):516-527 [FREE Full text] [Medline: 19515291]
21. Baker AL, Kavanagh DJ, Kay-Lambkin FJ, Hunt SA, Lewin TJ, Carr VJ, et al. Randomized controlled trial of cognitive-behavioural therapy for coexisting depression and alcohol problems: Short-term outcome. Addiction 2010 Jan;105(1):87-99. [doi: 10.1111/j.1360-0443.2009.02757.x] [Medline: 19919594]
22. Miller W, Rollnick S. Motivational interviewing: Helping people change. New York, NY: Guilford Press; 2013.
23. Vasilaki EI, Hosier SG, Cox WM. The efficacy of motivational interviewing as a brief intervention for excessive drinking: A meta-analytic review. Alcohol Alcohol 2006;41(3):328-335 [FREE Full text] [doi: 10.1093/alcalc/agl016] [Medline: 16547122]
24. Arkowitz H, Burke BL. Motivational interviewing as an integrative framework for the treatment of depression. In Arkowitz H, Westra HA, Miller WR, Rollnick S. eds. Motivational interviewing in the treatment of psychological problems. New York: Guilford Press; 2008.
25. Angus LE, Kagan F. Therapist empathy and client anxiety reduction in motivational interviewing: "She carries with me, the experience". J. Clin. Psychol 2009 Nov;65(11):1156-1167. [doi: 10.1002/jclp.20635] [Medline: 19760742]
26. Livingston JD, Milne T, Fang ML, Amari E. The effectiveness of interventions for reducing stigma related to substance use disorders: a systematic review. Addiction 2012 Jan;107(1):39-50 [FREE Full text] [doi: 10.1111/j.1360-0443.2011.03601.x] [Medline: 21815959]
27. Schaub MP, Blankers M, Lehr D, Boss L, Riper H, Dekker J, et al. Efficacy of an internet-based self-help intervention to reduce co-occurring alcohol misuse and depression symptoms in adults: Study protocol of a three-arm randomised controlled trial. BMJ Open 2016 Dec 25;6(5):e011457 [FREE Full text] [doi: 10.1136/bmjopen-2016-011457] [Medline: 27225652]
28. Deady M, Mills KL, Teesson M, Kay-Lambkin F. An online intervention for co-occurring depression and problematic alcohol use in young people: Primary outcomes from a randomized controlled trial. J Med Internet Res 2016 Mar 23;18(3):e71 [FREE Full text] [doi: 10.2196/jmir.5178] [Medline: 27009465]

29. Riper H, Spek V, Boon B, Conijn B, Kramer J, Martin-Abello K, et al. Effectiveness of E-self-help interventions for curbing adult problem drinking: A meta-analysis. J Med Internet Res 2011;13(2):e42 [FREE Full text] [doi: 10.2196/jmir.1691] [Medline: 21719411]
30. Buntrock C, Ebert D, Lehr D, Riper H, Smit F, Cuijpers P, et al. Effectiveness of a web-based cognitive behavioural intervention for subthreshold depression: Pragmatic randomised controlled trial. Psychother Psychosom 2015;84(6):348-358. [doi: 10.1159/000438673] [Medline: 26398885]
31. Saddichha S, Al-Desouki M, Lamia A, Linden IA, Krausz M. Online interventions for depression and anxiety - a systematic review. Health Psychol Behav Med 2014 Jan 1;2(1):841-881 [FREE Full text] [doi: 10.1080/21642850.2014.945934] [Medline: 25750823]
32. Insel T, Cuthbert B, Garvey M, Heinssen R, Pine DS, Quinn K, et al. Research domain criteria (RDoC): Toward a new classification framework for research on mental disorders. Am J Psychiatry 2010 Jul;167(7):748-751. [doi: 10.1176/appi.ajp.2010.09091379] [Medline: 20595427]
33. Statistics Canada. Health fact sheets: Heavy drinking 2015 URL: https://www150.statcan.gc.ca/n1/pub/82-625-x/2017001/article/14765-eng.htm [accessed 2018-07-15]
34. Saunders JB, Aasland OG, Babor TF, de la Fuente JR, Grant M. Development of the Alcohol Use Disorders Identification Test (AUDIT): WHO Collaborative Project on Early Detection of Persons with Harmful Alcohol Consumption--II. Addiction 1993 Jun;88(6):791-804. [Medline: 8329970]
35. Radloff L. The CES-D Scale. Applied Psychological Measurement 1977;1(3):385-401. [doi: 10.1177/014662167700100306]
36. Spitzer RL, Kroenke K, Williams JBW, Löwe B. A brief measure for assessing generalized anxiety disorder: The GAD-7. Arch Intern Med 2006 May 22;166(10):1092-1097. [doi: 10.1001/archinte.166.10.1092] [Medline: 16717171]
37. Dube P, Kurt K, Bair MJ, Theobald D, Williams LS. The p4 screener: Evaluation of a brief measure for assessing potential suicide risk in 2 randomized effectiveness trials of primary care and oncology patients. Prim Care Companion J Clin Psychiatry 2010 Dec;12(6) [FREE Full text] [doi: 10.4088/PCC.10m00978blu] [Medline: 21494337]
38. Keough MT, O'Connor RM, Colder CR. Testing the implicit and explicit cognitions underlying behavioral inhibition system-related drinking in young adults. Alcohol Clin Exp Res 2016 May;40(5):1065-1074. [doi: 10.1111/acer.13036] [Medline: 27059303]
39. Mohr DC, Cuijpers P, Lehman K. Supportive accountability: A model for providing human support to enhance adherence to eHealth interventions. J Med Internet Res 2011;13(1):e30 [FREE Full text] [doi: 10.2196/jmir.1602] [Medline: 21393123]
40. The WHOQOL Group. Development of the World Health Organization WHOQOL-BREF quality of life assessment. The WHOQOL Group. Psychol Med 1998 May;28(3):551-558. [Medline: 9626712]
41. World Health Organization. NIDA-Modified ASSIST-Prescreen V1 URL: http://www.drugabuse.gov/nidamed/screening/nmassist.pdf [accessed 2018-07-16]
42. Preacher KJ, Zyphur MJ, Zhang Z. A general multilevel SEM framework for assessing multilevel mediation. Psychol Methods 2010 Sep;15(3):209-233. [doi: 10.1037/a0020141] [Medline: 20822249]
43. Eysenbach G. CONSORT-EHEALTH: Improving and standardizing evaluation reports of Web-based and mobile health interventions. J Med Internet Res 2011;13(4):e126 [FREE Full text] [doi: 10.2196/jmir.1923] [Medline: 22209829]
44. Brorson HH, Ajo AE, Rand-Hendriksen K, Duckert F. Drop-out from addiction treatment: A systematic review of risk factors. Clin Psychol Rev 2013 Dec;33(8):1010-1024. [doi: 10.1016/j.cpr.2013.07.007] [Medline: 24029221]
45. Murray E, White IR, Varagunam M, Godfrey C, Khadjesari Z, McCambridge J. Attrition revisited: Adherence and retention in a web-based alcohol trial. J Med Internet Res 2013;15(8):e162 [FREE Full text] [doi: 10.2196/jmir.2336] [Medline: 23996958]

Abbreviations

AUDIT-C: Alcohol Use Disorders Identification Test brief version
CBT: cognitive behavioral therapy
CES-D: Center for Epidemiological Studies Depression Scale
GAD-7: Generalized Anxiety Disorder Scale-7th edition
MI: motivational interviewing
RCT: randomized controlled trial
TLFB: Timeline Followback
WHOQOL-BREF: The World Health Organization Quality of Life Assessment brief version

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Protocol

Evaluating the Long-Term Effectiveness of School-Based Depression, Anxiety, and Substance Use Prevention Into Young Adulthood: Protocol for the Climate School Combined Study

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Abstract

Background: Mental health and substance use disorders are the leading causes of global disability in children and youth. Both tend to first onset or escalate in adolescence and young adulthood, calling for effective prevention during this time. The Climate Schools Combined (CSC) study was the first trial of a Web-based combined universal approach, delivered through school classes, to prevent both mental health and substance use problems in adolescence. There is also limited evidence for the cost-effectiveness of school-based prevention programs.

Objective: The aim of this protocol paper is to describe the CSC follow-up study, which aims to determine the long-term efficacy and cost-effectiveness of the CSC prevention program for depression, anxiety, and substance use (alcohol and cannabis use) up to 7 years post intervention.

Methods: A cluster randomized controlled trial (the CSC study) was conducted with 6386 participants aged approximately 13.5 years at baseline from 2014 to 2016. Participating schools were randomized to 1 of 4 conditions: (1) control (health education as usual), (2) *Climate Substance Use* (universal substance use prevention), (3) *Climate Mental Health* (universal mental health prevention), or (4) *CSC* (universal substance use and mental health prevention). It was hypothesized that the CSC program would be more effective than conditions (1) to (3) in reducing alcohol and cannabis use (and related harms), anxiety, and depression symptoms as well as increasing knowledge related to alcohol, cannabis, anxiety, and depression. This long-term study will invite

follow-up participants to complete 3 additional Web-based assessments at approximately 5, 6, and 7 years post baseline using multiple sources of locator information already provided to the research team. The primary outcomes include alcohol and cannabis use (and related harms) and mental health symptoms. An economic evaluation of the program will also be conducted using both data linkage as well as self-report resource use and quality of life measures. Secondary outcomes include self-efficacy, social networks, peer substance use, emotion regulation, and perfectionism. Analyses will be conducted using multilevel mixed-effects models within an intention-to-treat framework.

Results: The CSC long-term follow-up study is funded from 2018 to 2022 by the Australian National Health and Medical Research Council (APP1143555). The first follow-up wave commences in August 2018, and the results are expected to be submitted for publication in 2022.

Conclusions: This is the first study to provide a long-term evaluation of combined universal substance use and mental health prevention up to 7 years post intervention. Evidence of sustained benefits into early adulthood would provide a scalable, easy-to-implement prevention strategy with the potential for widespread dissemination to reduce the considerable harms, burden of disease, injury, and social costs associated with youth substance use and mental disorders.

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KEYWORDS

alcohol abuse; prevention; depression; anxiety; costs and cost analysis; school; eHealth

Introduction

Background

Mental health and substance use disorders are the leading causes of global disability, accounting for 25% of total disability in children and youth [1]. Every year, mental and substance use disorders conservatively cost the Australian community over Aus $12.7 billion [2]. The burden of substance use and mental disorders now account for 1 in every 10 lost years of health globally [3]. The most common mental disorders are anxiety and depression [4,5], with the most commonly used substances in Western countries, such as Australia, being alcohol and cannabis. To reduce the cost and burden of depression, anxiety, and substance use, timely and effective prevention is critical.

Epidemiological studies show that between 40% [6] and 50% [7] of the population in Western countries will suffer from a depressive, anxiety, or substance use disorder during their lifetime. Furthermore, depression, anxiety, and substance use disorders typically emerge before the age of 25 years [8]. From the ages of 13 to 24 years, there is an increased susceptibility for the development of depression, anxiety, and substance use disorders. Longitudinal life course studies show that transitions from childhood to adolescence and from adolescence to young adulthood are marked by significant increases in anxiety disorders, depression, and substance use disorders [9]. In addition, even small elevations in mental health symptoms in adolescence increase the likelihood of developing a full-blown mental disorder later in life [10]. Substance use during adolescence is also a significant global problem, resulting in a number of adverse outcomes including violence, accidental injury, self-harm, suicide, and an increased risk of developing mental illness [11]. Although the majority of adolescents will not meet criteria for a full-blown substance use disorder [12], a substantial portion will use alcohol at harmful levels [13]. Data from nationally representative surveys consistently show rates of substance use (namely alcohol use) increase steeply between the ages of 13 and 18 years [14-16]. In the general population, approximately 25% of people with a substance use, anxiety, or mood disorder will experience comorbidity with another class of these disorders in any 12-month period [17]. Of particular concern, individuals with comorbid disorders are harder to treat, suffer a more chronic illness course, and experience poorer outcomes later in life than those with no disorder or single disorders [18,19].

To halt the escalation and associated burden of disease, prevention efforts need to be commenced before the onset and acceleration of substance use, depressive, and anxiety symptoms into well-established patterns and disorders. Adolescence is a key time to do this. School-based programs have been shown to reduce both substance use and depression and anxiety symptoms [20-22]. However, to date, prevention programs tend to target single disorders in isolation, ignoring the comorbidity and common risk factor shared by substance use and mental disorders [23,24]. Until recently, there were no prevention models targeting depression, anxiety, and substance use simultaneously.

Few studies have examined the effectiveness of prevention approaches for substance use, depression, and anxiety beyond secondary school. There is limited evidence from studies in the United States [25,26] that receiving the universal Life Skills Training substance use prevention program in year 6-7 (ages 12-13 years) reduced risk of alcohol-related problems and illicit drug use into early adulthood (ages 18-22 years). Further investigations of the Life Skills Training program have indicated that these reductions in substance use, in turn, demonstrated significant secondary benefits on depression symptoms at the age of 22 years [27]. According to recent reviews, the durability of universal prevention programs for anxiety and depression has not been investigated beyond 4 years post intervention and into the young adult years [28-30]. The secondary effects of prevention for anxiety and depression on substance use are rarely investigated and have been identified as a high priority future direction in prevention research [31]. Moreover, assessment over the longer term for interventions instigated in

adolescence is important as adolescents are increasingly exposed to drugs and alcohol, and personality vulnerabilities are triggered by the unique challenges associated with early adulthood [32].

The Climate School Combined Study: First Randomized Controlled Trial of Simultaneous Universal Prevention for Anxiety, Depression, and Substance Misuse

The Climate School Combined (CSC) study commenced in 2014 as the first randomized controlled trial (RCT) of a combined approach to preventing depression, anxiety, and substance misuse (focusing on alcohol and cannabis) in adolescence [33]. This study was a 4-armed, cluster RCT, in which participating schools were randomly allocated to 1 of 4 conditions: (1) *CSC intervention*; (2) *Climate Schools Substance Use*; (3) *Climate Schools Mental Health*, or (4) Control (health and physical education as usual). Participants allocated to the *CSC* intervention received 18 × 40-min classroom lessons focused on depression, anxiety, alcohol, and cannabis. Each lesson includes both computer-based and manualized classroom activities. The computer-based component is delivered on the Web to individual students who log on to view cartoon storylines that impart information about anxiety and depressive symptoms, alcohol, and cannabis. The classroom activities are delivered by the teacher and aim to reinforce the learning outcomes outlined in the cartoons and allow interactive communication between students. These lessons adopt a harm minimization approach in relation to substance use and utilize cognitive behavioral skills and strategies to assist students in identifying and reducing problematic mental health symptoms. Those allocated to *Climate Schools Substance Use* intervention received 12 × 40-min lessons focused on alcohol and cannabis use, those allocated to the *Climate Schools Mental Health* intervention received 6 × 40-min lessons focused on anxiety and depression, whereas those in the control condition received health education as usual. Further details about the intervention components and groups have been previously reported [33]. The primary aim of the original CSC study was to assess the effectiveness of delivering a comprehensive prevention strategy (the *CSC* intervention) targeting depression, anxiety, and substance use (alcohol and cannabis) in reducing the onset and escalation of mental health symptoms, substance use and related harms, and increasing knowledge in relation to these issues. A total of 71 schools and 6386 students aged 13 to 14 years at baseline participated in the trial. Although the initial phase of the study did not specifically aim to test the cost-effectiveness of the intervention, resource use questions used in cost-effectiveness analysis were included in the study from baseline (2014).

Sustaining Prevention Effects Into Young Adulthood: The Need for Longer-Term Follow-Up

At ages 17 to 18 years, the CSC trial cohort is now nearing early adulthood in 2018. This transition, from adolescence to early adulthood, represents a unique developmental period characterized by numerous personal and social role changes including new social relationships and living arrangements, increased financial and social independence, and pursuit of employment and/or higher education. Along with increased exposure to alcohol and cannabis during this period, mental health symptoms often become more pronounced with the onset of new challenges, increased autonomy, and formation of new friendship circles. A review of longitudinal epidemiological studies focusing on the transition from adolescence to young adulthood found that rates of any mental or substance use disorder more than doubled, as did the use of illicit drugs [9]. Specifically, substance use, anxiety, and depression begin to increase in adolescence and continue to increase significantly into early adulthood [34-36].

Despite evidence demonstrating that school-based prevention efforts can interrupt the trajectory of growth in substance use and mental health symptoms during adolescence [21,22,37], very little research has focused on whether these effects can be sustained into the critical period of young adulthood [38]. The majority of existing prevention programs have a very limited evidence base beyond 3 years [22,38,39]. It is therefore unclear whether prevention effects are sustained into young adulthood, when adult vocational and social roles are established, and rates of substance use and mental health problems are highest. Even small disruptions have potentially significant economic consequences, with economic modeling suggesting that even modest long-term reductions in substance use would lead to substantial societal benefits [40]. Evaluation of long-term outcomes and cost-effectiveness of school-based prevention programs for substance use, anxiety, and depression is a critical knowledge gap, and the long-term effectiveness of combining mental health and substance use prevention is unknown.

The Climate Schools Combined Long-Term Follow-Up Study

The CSC long-term follow-up study will be the first in the world to examine the long-term effectiveness of a combined approach to the universal prevention of anxiety, depression, and substance use disorders delivered on the Web. It will extend the follow-up of the existing CSC cohort by an additional 3 time points (5, 6, and 7 years post initial baseline assessment in 2014). There is limited evidence to suggest that when delivered in isolation, mental health and substance use prevention programs have secondary benefits on comorbid conditions [41,42]. This suggests the possibility of powerful multiplicative effects of mental health and substance use prevention when delivered in combination. This study will provide evidence on the long-term effectiveness of a combined approach to prevent mental health (anxiety and depression) and substance use (alcohol and cannabis) problems and evaluate the cost-effectiveness of such an approach. This combined approach will be compared with mental health and substance use prevention delivered in isolation and to education as usual (a control group). Primary outcomes include alcohol and cannabis use and related harms, and mental health symptoms. An economic evaluation of the program will utilize data linkage as well as self-reported resource use (use of health care staff time, facilities, and consumables) and quality of life measures. By investigating the long-term effects and cost-effectiveness of a combined approach to preventing mental health and substance use problems, this study will provide crucial information about which prevention approaches are most sustainable and whether and when additional booster sessions might be needed. To further understand intervention effects

over the long term, it is important to explore potential moderators and mediators of the intervention. Research has shown that emotion regulation [43], self-efficacy [44], personality domains (such as perfectionism) [45], social networks [46], and broad internalizing and externalizing domains [47] are important factors to consider in relation to substance use and mental health and will be considered as potential moderators and/or mediators in this study.

Cost-Effectiveness of Universal School-Based Prevention

There is limited evidence demonstrating the value for money of school-based programs to prevent depression, anxiety, and minimize substance abuse. An economic evaluation of school-based programs to prevent depression in adolescents aged 11 to 17 years demonstrated that both were cost-effective in an Australian context [48]. However, this was a modeled evaluation limited to the prevention of depression, based on a number of assumptions and used disability-adjusted life years as an outcome measure. A total of 4 cost-benefit analyses evaluated school-based programs to prevent substance use. The benefits of the prevention programs and the monetary benefits of reducing substance use over a lifetime outweighed the costs to deliver the programs in schools [49-51]. However, these were also model-based evaluations and conducted in the United States education and health systems. An economic evaluation conducted alongside an RCT of these interventions has not been undertaken nor has an economic evaluation of a combined Web-based approach to prevent mental and substance use disorders.

Aim

The study will conduct a long-term (7-year) follow-up of the first RCT of a combined Web-based substance use and mental health prevention approach addressing the following research questions:

1. RQ1: Is the combined approach used in the CSC program more effective in the long-term across the transition into early adulthood (ages 18-21 years) compared with: (1) universal substance use prevention (*Climate Substance Use)*, (2) universal mental health prevention (*Climate Mental Health)*, and (3) education as usual (control condition) for:
   - reducing the use and harmful use of alcohol and cannabis
   - reducing overall symptom levels of anxiety and depression
2. RQ2: How cost-effective is a combined approach to prevention over the long-term?

We hypothesize that the combined prevention model (CSC program) will be cost-effective compared with (1) school-based prevention as usual, (2) stand-alone universal school-based substance use prevention, and (3) stand-alone anxiety and depression prevention, where Aus $50,000 per quality-adjusted life year is taken as the benchmark for cost-effectiveness in Australia.

Methods

Ethics Approval and Consent to Participate

The study was approved by the University of Sydney Human Research Ethics Committee, Australia (2018/906), and all participants provided informed consent to participate in the original CSC study. All participants will provide additional informed consent before participating in further follow-up surveys.

Study Design

This trial is registered with the Australian and New Zealand Clinical Trials Registry: 12613000723785. A total of 88 schools from the Australian states of New South Wales, Western Australia, and Queensland were recruited to the CSC trial in 2014. A total of 17 schools withdrew after randomization (primarily due to time constraints). The final cohort at baseline consisted of 6386 year 8 students from 71 schools (mean age 13.5 years [SD 0.6], 54.84% [3502/6386] female, 81.24% [5188/6386] born in Australia). Participating schools were randomized to 1 of 4 conditions: (1) Control (health education as usual), (2) *Climate Substance Use* (universal substance use prevention), (3) *Climate Mental Health* (universal mental health prevention), or (4) *CSC* (universal substance use and mental health prevention). Blocked randomization was used, allocating schools to the 4 conditions in equal ratios in blocks of 4. The CONSORT diagram (see Multimedia Appendix 1) summarizes participant flow and retention rates through the study for each condition. Comprehensive information about the intervention content, delivery, and study design of the original CSC study has been published in the original CSC study protocol [33]. The completed CSC study assessments and timeline for extended follow-up assessments can be seen in Multimedia Appendix 2.

Procedure

The CSC long-term follow-up study will extend data collection up to 7 years post baseline. Using multiple sources of locator information already provided to the research team (eg, email addresses, address, phone number, and Facebook usernames), all participants will be invited to consent to take part in the long-term follow-up and then complete 3 Web-based assessments at approximately 5, 6, and 7 years post baseline. Participants in the state of Queensland complete school 1 year earlier than participants in New South Wales and Western Australia. To collect data from Queensland participants in their first year post school, follow-up will commence in Queensland from August 2018 to January 2019, whereas data collection will run from January 2019 to June 2019 in New South Wales and Western Australia. Participants will consent to take part in the longitudinal follow-up study and provide additional consent to release their Medicare Benefits Schedule and Pharmaceutical Benefits Scheme information to the research team. Subsequent contact with students will be made via email invitation or via school with reminder emails and texts sent once a week for 3 weeks. Those who cannot be reached via email will be contacted via alternative forms of locator information, including short messaging service (SMS) and social media. If no response is received, participants will be followed up via phone calls, and paper surveys will be mailed to their home address. Participants

will be contacted via the locator information provided until a response is received.

"Participants will be directed to the CSC website through a personalized URL to complete written consent procedures and complete the survey (approximately 30-45 min in duration) on the Web. Responses will be deidentified and linked over time using a unique identification code. Participants will be reimbursed Aus $20 in the form of a gift voucher for each survey occasion they complete. A duty of care procedure has been developed and approved by the University of New South Wales Human Research Ethics Committee and will be followed if a participant self-identifies as at risk of harm during the study. This includes automatic emails to participants with detailed information about support services if their response indicates they are at risk of harm.

Sample Size Calculations

Participants for this study come from 6386 students from 71 schools recruited to the original CSC study. Power calculations for the original trial were based on methods developed to detect intervention by time interactions in longitudinal cluster RCTs [52] and ensured adequate power to detect clinically significant differences across groups both in the total sample *and* in each of the 3 states of Australia where recruitment took place. These calculations accounted for 10% dropout at the school level and indicated that 2800 students recruited from 28 schools in each state (for a total of 8400 students) would achieve 80% power to detect a between-group mean difference of 0.15 (at the $P<.05$ level) with 7 measurement occasions. In our original study, we achieved a total sample size of 6386 students. Although this is not sufficient to do analyses at the state level, the total sample size is more than sufficient and far surpasses the 2800 required to detect the expected differences across the whole sample. As initiation and frequency of substance use as well as levels of depression and anxiety increase over the transition to early adulthood [9], larger effect sizes are expected over the longer-term follow-up. Thus, even allowing conservatively for dropout rates of >35%, the proposed follow-up study is adequately powered for the expected size of effect for *Climate Substance Use* ($d=0.15$), *Climate Mental Health* ($d=0.15$), and the *CSC* intervention ($d=0.2$). Power calculations based on the obtained sample, where there were at least 16 schools, and an average of at least 80 students per school in each intervention group show that the power to detect an effect size of $d=0.15$ at the final long-term follow-up would be >90%.

Measures

Where possible, measures have remained consistent from the original CSC study to the long-term follow-up study. Some measures have been amended or updated to be age appropriate as participants transition out of school. Details of all included measures in the long-term follow-up study are outlined below.

Demographic data including gender, age, country of birth, truancy rates, and academic performance were obtained at baseline to determine the equivalence of groups. All follow-up outcomes will be assessed by validated self-report measures, which have been shown to be valid and reliable in adolescent populations [53-55].

Primary Measures

Alcohol Use

Drinking behaviors in the past 6 months will be assessed using an adapted version of the Patterns of Alcohol index [56]. Participants will report the frequency and average quantity of their alcohol consumption in standard drinks, frequency of binge drinking (defined as consuming 5 or more standard drinks on 1 occasion), the maximum number of drinks consumed on 1 occasion, and the proportion of their friends or acquaintances who drink alcohol and drink to get drunk. From this scale, it will be possible to calculate dichotomous variables to determine whether participants have ever had a sip, full serve of alcohol, or binge drunk (consumed 5 or more standard drinks). This questionnaire has been used in previous *Climate Schools* trials [57-59] and allows for comparison with large-scale Australian cohorts. A standard drinks chart will be presented with these items to assist reporting. Emerging symptoms of alcohol use disorder will be screened for by a Diagnostic and Statistical Manual of Mental Disorders-fifth edition (DSM-5) symptom checklist [60]. This 16-item checklist examines the presence of symptoms in the past 12 months as specified in the DSM-5 and includes items such as, "during the past 12 months, have you tried unsuccessfully to reduce your use of alcohol?" Alcohol-related harms will be measured by the 24-item Brief Young Adult Alcohol Consequences Questionnaire [61]. Items capture a wide range of age-appropriate harms from mild (eg, fatigue) to more severe (eg, sexual victimization) consequences during the past year.

Cannabis Use

Cannabis use will be assessed by 4 items from the National Drug and Alcohol Strategy Household Survey (NDSHS) [62]. Items will assess whether participants have ever tried cannabis, their frequency of use in the past 6 months, and proportion of their friends and acquaintances who use cannabis. Emerging symptoms of cannabis use disorder will be screened by a 17-item DSM-5 symptom checklist, which assesses the absence or presence of symptoms in the past 12 months [60].

Other Substance Use

A total of 6 items from the NDSHS [62], allowing for comparison with a large representative group of Australians, will ask participants whether they have ever tried amphetamines, ecstasy, hallucinogens, sedatives, inhalants, or any other substance and their frequency of use in the last 6 months (on a 5-point scale ranging from "none" to "more than five times"). Questions will be presented alongside a table with alternative names for drugs. Cigarette and electronic cigarette use will be measured by 7 questions modified from Barrington-Trimis et al [63]. Questions assess whether participants have ever tried cigarettes or electronic cigarettes, their frequency of use in the past 6 months and 30 days, and the average quantity of cigarettes smoked per day in the past 30 days.

Mental Health Measures

Psychological distress in the past month will be assessed by the Kessler 6 scale [64] and the Distress Questionnaire-5 [60]. Depressive and anxiety symptoms during the past 2 weeks will be measured by the Patient Health Questionnaire-9 modified

for adolescents [65] and the 7-item Generalized Anxiety Disorder scale, respectively [66]. The 3-item Mini Social Phobia Inventory [67] will screen for social phobia, whereas the Community Assessment of Psychic Experiences Positive Scale-15 [68] will measure psychotic-like experiences during the past 3 months. A total of 3 dichotomous questions drawn from the Youth Risk Behavior Surveillance System [69] and 1 question from the Patient Health Questionnaire-9 [65] will assess suicidal ideation in the past 12 months, including thoughts of and plans to attempt suicide.

Resource Utilization

Participants' will be consented for access to Medicare Benefits Schedule and Pharmaceutical Benefits Scheme data providing detailed information on the number and cost of contacts with health care professionals and prescription medications reimbursed through these commonwealth-funded plans. These data will be obtained from the Department of Human Services for up to a 4.5-year period from the date of extraction. A retrospective 12-month questionnaire will also be used to capture resource use outside of Medicare Benefits Schedule and Pharmaceutical Benefits Scheme data, in addition to capturing some overlapping data for those participants who may not agree to this data access. The resource use questionnaire was adapted from the Client Services Receipt Inventory [70] and will assess the frequency of contact with health care professionals, other service utilization (eg, ambulance, self-help materials), overnight medical admissions, use of prescription medications, time off paid and unpaid work, support payments, and living arrangements.

Health-Related Quality of Life

Health outcomes will be assessed by the Child Heath Utility-9D [71], a pediatric health-related quality of life measure providing utility values for economic evaluations, which has been adapted for Australians aged 18 to 29 years [72].

Secondary Measures

Social Networks

All participants completing Web versions of the survey will also complete a social networks survey at each time point consisting of questions adapted from O'Malley et al [73] and Lau-Barraco et al [74]. Participants will be asked to nominate up to 6 people with whom they spent most of their free time with in the past 12 months. For each identified person, participants will be asked to report on this person's demographics, relationships, frequency and mode of contact, perceived mental health symptoms, perceived alcohol consumption, whether they are considered a drinking associate, and relationship closeness. The relationships and closeness between pairs of nominated individuals will also be rated. Although these questions were not included in the original phase of the study, a subsample of participants were asked to nominate their 6 closest friends in their year at school to provide information on their social networks in the original CSC study.

Other Measures

Other secondary measures that will be administered include the following: (1) Bandura's Resistive Self-Regulatory Efficacy Scale [75,76] will examine perceived self-efficacy to resist peer pressure to engage in high-risk activities; (2) the 8-item Frost Multidimensional Perfectionism Scale-Brief to measure perfectionism across 2 dimensions (striving and evaluative concerns) [77]; (3) the 11-item Emotion Regulation Questionnaire to assess individual differences in the use of 2 emotional regulation strategies (reappraisal and suppression) [78]; and (4) the Strengths and Difficulties Questionnaire 18+ to assess both internalizing and externalizing symptoms of participants [79].

Statistical Analysis

Intention-to-treat analyses will be carried out for all primary and secondary outcomes in the trial, including all participants in the groups they were initially randomized to. Multilevel mixed-effects regression models will be used to assess these outcomes. Where appropriate, generalized mixed-effects models will be applied, for example, using logistic regression for dichotomous outcomes.

Multilevel models are able to account for the clustered design of the trial by taking into account the expected correlations between the multiple observations of each participant and between participants in the same school [80]. Multilevel models will include random intercepts for schools and random intercepts and slopes for time for individuals. The best fitting random effects structure for each model will be determined using likelihood ratio tests and model fit statistics such as the Akaike information criterion.

Models will include dummy-coded intervention terms that compare each intervention with the reference control group and time terms reflecting the survey occasion, along with covariates such as gender to adjust for possible confounding. The effects of greatest interest for assessing the effectiveness of the interventions are intervention × time terms that provide baseline-adjusted estimates of how each intervention group has changed relative to control. Interpretable measures of effect size such as odds ratios and standardized mean differences will be calculated for all effects as well their accompanying CIs.

Given that some outcome data are expected to be missing due to loss to follow-up, the analysis must also account for missing data. As mixed-effects models employ maximum likelihood estimation, they produce unbiased estimates when missing data can be assumed to be either missing completely at random or missing at random [81] and are considered to be superior to other strategies for dealing with missing data [82].

Planned Comparisons

The primary aims of the original CSC trial were to assess the efficacy of the combined CSC intervention in comparison with the stand-alone *Climate Substance Use* intervention, *Climate Mental Health* intervention, and standard education received by the control group [83]. Therefore, planned comparisons for each outcome will compare *CSC versus* Control, *CSC versus Climate Mental Health*, and *CSC versus Climate Substance Use* including all participants allocated to each of these intervention groups.

Economic Evaluation

The cost to deliver each intervention will be combined with the additional resources used by participants over the follow-up period to calculate total costs from the Australian health sector and societal perspectives as recommended by current guidelines [84]. Intervention costs will comprise software development, staff, and teacher time to deliver interventions and usual care. Additional health care resources will be valued by applying standard Australian unit costs (ie, Independent Hospital Pricing Authority, Australian Bureau of Statistics wage rates) to the resource use units collected. The combined CSC intervention group will be compared with the stand-alone intervention groups and the control group in terms of both total costs and outcomes as assessed by an incremental cost-effectiveness ratio. Nonparametric bootstrapping will be used to obtain CIs for cost-effectiveness ratios, as parametric techniques are inappropriate for use on skewed variables and ratios. The sensitivity of the results will be tested against the variation in the utility weights and unit cost prices.

Additional Analyses: Moderation of Intervention Effects

To explore possible mechanisms for the interventions' effectiveness, planned moderation analyses will be conducted to examine whether measures of baseline risk moderate the intervention effects. Baseline measures of risk will be investigated in relation to alcohol and other substance use, harms related to substance use, and mental health symptoms.

Results

The CSC long-term follow-up study is funded from 2018 to 2022 by the Australian National Health and Medical Research Council (APP1143555). The first follow-up wave commences in August 2018, and the results are expected to be submitted for publication in 2022.

Discussion

Overall Aim

This paper outlines the study protocol and design of an extended long-term follow-up of the CSC study cohort into late adolescence and early adulthood. The study aims to (1) examine the long-term effectiveness of a combined universal mental health and substance use program (CSC program) in preventing substance use (and related harms) and reducing mental health symptoms up to 7 years post baseline and (2) evaluate the cost-effectiveness of the program over the long term. In addition, we will explore intervention effects on secondary outcomes including self-efficacy, social networks, peer substance use, emotion regulation, and perfectionism into young adulthood as well as key mediators and moderators of intervention effects.

Strengths and Limitations

This study will address a significant gap in knowledge by determining for the first time the longevity of school-based universal prevention for substance use and mental health delivered via the Web into young adulthood as well as conducting 1 of the first cost-effectiveness studies of Web-based prevention for mental health and substance use up to 7 years post baseline. Furthermore, this will be the first study to examine unique effects of combining substance use and mental health prevention over the long term. As with the original CSC study, 2 key limitations of the study are participant attrition and reliance on self-report for the majority of measures. Although follow-up rates for the original CSC study remained relatively high across survey waves (ranging from 67% to 88%), it is anticipated that the addition of a new round of consent and participants transitioning from school to postschool environments in this study will present additional challenges and increase study attrition. Anticipated barriers include incomplete and changing contact details, participant relocation (overseas or interstate for travel, study, or work opportunities), and a lack of follow-up support from teachers as participants complete school. To aid in participant follow-up, a set of detailed follow-up strategies will be developed, including a procedure using a wide range of mediums to contact participants (email, SMS, Facebook, phone calls, and mail out), obtaining contact details from one other person who is likely to know how to contact the participant should their contact details change, and adequately reimbursing participants for their time (Aus $20 reimbursement). Reliance on self-report data for the majority of collected measures may introduce bias related to social desirability, particularly in relation to illegal or risky behaviors such as drug use. Nonetheless, self-reported substance use has been shown to be both reliable and valid [53,54], especially when confidentiality is assured and when young people self administer surveys on the Web [55,85], both of which will occur in this study.

Conclusions

Harms relating to early substance use and development of mental health problems are a serious concern, and the transition into early adulthood represents a key risk period. Despite this, very little is currently known about the effectiveness of school-based prevention programs beyond school age. This study addresses a critical knowledge gap and will indicate if prevention approaches for anxiety, depression, and substance use can have lasting effects. Furthermore, this study will provide a critical economic evaluation of the long-term effects of a combined universal approach to prevent substance use and mental health problems among young people. This knowledge is vital to inform policy both nationally and internationally as economic modeling suggests substantial societal benefit can be gained from even modest reductions in substance use and mental health [48,50,86]. Evidence of sustained benefits into adulthood would provide a scalable and easy-to-implement prevention strategy that could be disseminated immediately, at minimal cost, to reduce the considerable harms, burden of disease, injury, and social costs associated with substance use and mental disorders.

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Conflicts of Interest

MT and NCN are both developers of the Climate Schools programs, as well as the Directors of Climate Schools Pty Ltd, which distributes the Climate Schools programs on a not-for-profit basis.

Multimedia Appendix 1
Consort diagram of the Climate Schools Combined study.
[PDF File (Adobe PDF File)102 KB - resprot_v7i11e11372_app1.pdf]

Multimedia Appendix 2
Completed Climate Schools Combined (CSC) Study assessments and timeline for extended follow-up assessments.
[PDF File (Adobe PDF File)113 KB - resprot_v7i11e11372_app2.pdf]

References

1. Erskine HE, Moffitt TE, Copeland WE, Costello EJ, Ferrari AJ, Patton G, et al. A heavy burden on young minds: the global burden of mental and substance use disorders in children and youth. Psychol Med 2015 May;45(7):1551-1563. [doi: 10.1017/S0033291714002888] [Medline: 25534496]
2. Lee Y, Chatterton ML, Magnus A, Mohebbi M, Le LK, Mihalopoulos C. Cost of high prevalence mental disorders: findings from the 2007 Australian National Survey of Mental Health and Wellbeing. Aust N Z J Psychiatry 2017 Dec;51(12):1198-1211. [doi: 10.1177/0004867417710730] [Medline: 28565923]
3. Patel V, Chisholm D, Parikh R, Charlson FJ, Degenhardt L, Dua T, et al. Addressing the burden of mental, neurological, and substance use disorders: key messages from Disease Control Priorities, 3rd edition. Lancet 2016 Apr 16;387(10028):1672-1685. [doi: 10.1016/S0140-6736(15)00390-6]
4. Kessler RC, Angermeyer M, Anthony JC, De Graaf R, Demyttenaere K, Gasquet I, et al. Lifetime prevalence and age-of-onset distributions of mental disorders in the World Health Organization's World Mental Health Survey Initiative. World Psychiatry 2007 Oct;6(3):168-176 [FREE Full text] [Medline: 18188442]
5. Steel Z, Marnane C, Iranpour C, Chey T, Jackson JW, Patel V, et al. The global prevalence of common mental disorders: a systematic review and meta-analysis 1980-2013. Int J Epidemiol 2014 Apr;43(2):476-493. [doi: 10.1093/ije/dyu038] [Medline: 24648481]
6. Slade T, McEvoy PM, Chapman C, Grove R, Teesson M. Onset and temporal sequencing of lifetime anxiety, mood and substance use disorders in the general population. Epidemiol Psychiatr Sci 2015 Feb;24(1):45-53. [doi: 10.1017/S2045796013000577] [Medline: 24229508]
7. Kessler RC, Berglund P, Demler O, Jin R, Merikangas KR, Walters EE. Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication. Arch Gen Psychiatry 2005 Jun;62(6):593-602. [doi: 10.1001/archpsyc.62.6.593] [Medline: 15939837]
8. Kessler RC, Amminger GP, Aguilar-Gaxiola S, Alonso J, Lee S, Ustün TB. Age of onset of mental disorders: a review of recent literature. Curr Opin Psychiatry 2007 Jul;20(4):359-364 [FREE Full text] [doi: 10.1097/YCO.0b013e32816ebc8c] [Medline: 17551351]
9. Costello EJ, Copeland W, Angold A. Trends in psychopathology across the adolescent years: what changes when children become adolescents, and when adolescents become adults? J Child Psychol Psychiatry 2011 Oct;52(10):1015-1025 [FREE Full text] [doi: 10.1111/j.1469-7610.2011.02446.x] [Medline: 21815892]
10. Fergusson DM, Horwood LJ, Ridder EM, Beautrais AL. Subthreshold depression in adolescence and mental health outcomes in adulthood. Arch Gen Psychiatry 2005 Jan;62(1):66-72. [doi: 10.1001/archpsyc.62.1.66] [Medline: 15630074]
11. Hall WD, Patton G, Stockings E, Weier M, Lynskey M, Morley KI, et al. Why young people's substance use matters for global health. Lancet Psychiatry 2016 Mar;3(3):265-279. [doi: 10.1016/S2215-0366(16)00013-4] [Medline: 26905482]
12. Kessler RC, Avenevoli S, Costello EJ, Georgiades K, Green JG, Gruber MJ, et al. Prevalence, persistence, and sociodemographic correlates of DSM-IV disorders in the National Comorbidity Survey Replication Adolescent Supplement.

Arch Gen Psychiatry 2012 Apr;69(4):372-380 [FREE Full text] [doi: 10.1001/archgenpsychiatry.2011.160] [Medline: 22147808]
13. Johnston LD, O'Malley PM, Miech RA, Bachman JA, Schulenberg JE. Deepblue. 2018. Monitoring the Future national survey results on drug use, 1975-2016: Overview, key findings on adolescent drug use URL: https://deepblue.lib.umich.edu/bitstream/handle/2027.42/142406/Overview%202017%20FINAL.pdf?sequence=1&isAllowed=y [accessed 2018-04-12]
14. White V, Bariola E. National Drug Strategy. Canberra: Drug Strategy Branch, Australian Government Department of Health and Ageing; 2012. Australian secondary school students' use of tobacco, alcohol, and over-the counter and illicit substances in 2011 URL: http://www.nationaldrugstrategy.gov.au/internet/drugstrategy/Publishing.nsf/content/BCBF6B2C638E1202CA257ACD0020E35C/$File/National%20Report_FINAL_ASSAD_7.12.pdf [accessed 2018-04-05] [WebCite Cache ID 72w4BYGfb]
15. White V, Bariola E. National Drug Strategy. Melbourne, Victoria: Centre for Behavioural Research in Cancer, The Cancer Council Victoria; 2016. Australian secondary school students' use of tobacco, alcohol, and over-the-counter and illicit substances in 2011 URL: http://www.nationaldrugstrategy.gov.au/internet/drugstrategy/Publishing.nsf/content/BCBF6B2C638E1202CA257ACD0020E35C/$File/National%20Report_FINAL_ASSAD_7.12.pdf [accessed 2018-10-08] [WebCite Cache ID 731nOyNUy]
16. White V, Williams T. National Drug Strategy. Canberra: Centre for Behavioural Research, Cancer Council Victoria; 2016. Australian secondary school students' use of tobacco, alcohol, and over-the-counter and illicit substances in URL: http://www.nationaldrugstrategy.gov.au/internet/drugstrategy/Publishing.nsf/content/E9E2B337CF94143CCA25804B0005BEAA/$File/National-report_ASSAD_2014.pdf [accessed 2018-10-05] [WebCite Cache ID 72w4Ryhg5]
17. Teesson M, Slade T, Mills K. Comorbidity in Australia: findings of the 2007 National Survey of Mental Health and Wellbeing. Aust N Z J Psychiatry 2009 Jul;43(7):606-614. [doi: 10.1080/00048670902970908] [Medline: 19530017]
18. Lubman DI, Allen NB, Rogers N, Cementon E, Bonomo Y. The impact of co-occurring mood and anxiety disorders among substance-abusing youth. J Affect Disord 2007 Nov;103(1-3):105-112. [doi: 10.1016/j.jad.2007.01.011] [Medline: 17291589]
19. Brière FN, Rohde P, Seeley JR, Klein D, Lewinsohn PM. Comorbidity between major depression and alcohol use disorder from adolescence to adulthood. Compr Psychiatry 2014 Apr;55(3):526-533 [FREE Full text] [doi: 10.1016/j.comppsych.2013.10.007] [Medline: 24246605]
20. Foxcroft DR, Tsertsvadze A. Universal school-based prevention programs for alcohol misuse in young people. Cochrane Database Syst Rev 2011 May 11(5):CD009113. [doi: 10.1002/14651858.CD009113] [Medline: 21563171]
21. Calear AL, Christensen H. Systematic review of school-based prevention and early intervention programs for depression. J Adolesc 2010 Jun;33(3):429-438. [doi: 10.1016/j.adolescence.2009.07.004] [Medline: 19647310]
22. Corrieri S, Heider D, Conrad I, Blume A, König H, Riedel-Heller SG. School-based prevention programs for depression and anxiety in adolescence: a systematic review. Health Promot Int 2014 Sep;29(3):427-441. [doi: 10.1093/heapro/dat001] [Medline: 23376883]
23. Carragher N, Teesson M, Sunderland M, Newton NC, Krueger RF, Conrod PJ, et al. The structure of adolescent psychopathology: a symptom-level analysis. Psychol Med 2016 Apr;46(5):981-994. [doi: 10.1017/S0033291715002470] [Medline: 26620582]
24. Catalano RF, Fagan AA, Gavin LE, Greenberg MT, Irwin CE, Ross DA, et al. Worldwide application of prevention science in adolescent health. Lancet 2012 Apr 28;379(9826):1653-1664 [FREE Full text] [doi: 10.1016/S0140-6736(12)60238-4] [Medline: 22538180]
25. Spoth R, Trudeau L, Redmond C, Shin C. Replication RCT of early universal prevention effects on young adult substance misuse. J Consult Clin Psychol 2014 Dec;82(6):949-963 [FREE Full text] [doi: 10.1037/a0036840] [Medline: 24821095]
26. Spoth RL, Clair S, Shin C, Redmond C. Long-term effects of universal preventive interventions on methamphetamine use among adolescents. Arch Pediatr Adolesc Med 2006 Sep;160(9):876-882. [doi: 10.1001/archpedi.160.9.876] [Medline: 16953009]
27. Trudeau L, Spoth R, Mason WA, Randall GK, Redmond C, Schainker L. Effects of adolescent universal substance misuse preventive interventions on young adult depression symptoms: mediational modeling. J Abnorm Child Psychol 2016 Feb;44(2):257-268 [FREE Full text] [doi: 10.1007/s10802-015-9995-9] [Medline: 25795013]
28. Corrieri S, Heider D, Conrad I, Blume A, König HH, Riedel-Heller SG. School-based prevention programs for depression and anxiety in adolescence: a systematic review. Health Promot Int 2014 Sep;29(3):427-441. [doi: 10.1093/heapro/dat001] [Medline: 23376883]
29. Stockings E, Degenhardt L, Dobbins T, Lee YY, Erskine HE, Whiteford HA, et al. Preventing depression and anxiety in young people: a review of the joint efficacy of universal, selective and indicated prevention. Psychol Med 2016 Jan;46(1):11-26. [doi: 10.1017/S0033291715001725] [Medline: 26315536]
30. Bennett K, Manassis K, Duda S, Bagnell A, Bernstein GA, Garland EJ, et al. Preventing child and adolescent anxiety disorders: overview of systematic reviews. Depress Anxiety 2015 Dec;32(12):909-918. [doi: 10.1002/da.22400] [Medline: 26282454]
31. O'Neil KA, Conner BT, Kendall PC. Internalizing disorders and substance use disorders in youth: comorbidity, risk, temporal order, and implications for intervention. Clin Psychol Rev 2011 Feb;31(1):104-112. [doi: 10.1016/j.cpr.2010.08.002] [Medline: 20817371]

32. Kendall PC, Kessler RC. The impact of childhood psychopathology interventions on subsequent substance abuse: policy implications, comments, and recommendations. J Consult Clin Psychol 2002 Dec;70(6):1303-1306. [doi: 10.1037/0022-006X.70.6.1303] [Medline: 12472302]
33. Teesson M, Newton NC, Slade T, Chapman C, Allsop S, Hides L, et al. The CLIMATE schools combined study: a cluster randomised controlled trial of a universal internet-based prevention program for youth substance misuse, depression and anxiety. BMC Psychiatry 2014 Feb 05;14:32 [FREE Full text] [doi: 10.1186/1471-244X-14-32] [Medline: 24499060]
34. Hankin BL, Young JF, Abela JR, Smolen A, Jenness JL, Gulley LD, et al. Depression from childhood into late adolescence: influence of gender, development, genetic susceptibility, and peer stress. J Abnorm Psychol 2015 Nov;124(4):803-816 [FREE Full text] [doi: 10.1037/abn0000089] [Medline: 26595469]
35. Beesdo K, Knappe S, Pine DS. Anxiety and anxiety disorders in children and adolescents: developmental issues and implications for DSM-V. Psychiatr Clin North Am 2009 Sep;32(3):483-524 [FREE Full text] [doi: 10.1016/j.psc.2009.06.002] [Medline: 19716988]
36. Hall WD, Patton G, Stockings E, Weier M, Lynskey M, Morley KI, et al. Why young people's substance use matters for global health. Lancet Psychiatry 2016 Mar;3(3):265-279. [doi: 10.1016/S2215-0366(16)00013-4] [Medline: 26905482]
37. Teesson M, Newton NC, Slade T, Carragher N, Barrett EL, Champion KE, et al. Combined universal and selective prevention for adolescent alcohol use: a cluster randomized controlled trial. Psychol Med 2017 Jul;47(10):1761-1770. [doi: 10.1017/S0033291717000198] [Medline: 28222825]
38. Stockings E, Hall WD, Lynskey M, Morley KI, Reavley N, Strang J, et al. Prevention, early intervention, harm reduction, and treatment of substance use in young people. Lancet Psychiatry 2016 Mar;3(3):280-296. [doi: 10.1016/S2215-0366(16)00002-X] [Medline: 26905481]
39. Bennett K, Manassis K, Duda S, Bagnell A, Bernstein GA, Garland EJ, et al. Preventing child and adolescent anxiety disorders: overview of systematic reviews. Depress Anxiety 2015 Dec;32(12):909-918. [doi: 10.1002/da.22400] [Medline: 26282454]
40. Nherera L, Jacklin P. Nice. 2009 Mar. A model to assess the cost-effectiveness of alcohol education developed for NICE public health guidance on personal, social, health and economic (PSHE) education URL: https://www.nice.org.uk/guidance/gid-phg0/documents/pshe-additional-consultation-on-the-evidence-alcohol-cost-effectiveness-modelling-report2 [accessed 2018-10-07] [WebCite Cache ID 730QijMpW]
41. Trudeau L, Spoth R, Mason WA, Randall GK, Redmond C, Schainker L. Effects of adolescent universal substance misuse preventive interventions on young adult depression symptoms: mediational modeling. J Abnorm Child Psychol 2016 Feb;44(2):257-268 [FREE Full text] [doi: 10.1007/s10802-015-9995-9] [Medline: 25795013]
42. O'Neil KA, Conner BT, Kendall PC. Internalizing disorders and substance use disorders in youth: comorbidity, risk, temporal order, and implications for intervention. Clin Psychol Rev 2011 Feb;31(1):104-112. [doi: 10.1016/j.cpr.2010.08.002] [Medline: 20817371]
43. Aldao A, Nolen-Hoeksema S, Schweizer S. Emotion-regulation strategies across psychopathology: a meta-analytic review. Clin Psychol Rev 2010 Mar;30(2):217-237 [FREE Full text] [doi: 10.1016/j.cpr.2009.11.004]
44. Choi HJ, Krieger JL, Hecht ML. Reconceptualizing efficacy in substance use prevention research: refusal response efficacy and drug resistance self-efficacy in adolescent substance use. Health Commun 2013;28(1):40-52 [FREE Full text] [doi: 10.1080/10410236.2012.720245] [Medline: 23330857]
45. Curran T, Hill AP. Perfectionism is increasing over time: a meta-analysis of birth cohort differences from 1989 to 2016. Psychol Bull 2017 Dec 28 Epub ahead of print. [doi: 10.1037/bul0000138] [Medline: 29283599]
46. Jeon KC, Goodson P. US adolescents' friendship networks and health risk behaviors: a systematic review of studies using social network analysis and Add Health data. PeerJ 2015;3:e1052 [FREE Full text] [doi: 10.7717/peerj.1052] [Medline: 26157622]
47. Kotov R, Krueger RF, Watson D, Achenbach TM, Althoff RR, Bagby RM, et al. The Hierarchical Taxonomy of Psychopathology (HiTOP): a dimensional alternative to traditional nosologies. J Abnorm Psychol 2017 May;126(4):454-477. [doi: 10.1037/abn0000258] [Medline: 28333488]
48. Lee YY, Barendregt JJ, Stockings EA, Ferrari AJ, Whiteford HA, Patton GA, et al. The population cost-effectiveness of delivering universal and indicated school-based interventions to prevent the onset of major depression among youth in Australia. Epidemiol Psychiatr Sci 2017 Oct;26(5):545-564. [doi: 10.1017/S2045796016000469] [Medline: 27509769]
49. Caulkins JP, Nicosia N. What economics can contribute to the addiction sciences. Addiction 2010 Jul;105(7):1156-1163 [FREE Full text] [doi: 10.1111/j.1360-0443.2010.02915.x] [Medline: 20331545]
50. Aos S, Lieb R, Mayfield J, Miller M, Pennucci A. Benefits and Costs of Prevention and Early Intervention Programs for Youth.: Washington State Institute for Public Policy; 2004 Sep. URL: http://www.wsipp.wa.gov/ReportFile/881/Wsipp_Benefits-and-Costs-of-Prevention-and-Early-Intervention-Programs-for-Youth_Summary-Report.pdf [WebCite Cache ID 730GAC1jG]
51. Miller T, Hendrie D. Samhsa.: Department of Health and Human Services Pub; 2008. Substance abuse prevention dollars and cents: a cost-benefit analysis URL: https://www.samhsa.gov/sites/default/files/cost-benefits-prevention.pdf [accessed 2018-10-07] [WebCite Cache ID 730Gl0aqJ]

52. Heo M, Leon AC. Sample size requirements to detect an intervention by time interaction in longitudinal cluster randomized clinical trials. Stat Med 2009 Mar 15;28(6):1017-1027 [FREE Full text] [doi: 10.1002/sim.3527] [Medline: 19153969]
53. Del Boca FK, Darkes J. The validity of self-reports of alcohol consumption: state of the science and challenges for research. Addiction 2003 Dec;98 Suppl 2:1-12. [Medline: 14984237]
54. Ramo DE, Liu H, Prochaska JJ. Reliability and validity of young adults' anonymous online reports of marijuana use and thoughts about use. Psychol Addict Behav 2012 Dec;26(4):801-811 [FREE Full text] [doi: 10.1037/a0026201] [Medline: 22082344]
55. Brener ND, Billy JO, Grady WR. Assessment of factors affecting the validity of self-reported health-risk behavior among adolescents: evidence from the scientific literature. J Adolesc Health 2003 Dec;33(6):436-457. [doi: 10.1016/S1054-139X(03)00052-1] [Medline: 14642706]
56. McBride N, Farringdon F, Midford R, Meuleners L, Phillips M. Harm minimization in school drug education: final results of the School Health and Alcohol Harm Reduction Project (SHAHRP). Addiction 2004 Mar;99(3):278-291. [doi: 10.1111/j.1360-0443.2003.00620.x] [Medline: 14982537]
57. Newton N, Andrews G, Teesson M, Vogl LE. Delivering prevention for alcohol and cannabis using the internet: a cluster randomised controlled trial. Prev Med 2009 Jun;48(6):579-584. [doi: 10.1016/j.ypmed.2009.04.009] [Medline: 19389420]
58. Newton NC, Teesson M, Vogl LE, Andrews G. Internet-based prevention for alcohol and cannabis use: final results of the Climate Schools course. Addiction 2010 Apr;105(4):749-759. [doi: 10.1111/j.1360-0443.2009.02853.x] [Medline: 20148791]
59. Vogl L, Teesson M, Andrews G, Bird K, Steadman B, Dillon P. A computerized harm minimization prevention program for alcohol misuse and related harms: randomized controlled trial. Addiction 2009 Apr;104(4):564-575. [doi: 10.1111/j.1360-0443.2009.02510.x] [Medline: 19335655]
60. Batterham PJ, Sunderland M, Carragher N, Calear AL, Mackinnon AJ, Slade T. The Distress Questionnaire-5: population screener for psychological distress was more accurate than the K6/K10. J Clin Epidemiol 2016 Mar;71:35-42. [doi: 10.1016/j.jclinepi.2015.10.005] [Medline: 26464194]
61. Kahler CW, Strong DR, Read JP. Toward efficient and comprehensive measurement of the alcohol problems continuum in college students: the brief young adult alcohol consequences questionnaire. Alcohol Clin Exp Res 2005 Jul;29(7):1180-1189. [doi: 10.1097/01.ALC.0000171940.95813.A5] [Medline: 16046873]
62. 2010 National Drug Strategy Household Survey report.: Australian Institute of Health and Welfare; 2011. URL: https://www.aihw.gov.au/reports/illicit-use-of-drugs/2010-ndshs/contents/table-of-contents [WebCite Cache ID 730HidO5Z]
63. Barrington-Trimis JL, Berhane K, Unger JB, Cruz TB, Huh J, Leventhal AM, et al. Psychosocial factors associated with adolescent electronic cigarette and cigarette use. Pediatrics 2015 Aug;136(2):308-317 [FREE Full text] [doi: 10.1542/peds.2015-0639] [Medline: 26216326]
64. Kessler RC, Andrews G, Colpe LJ, Hiripi E, Mroczek DK, Normand SL, et al. Short screening scales to monitor population prevalences and trends in non-specific psychological distress. Psychol Med 2002 Aug;32(6):959-976. [doi: 10.1017/S0033291702006074] [Medline: 12214795]
65. Johnson JG, Harris ES, Spitzer RL, Williams JB. The patient health questionnaire for adolescents: validation of an instrument for the assessment of mental disorders among adolescent primary care patients. J Adolesc Health 2002 Mar;30(3):196-204. [doi: 10.1016/S1054-139X(01)00333-0] [Medline: 11869927]
66. Spitzer RL, Kroenke K, Williams JB, Löwe B. A brief measure for assessing generalized anxiety disorder: the GAD-7. Arch Intern Med 2006 May 22;166(10):1092-1097. [doi: 10.1001/archinte.166.10.1092] [Medline: 16717171]
67. Ranta K, Kaltiala-Heino R, Rantanen P, Marttunen M. The Mini-Social Phobia Inventory: psychometric properties in an adolescent general population sample. Compr Psychiatry 2012 Jul;53(5):630-637. [doi: 10.1016/j.comppsych.2011.07.007] [Medline: 21944882]
68. Capra C, Kavanagh DJ, Hides L, Scott JG. Current CAPE-15: a measure of recent psychotic-like experiences and associated distress. Early Interv Psychiatry 2017 Dec;11(5):411-417. [doi: 10.1111/eip.12245] [Medline: 25962504]
69. Centers for Disease Control and Prevention. 2018. Youth Risk Behavior Surveillance System 2017 URL: https://www.cdc.gov/healthyyouth/data/yrbs/questionnaires.htm [WebCite Cache ID 730IdX9aB]
70. Beecham J, Knapp M. Costing psychiatric interventions. In: Thornicroft G, Brewin C, Wing J, editors. Measuring Mental Health Needs (Second Edition). London: Gaskell; 1992:179-190.
71. Stevens KJ. Working with children to develop dimensions for a preference-based, generic, pediatric, health-related quality-of-life measure. Qual Health Res 2010 Mar;20(3):340-351. [doi: 10.1177/1049732309358328] [Medline: 20054040]
72. Ratcliffe J, Couzner L, Flynn T, Sawyer M, Stevens K, Brazier J, et al. Valuing Child Health Utility 9D health states with a young adolescent sample: a feasibility study to compare best-worst scaling discrete-choice experiment, standard gamble and time trade-off methods. Appl Health Econ Health Policy 2011;9(1):15-27. [doi: 10.2165/11536960-000000000-00000] [Medline: 21033766]
73. O'Malley AJ, Arbesman S, Steiger DM, Fowler JH, Christakis NA. Egocentric social network structure, health, and pro-social behaviors in a national panel study of Americans. PLoS One 2012;7(5):e36250 [FREE Full text] [doi: 10.1371/journal.pone.0036250] [Medline: 22615760]

74. Lau-Barraco C, Braitman AL, Leonard KE, Padilla M. Drinking buddies and their prospective influence on alcohol outcomes: alcohol expectancies as a mediator. Psychol Addict Behav 2012 Dec;26(4):747-758 [FREE Full text] [doi: 10.1037/a0028909] [Medline: 22732054]
75. Bandura A. Guide for constructing self-efficacy scales. In: Pajares F, Urdan T, editors. Self-Efficacy Beliefs of Adolescents. Greenwich, CT: Information Age Publishing; 2006:307-337.
76. Bandura A, Caprara GV, Barbaranelli C, Gerbino M, Pastorelli C. Role of affective self-regulatory efficacy in diverse spheres of psychosocial functioning. Child Dev 2003;74(3):769-782. [doi: 10.1111/1467-8624.00567] [Medline: 12795389]
77. Burgess AM, Frost RO, DiBartolo PM. Development and validation of the Frost Multidimensional Perfectionism Scale–Brief. J Psychoeduc Assess 2016 Aug 03;34(7):620-633. [doi: 10.1177/0734282916651359]
78. Gross JJ, John OP. Individual differences in two emotion regulation processes: implications for affect, relationships, and well-being. J Pers Soc Psychol 2003;85(2):348-362. [doi: 10.1037/0022-3514.85.2.348] [Medline: 12916575]
79. Goodman R, Meltzer H, Bailey V. The Strengths and Difficulties Questionnaire: a pilot study on the validity of the self-report version. Eur Child Adolesc Psychiatry 1998 Sep;7(3):125-130. [doi: 10.1007/s007870050057] [Medline: 9826298]
80. Fitzmaurice G, Laird N, Ware J. Applied Longitudinal Analysis, 2nd Ed. Hoboken: Wiley; 2011.
81. Hox J. Multilevel Analysis: Techniques and Applications, 2nd Ed. New York: Routledge; 2010.
82. Schafer JL, Graham JW. Missing data: our view of the state of the art. Psychol Methods 2002 Jun;7(2):147-177. [doi: 10.1037/1082-989X.7.2.147] [Medline: 12090408]
83. Newton NC, Teesson M, Barrett EL, Slade T, Conrod PJ. The CAP study, evaluation of integrated universal and selective prevention strategies for youth alcohol misuse: study protocol of a cluster randomized controlled trial. BMC Psychiatry 2012 Aug 20;12:118 [FREE Full text] [doi: 10.1186/1471-244X-12-118] [Medline: 22906138]
84. Sanders GD, Neumann PJ, Basu A, Brock DW, Feeny D, Krahn M, et al. Recommendations for conduct, methodological practices, and reporting of cost-effectiveness analyses: second panel on cost-effectiveness in health and medicine. J Am Med Assoc 2016 Sep 13;316(10):1093-1103. [doi: 10.1001/jama.2016.12195] [Medline: 27623463]
85. Gnambs T, Kaspar K. Disclosure of sensitive behaviors across self-administered survey modes: a meta-analysis. Behav Res Methods 2015 Dec;47(4):1237-1259. [doi: 10.3758/s13428-014-0533-4] [Medline: 25410404]
86. Collins DJ, Lapsley HM. The costs of tobacco, alcohol and illicit drug abuse to Australian society in 2004/05. Canberra: Australian Governement Department of Health and Ageing; 2008. URL: https://www.health.gov.au/internet/drugstrategy/publishing.nsf/Content/34F55AF632F67B70CA2573F60005D42B/$File/mono64.pdf [accessed 2018-04-08] [WebCite Cache ID 730CgJ4tM]

Abbreviations

CSC: Climate Schools Combined
DSM-5: Diagnostic and Statistical Manual of Mental Disorders-fifth Edition
NDSHS: National Drug and Alcohol Strategy Household Survey
RCT: randomized controlled trial
SMS: short messaging service

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Protocol

Patterns of Patients' Interactions With a Health Care Organization and Their Impacts on Health Quality Measurements: Protocol for a Retrospective Cohort Study

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Abstract

Background: Data collected by health care organizations consist of medical information and documentation of interactions with patients through different communication channels. This enables the health care organization to measure various features of its performance such as activity, efficiency, adherence to a treatment, and different quality indicators. This information can be linked to sociodemographic, clinical, and communication data with the health care providers and administrative teams. Analyzing all these measurements together may provide insights into the different types of patient behaviors or more accurately to the different types of interactions patients have with the health care organizations.

Objective: The primary aim of this study is to characterize usage profiles of the available communication channels with the health care organization. The main objective is to suggest new ways to encourage the usage of the most appropriate communication channel based on the patient's profile. The first hypothesis is that the patient's follow-up and clinical outcomes are influenced by the patient's preferred communication channels with the health care organization. The second hypothesis is that the adoption of newly introduced communication channels between the patient and the health care organization is influenced by the patient's sociodemographic or clinical profile. The third hypothesis is that the introduction of a new communication channel influences the usage of existing communication channels.

Methods: All relevant data will be extracted from the Clalit Health Services data warehouse, the largest health care management organization in Israel. Data analysis process will use data mining approach as a process of discovering new knowledge and dealing with processing data extracted with statistical methods, machine learning algorithms, and information visualization tools. More specifically, we will mainly use the k-means clustering algorithm for discretization purposes and patients' profile building, a hierarchical clustering algorithm, and heat maps for generating a visualization of the different communication profiles. In addition, patients' interviews will be conducted to complement the information drawn from the data analysis phase with the aim of suggesting ways to optimize existing communication flows.

Results: The project was funded in 2016. Data analysis is currently under way and the results are expected to be submitted for publication in 2019. Identification of patient profiles will allow the health care organization to improve its accessibility to patients and their engagement, which in turn will achieve a better treatment adherence, quality of care, and patient experience.

Conclusions: Defining solutions to increase patient accessibility to health care organization by matching the communication channels to the patient's profile and to change the health care organization's communication with the patient to a highly proactive one will increase the patient's engagement according to his or her profile.

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KEYWORDS

health communication; population characteristics; eHealth; mHealth; telehealth; health information systems; consumer health informatics; delivery of health care; machine learning

Introduction

Background

Health care organizations and patients communicate with each other using various communication channels [1,2]. Some of these communication channels are traditional: face-to-face meetings with a physician or a nurse, face-to-face interactions with the administrative staff, and phone calls. However, in the past decade, many health care organizations introduced novel methods of digital communication with patients such as text messages, emails, video calls, websites, and mobile apps. The communication channels between the health care organization and its patients have been examined and analyzed in previous studies [3-10].

Data mining and machine learning methodologies have been used to define or redefine clusters of patients according to their state of health and other sociodemographic data [11,12]. Recently, process mining has been used to try to improve communication between consumers and health care providers [13]. However, no studies attempting to cluster patients by combining medical, sociodemographic, or communication characteristics have been conducted and certainly not in a population as large as the one proposed in this study. We expect that such research will improve communication between patients, service providers, and medical organizations and will improve the quality of treatment and treatment effectiveness and responsiveness.

Aims and Objectives

Finding the circumstances and the extent to which different population segments use different communication channels, and specifically, the extent to which usage of newly introduced channels replaces the usage of more traditional channels will help us learn about the effectiveness of these new channels. Tying these population segments' communication behavior with their sociodemographic profiles and health outcomes will help us establish the association between the 3, and it may help drive the hypotheses as to the causation. In addition, identifying communication-based population segments may help health care providers to use the most appropriate channels with each population segment, leading to more efficient and targeted communications, for example, identifying and quantifying the early adopters group will help the health care organization to estimate the usage level of a newly developed communication channel, its effectiveness in driving the intended message, and to some extent, its effect on health outcomes. Accordingly, this will also allow to improve the quality of treatment, treatment effectiveness, and responsiveness.

The aims of this retrospective data study are to assist health care policy makers to improve and personalize the communication between patients and health care professionals (eg, physicians and nurses). Communication improvement includes enhancing the accessibility of health care professionals by expanding the capabilities of current communication channels and introducing new ones. These communications will help to improve patient engagement with the treatment process, increase patient responsiveness to follow-up requirements and treatment, and improve patient experience with health care services. More specifically, the primary aim of this study is to characterize usage profiles in the available communication channels in the Clalit Health Services (Clalit), each one of them without considering the others and then all of them together. The second aim is to establish relationships between communication profiles, sociodemographic, and medical patients' profiles. The main objective is to suggest new ways to encourage the usage of the most appropriate communication channel based on the patient's profile. A secondary objective is to suggest ways for improving communication between the patient and the health care organization mainly through technological means.

Hypotheses

The first hypothesis is that the patient's follow-up and clinical outcomes are influenced by the patient's preferred channel(s) of communication with the health care organization. If this hypothesis is validated, the research will quantify the phenomenon.

The second hypothesis is that the adoption of newly introduced communication channels between the patient and the health care organization is influenced by the patient's sociodemographic and/or clinical profile. If this hypothesis is validated, the research will identify sociodemographic and/or clinical attributes that affect the adoption of newly introduced communication channels.

The third hypothesis is that the introduction of a new communication channel influences the usage of existing communication channels. If this hypothesis is validated, the research will characterize the changes in usage of existing communication channels once a new communication channel is introduced.

Methods

Materials

This is a data-based study that analyzes information stored in Clalit electronic medical records (EMRs) and in logs documenting access to various communication channels between patients and Clalit, such as the internet personal health records, and telephone logs. Researchers have full access to Clalit EMRs and logs on the entire insured population of 4.53 million patients in 2015, which constitute 54% of the Israeli population of 8.38 million as of 2015. Data collected include demographic, clinical, and pharmacological information. In addition, we plan to conduct interviews with a representative sample of the patients to learn directly about the patients' perceptions, their relationship with the various means of communication, patterns of use, and suggestions for improvement. We hope that this survey will provide supplementary information to the one we will receive from analyzing the data.

Clinical data from community and hospital settings and pharmacological data are routinely collected in the data warehouses (DWHs) of the health maintenance organization (HMO) and classified into the appropriate data world (eg, appointment scheduling, consultation with a physician, appointment with a specialist, diagnosis during hospitalization, medical services, and prescriptions). The information recorded includes sociodemographic data (gender, marital status, number of children at home, age, origin, socioeconomic status (SES), and place of residence), medical information (dates of specialist appointment, physician license number and the corresponding specialization, diagnoses, date of each diagnosis, prescriptions, acquisition of prescriptions, laboratory results, and imaging), and communication data (appointment date, date the appointment occurred, time elapsed between the scheduled appointment and the actual appointment, and the way the appointment was scheduled—through a medical secretary, call center, website, or mobile app). All relevant pieces of information include a patient identifier, which allows compiling all data relevant to a specific patient into a single record.

The information to be analyzed is extracted from the EHR DWH of Clalit and includes data collected between 2008 and 2016 for all relevant patients. The long duration of the study will allow us to identify changes in the ways patients interact with the HMO as a function of time and as a function of new communication channels the HMO introduced (eg, website, mobile apps, and the use of the short message service [SMS] text messaging). Accordingly, the patient can start or stop using 1 or more channels to interact with the HMO. The patients included in this study are aged 21 years and over and are members of Clalit for at least 1 year before 2008 and are still alive in 2016. We will focus our study on patients with chronic disease because we want to examine long-term adherence and efficacy. In addition, patients who suffer from 1 chronic disease or more have a high rate of resource consumption. In the United States, for example, 86% of health care spending is devoted to patients with chronic diseases [14]. In particular, we will examine diabetic patients, who in 2001 accounted for about 20% of the patient population [15]. We hope that the study will help optimize the processes in which these patients participate. The incidence of chronic diseases in general and of diabetes in particular is increasing over the years due to several factors, most notably the aging of the Israeli population. According to Clalit data, as of the end of 2014, more than 40% of the insured population had at least 1 diagnosis that is defined as chronic (eg, diabetes, asthma, heart disease, mental illness, and cancer). Patients with diabetes constitute more than 300,000 individuals with our inclusion criteria [16,17]. The profiles that will be found will help define the recommendations and policies that will improve communication with specific subpopulation groups and will increase the effectiveness of treatment and patient adherence. Chronic diseases are not spread uniformly by age; however, given the high cost of treating patients with chronic diseases, we believe it is more useful to concentrate on these patients despite this bias.

Ethics

Ethical approval for the study was granted by the Clalit ethical committee (147-15-COM2; January 26, 2016).

Methodologies

The communication between health care providers (ie, physicians, nurses, hospitals, and more globally, HMOs) and patients is studied by focusing, generally, only on 1 or 2 of the channels [1-12]. To fulfill our research aims and objectives, our analysis will consist of characterizing the usage profiles of existing nontechnological and technological communication channels over a period of 9 years, taking into account that Clalit has added and changed over the time the methods by which patients contact health care professionals (eg, the introduction of Web and mobile apps). Then, the sociodemographic and clinical profiles of each one of the different communication channels' usage profiles will be defined. This will allow us to qualitatively evaluate the influence of the communication profile on patient's engagement and follow-up quality.

As part of the analysis, we will evaluate impacts of new communication channels introduced over the research period. This will allow us to suggest future improvements to the communication between the patient and physician or nurse, with the aim of improving the work processes of the health organization.

This research is based on knowledge discovery in databases (KDD) methodologies [18,19]. KDD is an interdisciplinary discipline that deals with methodologies for the extraction and identification of valid, new, nontrivial patterns of data that have the potential to be useful and understandable [18-20]. The continued increase in the amounts of data available, a product of the unprecedented development of computer and communications technologies over the past two decades, created a unique opportunity to implement KDD methodologies. Data science experts from different disciplines are therefore challenged to find new and effective ways to extract and generate new knowledge from existing data.

In the analysis phase, we will use one-dimensional and multidimensional statistical methods as well as different data mining algorithms. The data mining stage is part of the KDD process and focuses mainly on the discovery of unknown

patterns. For this purpose, we will use and tune, if necessary, data mining [21] and machine learning [22] algorithms for dealing with the multidimensional dataset (ie, sociodemographics, bio-clinical, and communication-related data over time), which will be explored in this study. The patterns found in this stage are then evaluated and interpreted to form the knowledge extracted from the KDD process.

The KDD process that will be developed and implemented in this research includes data collection and integration, early processing and cleaning of data, development and implementation of data mining algorithms to discover new knowledge and a qualitative research [18-20].

Data Acquisition

Clalit DWH is the main source of information the research uses, and a replication for research purposes is updated on a weekly basis. The data extracted from Clalit DWH for each patient comprise the following information:

1. Sociodemographic data
   - Date and country of birth and date of immigration when relevant
   - Date of death (allowing exclusion)
   - Start and end date of membership (allowing exclusion)
   - Gender
   - Ethnic sector (general Jewish, Arab, and ultra-orthodox Jewish)—the ethnic sector is determined according to the clinic at which the member receives primary care medicine. It is computed by the Clalit computer services unit by integrating geostatistical data from the Israeli Central Bureau of Statistics
   - Clinic-level SES (3 categories: low, mid, and high)—the SES is determined according to the clinic at which the member receives primary care medicine. It is computed by the Clalit computer services unit by integrating geostatistical data from the Israeli Central Bureau of Statistics
2. Bio-clinical
   - Body mass index (BMI) category (underweight, normal, overweight, obese, or unknown) [23]
   - Smoking status (current, past, never, or unknown)
   - Last available glycated hemoglobin (HbA_{1c}) measurement reflecting the level of blood sugar control in patient with diabetes
   - Last available lipidemic profiling (high-density lipoprotein, low-density lipoprotein, triglycerides, and total cholesterol)
   - Adjusted clinical groups (ACG) [24]
   - Comorbidities according to the Clalit chronic diseases registry [15]
   - Proportion of days covered by treatment of diabetes when relevant based on purchase of drugs used in diabetes and more particularly by blood glucose lowering drugs excluding insulin (Anatomical Therapeutic Chemical Classification System codes starting with A10B) [25]
3. Communication or contacts with the HMO data
   - Appointments scheduling (through a medical secretary—data available since 2009, call center—data available since 2009, website—since 2011, or mobile app—since 2012)
   - Consultations with a physician or a nurse
   - Hospitalizations
   - Consultations at an emergency department
   - Nonqueue requests (eg, request for periodic checks, prescription renewal, and sick leave certificate) done without visiting but only by sending a request to a physician through a call to a medical secretary or a nurse or by completing a paper or an electronic form
   - Any purchases in a pharmacy of the HMO or purchase related to a prescription in other pharmacies having an agreement with the HMO
   - Prescription renewals by SMS—since 2015.

Data Preprocessing

Data Cleansing

After integrating the data collected and extracted from the Clalit's DWH, we will prepare it for analysis. This stage includes cleansing of the data collected by Clalit's DWH when necessary. The main objective of this phase is to reduce noise by detecting and removing or correcting outliers [26] in the dataset by evaluating the quality of the data [21]. An outlier is a data measurement that is inconsistent with other historical measurement data of the same individual (eg, outlaying height value, an exceptionally high number of consultations with a physician—a few hundred per year-). When a measurement-specific (eg, BMI) algorithm has been developed in-house by Clalit Research Institute (CRI) for epidemiological studies, outlier detection and data correction will be processed using it. For example, an algorithm screens data on BMI, weight, and height, to detect and handle outliers in the recording of 1 of these 3 measurements (eg, due to mistyping). When the CRI algorithms will not be relevant, outliers will be detected with statistical approaches such as median absolute deviation to find outliers (nonparametric due to lack of knowledge regarding the data distribution [27] and/or machine learning algorithms such as k-means [28]).

Data related to communication between patient and Clalit have not yet been fully processed and cleansed before, and accordingly, we may need to develop special cleaning and correction algorithms for these data. If data correction algorithms and/or algorithms that deal with cases of missing information do not exist for any given data in our database [29,30], we will use appropriate machine learning algorithms and/or statistical approaches [31,32] to correct and/or deal with missing data where needed. Examples of potential problems that we might encounter are identifying irrelevant entries (eg, entries related to quality assurance traffic and testing and entries that are not the result of human activity) and lack of full documentation. In addition, interface exposed to the user is a *breathing* interface and changes over time depending on the services that the HMO chooses to provide through the Web-based and app services. A new version of the website, for example, is released every 6 months. Data processing and analysis should reflect these changes.

Data Transformation

Many methods of machine learning and data mining require, as part of the preprocessing phase, a data reformulation such as a new categorization or a new grouping of numerical, categorical, or textual data to reduce the number of values each attribute has [28].

This step involves the use of techniques for reducing the number of dimensions or transduction methods to reduce the number of variables for analysis or to find invariant representations of the data [26,33-35].

For example, if we consider attributes with continuous values such as laboratory tests or clinical measurement having existing and defined scales in the literature, we will reformulate them into categorical values as a part of the dataset dimension reduction. For example, HbA_{1c} values may be divided into 5 categories: excellent control (<6.5%), good control (6.5% to 7.5%), moderate control (7.5% to 8.9%), poor control (≥9%), and not available [36,16].

However, for attributes that do not have predefined scales in the literature or which are specific to Clalit, such as the number of appointments by using the HMO website or the number of visits to a physician per year, we will use the k-means clustering algorithm for discretization purposes in 6 groups of resource consumption: "No" (meaning not consuming of the related resource, so excluded from the k-means run and assigned to this group), "Small," "Small-Moderate," "Moderate," "Moderate-Large," and "Large." The cluster bounds are validated, if necessary, by a domain expert (ie, a public health practitioner having some experience with the Clalit data).

Data Mining

For identifying population clusters, different machine learning methods and algorithms must be used. The main aim is to characterize usage profiles in the available communication channels. Considering the fact that we do not have prior knowledge on the data, we will use unsupervised machine learning algorithms [37-43] and will more particularly focus on k-means [38] and hierarchical clustering [37]. We choose to use these specific algorithms because they are relatively simple to communicate with people having less technical knowledge, such as decision and policy makers of the HMO, which will get the final analysis report and will need to implement its recommendations.

The first data mining goal is to find the number of hidden k clusters in the "Communication/contacts with the HMO data" or in other words, the number of different types of patient communication profiles. This will be performed on the available data of the year 2016 because by that time, data cleansing will be fully performed. As communication channels constantly evolve, we chose the most recent year to be the reference point to which previous years, with less communication channels, are compared with. The "Communication/contacts with the HMO data" of 2016 will be clustered as follows:

1. For each k between 2 and 100, 100 randomly selected samples of 20% of the cohort will be generated
2. For each sample, k-means will be run
3. For each run, the Ray-Turi criterion [44] will be computed
4. The results of the overall Ray-Turi criterion computation will be plotted on a graph
5. The elbow will be manually defined on the previously built plot for finding the relevant k.

Each cluster relates to a type of patient communication. This step allows reducing the patient communication profiles from the number of patients included into the cohort (more than 300,000 if we consider patients with diabetes) to a small one (at most less than a few dozen).

The second data mining goal is to generate a hierarchical clustering of the previously discovered clusters to allow understanding the similarities and dissimilarities between the communication patterns.

Descriptive statistics of sociodemographic, bio-medical, and communication data will be generated for each cluster.

On the basis of the previously built k clusters of "Communication/contacts with the HMO data" of 2016 and the related hierarchical clustering, we will generate descriptive statistics for each patient communication profiles (ie, cluster or set of patients) over the years (2008-2015).

Information Visualization

To provide user-friendly tools to decision and policy makers [45], allowing them to understand the different patient communication profiles and the strengths and weaknesses of each one, we will build heat maps for each year between 2008 and 2016 based on the previously generated hierarchical clustering of 2016 data.

Process Mining

Furthermore, we plan to implement algorithms and approaches from the field of process mining [46] to identify the changes in communication profiles over time, which may be the cause of treatment adherence changes. For example, process mining will allow us to model how patients with a similar communication profile (ie, patients within the same cluster) have changed their communication patterns with the HMO using the following channels:

1. Consulting with physicians and/or nurses
2. Scheduling appointments by using 1 or more of the following channels: through a medical secretary—data available since 2009, call center—data available since 2009, website—since 2011, or mobile app—since 2012
3. Overall interaction with the HMO (using the overall services).

Qualitative Research

Qualitative research of focus groups is the most effective means to fully understand factors that encourage or delay the use of communication interfaces with the health care organization. Focus groups enable the collection of information from a multicultural population [47] and discussion of new ideas that do not arise during personal interviews [48]. We designed the qualitative part of the proposed study based on the guidelines presented by King et al [49]. The qualitative part of the research will include between 1 and 8 focus groups depending on their

usage level of the communications channels with Clalit. Each one of the focus groups will include up to 8 patients from the same area. Participants in the focus groups will be asked to complete a short sociodemographic questionnaire and sign an informed consent form. During the focus group meeting, the group facilitator will record the discussion and make important notes related to the participants' nonverbal communication.

A guideline questionnaire for the focus groups will be constructed with the assistance of experts in the field and relevant literature. This questionnaire will evaluate factors that encourage or delay the use of communication channels with Clalit. The guiding questionnaire will include up to 10 open questions that will facilitate responses providing critical information, for example, "What factors contribute or will contribute to your use of the communication channel X?"; "What factors delay or will delay your usage of communication channel X?"; or "How do you think that communication channel X can be improved?". The guiding questionnaire will be used to explore aspects that are relevant for better understanding the topic and will facilitate expanding the discussion to areas that the participants consider to be most significant.

The discussions in the focus groups will be recorded and transcribed. The transcripts of the focus group discussion will be analyzed in a phenomenological approach that emphasizes the patient's unique and subjective perception through qualitative content analysis [50]. The coding process will begin with open coding (ie, identification of major categories), following by axial coding that results from 1 core phenomenon. Next, the data will be categorized according to this core phenomenon [51] and will be reviewed by external domain experts to ensure objectivity [49]. Sandelowski [52] notes that through qualitative content analysis, researchers can add new information to the existing one and gain new insights. The encoding and analysis will be performed by the principal investigators and the associate investigators, with the same encoding rules for guaranteeing homogeneous and consistent encoding [49]. In cases of disagreement regarding the encoding, an expanded forum will be held in which the majority decision prevails.

Results

This project was funded in 2016, and the research project is scheduled to be completed in 2019.

A preliminary analysis has been performed on the data of the year 2015 related to 309,460 patients with diabetes in 2015, aged 32 years and above, having the disease treated by Clalit for more than 7 years. Overall, 7 main communication patterns have been discovered.

The first cluster is of patients with relatively low contacts with the HMO in comparison with the rest of the population. Patients in these 2 groups tend to be relatively young (median age: 64 years) and less morbid (ACG between 3 and 4). Although patients in the first group tend to have a poor follow-up quality, 21.21% (18,779/88,524) of the patients were missing BMI measurement and 23.09% (20,436/88,524) were missing their HbA_{1c} measurement in 2015; patients in the second cluster have an average follow-up quality: only 7.72% (6228/80,714) of the patients did not perform a BMI measurement and only 10.56% (8527/80,714) did not perform a HbA_{1c} measurement. A possible explanation for this difference may be related to the tendency of the patients in the second group to resort mainly to human contact (face-to-face or by phone).

The next 2 clusters are of early adopters of technology. These diabetic patients interacted in 2015 with Clalit mainly through new digital platforms: the website (first group) or the mobile app (the second group). These patients also tend to use lesser medical services compared with the rest of the population, and their follow-up quality was better than the rest of the population: only 4.64% (1212/26,098) and 6.10% (1593/26,098) of the first group did not perform BMI and HbA_{1c} tests in 2015, respectively, whereas 5.05% (603/11,945) and 6.93% (826/11,945) of the second group did not perform BMI and HbA_{1c} tests in 2015, respectively.

The patients included in the fifth cluster are mainly using nursing services. They also tend not to schedule appointments. This subpopulation has a low SES (40.79%, 14,531/35,624). However, the follow-up of these patients is quite good (with 3.17% [1128/35,624] and 6.05% [2155/35,624] of these patients missing their BMI and HbA_{1c} measurements, respectively). This is a clear effect of the nursing personnel involvement.

Patients in the last 2 clusters tend to be older than the rest of the patient population (aged more than 70 years) and with relatively high morbidity (ACG=5). Patients in the sixth cluster tend to be consumers of medical services that involve access to a human being, whereas patients in the seventh cluster tend to be heavy users of all medical services. They also tend to have one of the best follow-up rates: only 1.64% (825/38,070) and 4.38% (1668/38,070) of the patients in the sixth cluster have missed their BMI and HbA_{1c} measurements, respectively, in 2015, whereas only 4.22% (1203/28,485) and 6.40% (1822/28,485) of the patients in the seventh cluster have missed their BMI and HbA_{1c} measurements, respectively, in 2015.

Discussion

Overview

This research protocol deals with the identification of patient communication profiles. This knowledge will help the health care organization to increase the accessibility of patients to the services the health care organization provides and to improve patients' engagement with the treatment process. This, in turn, may motivate the patient to achieve a better treatment adherence, improve quality of care, and generate better patient experience.

Expected Results and Future Directions

Analysis of communication patterns over time may reveal long-term behavior patterns as well as identify patterns at a higher abstraction level (eg, early adopters of technology and early adopters of services). It should be noted that the research is planned to be performed on data from a period that witnessed a significant yet gradual change in the communication channels Clalit provides its patients. Analyzing the response of the patient population to these changes will hopefully help improve the

available communication channels as well as assist in formulating realistic expectations from the introduction of new communication channels, taking into consideration also the sociodemographic characteristics and clinical constraints as well as their previous communication patterns with the HMO.

By tuning its communication tools to patients' preferences (eg, by translating the user interfaces of the electronic communications tools—website or apps—from Hebrew to other languages such as Arabic, English, Russian, Amharic, French, and Spanish), the health organization would (1) improve and increase accessibility to health care services, achieve better patient engagement and responsiveness to treatment, and improve quality of treatment and treatment experience within existing budgetary constraints and (2) increase patients' engagement with the treatment process by transforming the communication scheme with each patient to a more proactive scheme, so as to better fit their profile.

Strengths and Limitations

Clalit insured and provided medical services to approximately 4.53 million patients in 2015 and is the largest health care provider in Israel. The data available spans all treatment providers including hospitals' end emergency units. Nevertheless, overall ethnic distribution of the Clalit population does not fully reflect the overall Israeli demographic composition. The Clalit members comprise, in comparison with the Israeli general population, (1) a higher proportion of Arabs and a lower proportion of ultra-orthodox members and (2) a higher proportion of members having a low SES.

Another potential limitation is the decision to analyze only patients with diabetes. These patients may exhibit behaviors that are unique to this specific chronic disease and may not be shared by other chronic patients. Nevertheless, diabetes is 1 of the most common chronic diseases, with prevalence of approximately 7% within Clalit's insured population.

Finally, this research is conducted on data of Israeli patients. The structure of the Israeli health care system as well as Israeli culture and norms may affect patients' behavior and may not apply to patients in other geographical locations.

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Conflicts of Interest

None declared.

References

1. Axén I, Bodin L, Bergström G, Halasz L, Lange F, Lövgren PW, et al. Clustering patients on the basis of their individual course of low back pain over a six month period. BMC Musculoskelet Disord 2011 May 17;12:99 [FREE Full text] [doi: 10.1186/1471-2474-12-99] [Medline: 21586117]
2. Rai A, Chen L, Pye J, Baird A. Understanding determinants of consumer mobile health usage intentions, assimilation, and channel preferences. J Med Internet Res 2013 Aug 2;15(8):e149 [FREE Full text] [doi: 10.2196/jmir.2635] [Medline: 23912839]
3. Hoffman AS, Volk RJ, Saarimaki A, Stirling C, Li LC, Härter M, et al. Delivering patient decision aids on the internet: definitions, theories, current evidence, and emerging research areas. BMC Med Inform Decis Mak 2013;13 Suppl 2:S13 [FREE Full text] [doi: 10.1186/1472-6947-13-S2-S13] [Medline: 24625064]
4. Beck F, Richard J, Nguyen-Thanh V, Montagni I, Parizot I, Renahy E. Use of the internet as a health information resource among French young adults: results from a nationally representative survey. J Med Internet Res 2014 May 13;16(5):e128 [FREE Full text] [doi: 10.2196/jmir.2934] [Medline: 24824164]
5. Moick M, Terlutter R. Physicians' motives for professional internet use and differences in attitudes toward the internet-informed patient, physician-patient communication, and prescribing behavior. Med 2 0 2012 Jul 6;1(2):e2 [FREE Full text] [doi: 10.2196/med20.1996] [Medline: 25075230]
6. Kritz M, Gschwandtner M, Stefanov V, Hanbury A, Samwald M. Utilization and perceived problems of online medical resources and search tools among different groups of European physicians. J Med Internet Res 2013 Jun 26;15(6):e122 [FREE Full text] [doi: 10.2196/jmir.2436] [Medline: 23803299]
7. Dugdale DC, Epstein R, Pantilat SZ. Time and the patient-physician relationship. J Gen Intern Med 1999 Jan;14 Suppl 1:S34-S40 [FREE Full text] [doi: 10.1046/j.1525-1497.1999.00263.x] [Medline: 9933493]
8. Weiner JP. Doctor-patient communication in the e-health era. Isr J Health Policy Res 2012 Aug 28;1(1):33 [FREE Full text] [doi: 10.1186/2045-4015-1-33] [Medline: 22929000]
9. Peleg R, Avdalimov A, Freud T. Providing cell phone numbers and email addresses to patients: the physician's perspective. BMC Res Notes 2011 Mar 23;4:76 [FREE Full text] [doi: 10.1186/1756-0500-4-76] [Medline: 21426591]
10. Peleg R, Nazarenko E. Providing cell phone numbers and e-mail addresses to patients: the patient's perspective, a cross sectional study. Isr J Health Policy Res 2012 Aug 28;1(1):32 [FREE Full text] [doi: 10.1186/2045-4015-1-32] [Medline: 22929801]

11. Henao R, Murray J, Ginsburg G, Carin L, Lucas JE. Patient clustering with uncoded text in electronic medical records. AMIA Annu Symp Proc 2013;2013:592-599 [FREE Full text] [Medline: 24551361]
12. Sewitch MJ, Leffondré K, Dobkin PL. Clustering patients according to health perceptions: relationships to psychosocial characteristics and medication nonadherence. J Psychosom Res 2004 Mar;56(3):323-332. [doi: 10.1016/S0022-3999(03)00508-7] [Medline: 15046970]
13. Webster C. EHR business process management: from process mining to process improvement to process usability. 2012 Feb 20 Presented at: Healthcare Systems Process Improvement Conference; February 20, 2012; Las Vegas, USA URL: http://wareflo.com/HSPI2012/ehr-bpm-process-mining-webster-2012-shs-conf.pdf
14. Gerteis J, Izrael D, Deitz D, LeRoy L, Ricciardi R, Miller T, et al. Healthcare Utilization and Costs. In: Multiple Chronic Conditions Chartbook. Rockville, MD: Agency for Healthcare Research and Quality; Apr 2014:7-14.
15. Rennert G, Peterburg Y. Prevalence of selected chronic diseases in Israel. Isr Med Assoc J 2001 Jun;3(6):404-408 [FREE Full text] [Medline: 11433630]
16. Karpati T, Cohen-Stavi CJ, Leibowitz M, Hoshen M, Feldman BS, Balicer RD. Towards a subsiding diabetes epidemic: trends from a large population-based study in Israel. Popul Health Metr 2014 Oct 30;12(1):32 [FREE Full text] [doi: 10.1186/s12963-014-0032-y] [Medline: 25400512]
17. Israel Center for Disease Control. Israel: Ministry of Health; 2017. Highlights of Health in Israel 2016 URL: https://www.health.gov.il/publicationsfiles/highlights_of_health_in_israel2016.pdf [WebCite Cache ID 735U5lE3I]
18. Fayyad U, Piatetsky-Shapiro G, Smyth P. From data mining to knowledge discovery: an overview. In: Advances in knowledge discovery and data mining. CA, USA: American Association for Artificial Intelligence; 1996.
19. Fayyad U, Piatetsky-Shapiro G, Smyth P. The KDD process for extracting useful knowledge from volumes of data. Communications of the ACM 1996 Nov;39(11):27-34 [FREE Full text] [doi: 10.1145/240455.240464]
20. Frawley WJ, Piatetsky-Shapiro G, Matheus C. Knowledge discovery in databases: an overview. AI Mag 1992 Sep;13(3):57-70. [doi: 10.1609/aimag.v13i3.1011]
21. Zaki MJ, Meira Jr W. Data Mining and Analysis: Fundamental Concepts and Algorithms. Cambridge: Cambridge University Press; May 2014.
22. Mitchell TM. Machine Learning. New York, NY, USA: McGraw-Hill, Inc; 1997.
23. National Heart Lung and Blood Institute. The Practical Guide Identification, Evaluation, and Treatment of Overweight and Obesity in Adults URL: https://www.nhlbi.nih.gov/files/docs/guidelines/prctgd_c.pdf [accessed 2018-10-11]
24. Reid RJ, Roos NP, MacWilliam L, Frohlich N, Black C. Assessing population health care need using a claims-based ACG morbidity measure: a validation analysis in the Province of Manitoba. Health Serv Res 2002 Oct;37(5):1345-1364 [FREE Full text] [doi: 10.1111/1475-6773.01029] [Medline: 12479500]
25. WHO Collaborative Centre for Drug Statistics Methodology. 2017. Guidelines for ATC classification and DDD assignment 2018 URL: https://www.whocc.no/filearchive/publications/guidelines.pdf [accessed 2018-10-11] [WebCite Cache ID 735UGNsOl]
26. Ben-Gal I. Outlier Detection. In: Maimon O, Rokach L, editors. Data mining and knowledge discovery handbook. New York, NY: Springer; 2010:117-130.
27. Leys C, Ley C, Klein O, Bernard P, Licata L. Detecting outliers: do not use standard deviation around the mean, use absolute deviation around the median. J Exp Soc Psychol 2013 Jul;49(4):764-766. [doi: 10.1016/j.jesp.2013.03.013]
28. Bansal R, Gaur N, Singh S. Outlier Detection: Applications and techniques in Data Mining. 2016 Presented at: The 6th International Conference - Cloud System and Big Data Engineering (Confluence); January 14-15, 2016; Noida, India URL: https://ieeexplore.ieee.org/document/7508146 [doi: 10.1109/CONFLUENCE.2016.7508146]
29. Rahm E, Do HH. Data cleaning: problems and current approaches. Bull Tech Comm Data Eng 2000 Jan;23(4):3-13 [FREE Full text]
30. Han J, Kamber M, Pei J. Data Mining: Concepts and Techniques. Canada: Elsevier Science; 2011.
31. Escalante HJ. Semanticscholar. 2005. A Comparison of Outlier Detection Algorithms for Machine Learning URL: https://pdfs.semanticscholar.org/cf06/9b7460ce1b5a0434a6a19f420544a780f35d.pdf [accessed 2018-10-11] [WebCite Cache ID 735M1NrEO]
32. Chandola V, Banerjee A, Kumar V. Anomaly detection: a survey. ACM Comput Surv 2009 Jul 1;41(3):1-58. [doi: 10.1145/1541880.1541882]
33. Ahmad T, Pencina MJ, Schulte PJ, O'Brien E, Whellan DJ, Piña IL, et al. Clinical implications of chronic heart failure phenotypes defined by cluster analysis. J Am Coll Cardiol 2014 Oct 28;64(17):1765-1774 [FREE Full text] [doi: 10.1016/j.jacc.2014.07.979] [Medline: 25443696]
34. Fodor IK. A survey of dimension reduction techniques. United States of America: Lawrence Livermore National Lab, CA (US); May 9, 2002.
35. Cunningham P. University College Dublin. 2007. Dimension Reduction URL: http://citeseerx.ist.psu.edu/viewdoc/download?doi=10.1.1.98.1478&rep=rep1&type=pdf
36. World Health Organization. Use of Glycated Haemoglobin (HbA1c) in the Diagnosis of Diabetes Mellitus: Abbreviated Report of a WHO Consultation. Geneva: World Health Organization; 2011.

37. Rokach L. A survey of clustering algorithms. In: Maimon O, Rokach L, editors. Data mining and knowledge discovery handbook, 2nd ed. New York, NY: Springer; 2010:269-298.
38. MacQueen JB. Some methods for classification and analysis of multivariate observations. 1967 Presented at: Proceedings of the Fifth Berkeley Symposium on Mathematical Statistics and Probability; 1967; Berkeley, California p. 281-297.
39. Ester M, Kriegel HP, Sander J, Xu X. A density-based algorithm for discovering clusters in large spatial databases with noise. In: Proceedings of the Second International Conference on Knowledge Discovery and Data Mining. 1996 Presented at: Proceedings of the Second International Conference on Knowledge Discovery and Data Mining; August 2-4, 1996; Portland, Oregon p. 226-231 URL: https://www.aaai.org/Library/KDD/kdd96contents.php
40. Ankerst M, Breunig M, Kriegel H, Sander J. Optics: ordering points to identify the clustering structure. In: SIGMOD '99 Proceedings of the ACM SIGMOD international conference on Management of data. New York, NY, USA: ACM; 1999 Presented at: ACM SIGMOD international conference on Management of data; May 31-June 3, 1999; New York p. 49-60 URL: https://dl.acm.org/citation.cfm?id=304187
41. Madeira SC, Oliveira AL. Biclustering algorithms for biological data analysis: a survey. IEEE/ACM Trans Comput Biol Bioinform 2004;1(1):24-45. [doi: 10.1109/TCBB.2004.2] [Medline: 17048406]
42. Zhao H, Wee-Chung Liew A, Wang DZ, Yan H. Biclustering analysis for pattern discovery: current techniques, comparative studies and applications. Curr Bioinform 2012 Mar 1;7(1):43-55. [doi: 10.2174/157489312799304413]
43. Aggarwal C, Han J, editors. Frequent Pattern Mining. Switzerland: Springer International Publishing; 2014.
44. Ray S, Turi R. Determination of number of clusters in k-means clustering and application in colour image segmentation. 1999 Presented at: The 4th international conference on advances in pattern recognition and digital techniques; 1999; Calcutta, India URL: http://citeseerx.ist.psu.edu/viewdoc/summary?doi=10.1.1.587.3517
45. Card S, Mackinlay J, Shneiderman B, editors. Readings in Information Visualization: Using Vision to Think. USA: Elsevier Science; 1999.
46. van der Aalst W. Process Mining. Berlin Heidelberg: Springer; 2016.
47. Culley L, Hudson N, Rapport F. Using focus groups with minority ethnic communities: researching infertility in British South Asian communities. Qual Health Res 2007 Jan;17(1):102-112. [doi: 10.1177/1049732306296506] [Medline: 17170248]
48. Kidd PS, Parshall MB. Getting the focus and the group: enhancing analytical rigor in focus group research. Qual Health Res 2000 May;10(3):293-308. [doi: 10.1177/104973200129118453] [Medline: 10947477]
49. King G, Verba S, Keohane RO. Designing Social Inquiry: Scientific Inference in Qualitative Research. Princeton: Princeton University Press; 1994.
50. Stewart DW, Shamdasani PN. Focus Groups: Theory and Practice (Applied Social Research Methods), 3rd ed. USA: SAGE Publications; 2018.
51. Lewis S. Qualitative inquiry and research design: choosing among five approaches. Health Promot Pract 2015 Apr 2;16(4):473-475. [doi: 10.1177/1524839915580941]
52. Sandelowski M. Whatever happened to qualitative description? Res Nurs Health 2000 Aug;23(4):334-340. [Medline: 10940958]

Abbreviations

ACG: adjusted clinical groups
BMI: body mass index
Clalit: Clalit Health Services
CRI: Clalit Research Institute
DWH: data warehouse
EMR: electronic medical record
HMO: health maintenance organization
HbA_{1c}: glycated hemoglobin
KDD: knowledge discovery in databases
SES: socioeconomic status
SMS: short message service

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Protocol

Testing a Web-Based Interactive Comic Tool to Decrease Obesity Risk Among Minority Preadolescents: Protocol for a Pilot Randomized Control Trial

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Abstract

Background: Childhood obesity is a public health crisis, particularly in low-income, minority populations in the United States. Innovative and technology-enhanced interventions may be an engaging approach to reach at-risk youth and their parents to improve dietary behaviors and feeding practices. However, such tools are limited, especially ones that are theory-based; co-developed with user-centered approaches; tailored to low-income, minority preadolescents; and include parent-focused content.

Objective: The objectives of this study include assessing the feasibility and acceptability and exploring the potential impact of the *Intervention INC* (Interactive Nutrition Comics for urban, minority preadolescents) Web-based tool, which is focused on decreasing childhood obesity risk in black/African American and Latino children aged 9 to 12 years.

Methods: *Intervention INC* is underpinned by the narrative transportation theory, social cognitive theory, and health belief model, and it was co-developed by children and parents from the intended population. The child component consists of a 6-chapter interactive nutrition comic optimized for use on tablet devices, a goal-setting and self-assessment feature, and weekly text/email messages and reminders. The parental component consists of 6 Web-based newsletters, access to the child comic, and weekly text/email messages and reminders. The tool was evaluated using a pilot, single-blind, 2-group randomized controlled study design. Child-parent dyads were randomized to either the experimental or comparison group and assigned to a targeted behavior (increase fruit/vegetable or water intake) based on initial screening questions. Data were collected at 4 time points: baseline (T1), intervention midpoint (T2), intervention endpoint (T3), and 3 months postintervention (T4). Primary measures comprise usage, usability, and feasibility of the Web-based tool. Secondary measures comprise dietary knowledge, preferences, and intake and anthropometric measures (for child) and feeding practices and home food environment (for parent).

Results: Study enrollment was completed in November 2017. A total of 89 child-parent dyads were randomized to either the experimental (n=44) or comparison (n=45) group. Data analysis is currently being conducted.

Conclusions: This study aims to implement and assess an innovative approach to deliver health messages and resources to at-risk minority preadolescents and their parents. If found to be acceptable, engaging, feasible, and a potential approach to improve dietary behaviors, a full-fledged randomized controlled trial will be conducted to assess its efficacy and potential impact.

Trial Registration: ClinicalTrials.gov NCT03165474; https://clinicaltrials.gov/ct2/show/NCT03165474 (Archived by WebCite at http://www.webcitation.org/73122IjgP)

International Registered Report Identifier (IRRID): RR1-10.2196/10682

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KEYWORDS

mHealth; pediatric obesity; vulnerable populations; minority; diet; child; parents

Introduction

Childhood obesity continues to be a serious clinical and public health issue in the United States. Over the last three decades, the rate of childhood obesity has tripled, with 17.0% of children aged 2 to 19 years now considered obese [1]. Although the US childhood obesity rate has leveled off in recent years, the challenge remains pronounced among certain populations, particularly in low-income, minority groups. Latino and black/African American children have the highest rates at 21.9% and 19.5%, respectively [1]. This epidemic has profound short- and long-term consequences as it not only leads to negative health outcomes such as type 2 diabetes and cardiovascular disease and can compromise a child's quality of life but also increases the risk of adult morbidity and mortality [1-6].

Effective yet innovative interventions are needed to capture the attention of children living in a multimedia environment. Visual narratives such as comics may engage today's youth population around health topics and promote positive psychosocial and behavioral outcomes [7-9]. Moreover, narrative-based health communication interventions can be effective with populations that have strong storytelling traditions such as Latino and African American communities, especially when cultural elements are incorporated [10-13]. Furthermore, the pervasiveness of technology and new media use in children, particularly within black and Latino populations, highlights opportunities and new avenues to engage with this priority population [14-16].

Web-based and technology-enhanced interventions, particularly if developed with user-centered approaches and informed by theory [17], also have the potential to increase access, improve convenience, decrease cost, and increase participant engagement with dietary behavior change strategies, especially among culturally diverse and hard-to-reach communities [18-21]. Indeed, some recent studies have indicated that Web-based programs could improve dietary behaviors in school-aged children [22-25]. However, such interventions tailored to minority youth are limited, especially those which have been co-designed by and/or developed for this population [26-30]. Lifestyle interventions developed to be culturally tailored or culturally relevant have the potential to be more readily adopted by at-risk minority populations [31-34]. Furthermore, this gap in tailored health promotion tools is particularly apparent within the preadolescent population, which is an understudied, yet critical stage of development. Not only does obesity prevalence increase when children transition into adolescence [35] but food preferences and behaviors established during this developmental period often continue into adulthood [36-39].

Despite the increase in childhood obesity studies using technology, mobile health (mHealth), and interactive media, there remain few systematic reviews of this literature and none specific to or tailored for minority/at-risk youth [40-43]. Broad recommendations for future work in this area highlight the need to identify the most effective approaches and strategies to impact behavioral and related health outcomes. In addition, knowledge gaps and challenges related to the implementation and adoption of technology-enhanced interventions exist (eg, identification and recruitment of at-risk, low-income minorities with internet access), which limit their potential effectiveness [40].

The purpose of this paper is to describe the protocol for the implementation and assessment of the *Intervention INC* (Interactive Nutrition Comics for urban, minority preadolescents) Web-based tool, which focuses on decreasing childhood obesity risk in Latino and black/African American children aged 9 to 12 years. This intervention builds on previous research and recommendations for childhood obesity interventions as it is theory-guided, focused on improving key dietary-related health behaviors, delivered via a narrative-based comic medium, and enhanced through an engaging mHealth platform, and it was developed with the intended population (Latino and black/African American preadolescents). The objectives of the study include assessing the feasibility and acceptability and exploring the potential impact of the intervention on dietary behaviors using a pilot, single-blind, 2-group randomized study design.

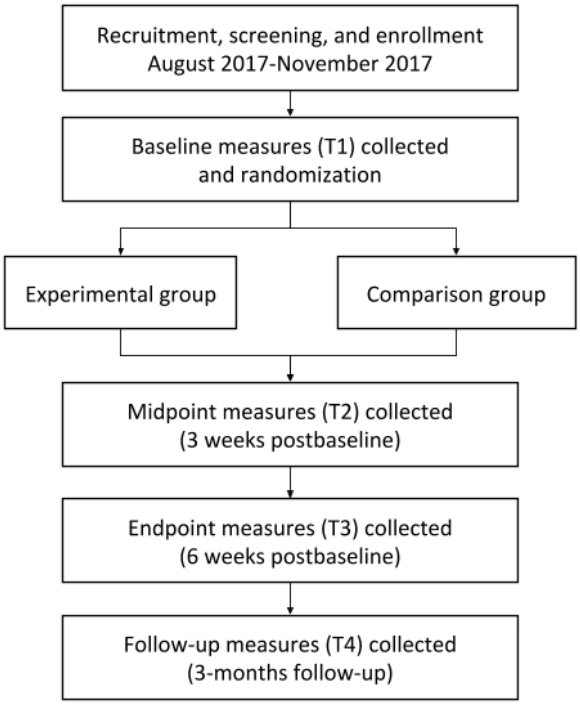
Methods

Study Design

The *Intervention INC* study is a pilot, single-blind, 2-group randomized controlled trial (RCT) that evaluated a 6-week intervention, with a 3-month follow-up period (see Figure 1). Child-parent dyads were enrolled into the study on a rolling basis between August and November 2017. Dyads were randomized to either the experimental group, in which the child received a Web-based comic with health messages primarily promoting either fruit/vegetable (F/V) or water consumption or the comparison group, in which the child received Web-based newsletters with health information similarly promoting primarily F/V or water consumption. Parents of both groups received Web-based health newsletters; however, parents in the experimental group were also given access to the child comic. Dyads were blinded to group assignment. Data were collected at 4 different time points: baseline (T1), intervention midpoint or 3 weeks postbaseline (T2), intervention endpoint or 6 weeks postbaseline (T3), and 3-month follow-up postintervention (T4).

The study was approved by the Hunter College institutional review board and is registered with the Clinical Trials Registry (NCT03165474). Adult consent, parental permission, and child assent were obtained at baseline before the commencement of any study procedures.

Figure 1. Study design of *Intervention INC*.



Study Population

Child

Children residing in New York City (NYC) were recruited based on the following inclusion/exclusion criteria: self-identifies as black/African American and/or Latino; aged between 9 and 12 years (preadolescents) at the time of scheduled baseline visit, reads and speaks in English; has a body mass index (BMI) percentile at or above 5% at baseline (categorized as healthy, overweight, or obese); has regular internet access via a tablet device, mobile phone or computer/laptop; has regular access to a phone with texting capability; is comfortable reading/viewing material on electronic devices; is comfortable speaking with study staff about thoughts/experiences while participating in the study; has no allergies, food aversions, food disorders, or medications with side-effects that may impact participation in the study; does not have a pacemaker or heart condition; and has a legal parent/guardian willing to participate in the study.

It should be noted that original criteria included a BMI percentile at or above 85% (categorized as overweight/obese). Due to recruitment challenges and evidence highlighting that most youth, regardless of BMI status (healthy, overweight, or obese), do not consume the daily recommended amount of fruits/vegetables and water [44-46], the criterion was changed to expand the BMI percentile range to include healthy-weight children (BMI percentile at or above 5%). In addition, the criterion regarding comfort level of child speaking with study staff was added after recruitment began due to observations at initial baseline visits of some children who were unable/unwilling to verbalize their thoughts/experiences.

Parent/Guardian

Parents/guardians were recruited based on the following inclusion/exclusion criteria: legal parent/guardian of child willing to participate in the study; reads and speaks in English or Spanish; primarily responsible for preparing/purchasing food for child; has regular internet access via a tablet device, smartphone, or computer/laptop; has regular access to a phone with text messaging capability; comfortable reading/viewing material on electronic devices; and able to attend in-person study visits and complete online questionnaires with their child over the full duration of the study.

Recruitment

Several recruitment approaches (with bilingual materials) were utilized to enroll child-parent dyads. Recruitment letters were sent to the parent/guardian of eligible child patients (based on age, race/ethnicity, and BMI percentile criteria) who had received care at a community-based clinic (partnering organization) in upper Manhattan, NYC, within the last 2 years. We also intended to send recruitment letters to similar child patients of a government-insured medical clinic based in Upper Manhattan, NYC. However, barriers related to accessing patient data were encountered, thus preventing the use of this approach. Once the BMI percentile criterion was changed (see Study Population section above), recruitment approaches were expanded to include local community flyering in East Harlem/Upper Manhattan, posting inside/near local businesses, housing complexes, community centers, schools, and churches. Through several partnerships with local schools and community initiatives, recruitment efforts also occurred via tabling at community and school events.

Interested parents/guardians had the option to call, text, or email study staff to receive more information about the study. Those receiving recruitment letters also received a recruitment call to assess interest in the study and receive additional information. Interested parents/guardians completed a screening form via phone/email to determine study eligibility. Eligible participants

were scheduled to attend a baseline (T1) visit where the child's height and weight were measured to determine if their BMI percentile was at or above 5%.

To minimize attrition, child participants were compensated up to US $70 in gift cards and parent/guardian participants up to US $65 for completing data collection. Compensation was distributed in increasing amounts at each time point (T1: child US $10, parent/guardian US $15; T2: child US $15; T3: child US $20, parent/guardian US $20; and T4: child US $25, parent/guardian US $30). Each participant had the option to select a gift card from either a large department store retailer, a discount supermarket chain, a supermarket chain specializing in selling organic products, or a sporting goods retailer. Participants also received a round-trip metro card for any in-person study visits. If a dyad completed data collection at all 4 time points, they were entered into a raffle for a US $100 gift card.

Sample Size

The sample size for this study was determined to reliably assess feasibility, acceptability, and preliminary efficacy of the intervention. We aimed to enroll a total sample size of 82 dyads (41 per group) [47,48], which allows for assessment of (1) intervention usage, usability, and feasibility/acceptability of study implementation and (2) both the within and between-group effect sizes as well as preliminary intervention efficacy based on mixed-models methodology (d=0.5, power=.80, alpha=.05, intraclass correlation coefficient=.6, 4 repeated measures), after taking into consideration estimated attrition of 20%. This sample size also allows to characterize potential sociodemographic moderators of the intervention as well as guide power calculations for a subsequent full-fledged RCT.

Randomization

At baseline (after height and weight data were collected), eligible participants were randomized to either the experimental group or comparison group using a minimization allocation strategy (performed using the QMinim Web-based app created by Mahmoud Saghaei [49]). Randomization was performed at the dyad level and was balanced on child ethnicity (Hispanic or non-Hispanic) and BMI category (normal, overweight, or obese). Randomization was revealed at T4.

Experimental Group Description

Interviews/focus groups, usability testing, and continuous quality improvement feedback on multiple prototypes with children and parents/guardians from our priority populations were used to inform development of *Intervention INC*, a theory-guided, interactive Web-based tool promoting healthy dietary behaviors (increased F/V and water intake), with the goal of reducing childhood obesity risk in black/African American and Latino preadolescents. Table 1 outlines the multiple phases and related research activities of the design and development process, which ultimately led to the final product that was tested in the pilot randomized trial. Details of the formative and development phases of *Intervention INC* are included in another manuscript (currently under review). *Intervention INC* comprises a 6-chapter comic with embedded goal-setting and messaging components. The tool is hosted on a password-protected website and optimized for use on tablet devices and touch-screen computer/laptop devices. All study participants received training on how to use the website at baseline.

Theoretical Framework

The narrative transportation theory (NTT), social cognitive theory (SCT), and health belief model (HBM) provided the theoretical framework for the *Intervention INC* tool. Comics, in particular manga comics (also known as Japanese comic art), are a unique form of multimodal narrative media that stimulate a reader's attention by combining detailed visual images and text to create more of a subjective or personal viewpoint of a story [50]. The NTT explains how narrative communication, such as manga comics, could contribute to changes in health-related beliefs and behaviors by transporting the reader into the narrative world [51]. According to the NTT, transportation into a narrative world is believed to lead to acceptance of persuasive messages within a story through multiple mechanisms [52-54]. This theory also suggests that images are most impactful when they are embedded in a story rather than provided in isolation, as it could enhance the narrative influence [55]. Therefore, visual images relevant to the story's message, such as those incorporated in manga comics, may further impact attitudes and beliefs. Furthermore, Latino and African American communities have strong storytelling traditions; thus, narrative-based health communication interventions could be effective with such populations, especially when culturally grounded messages and character experiences are depicted within relatable contexts [10].

SCT is a frequently used framework in effective dietary behavior change interventions [56,57], and it also lends explanation to ways in which a manga comic may influence health behavior in youth [7,8]. Exposure to characters in the storylines may facilitate observational learning and influence health behaviors, particularly when readers relate to the characters in the comics and consider them role models [58]. The development of entertainment-education narratives draws greatly on SCT by using role models to perform new behaviors [59-61]. SCT also supports self-regulatory behavior change procedures such as goal setting, self-monitoring, and feedback [58].

Table 1. Phases of *Intervention INC* tool design and development.

Phase	Activities	Objectives
Formative	Focus groups/interviews with children and parents	Identify factors influencing child dietary behaviors; assess technology use; and identify preferred comic storylines and characters
Development	Internal development of initial Web-based tool concepts; co-designing of Web-based tool content and design with children and parents; and usability testing of Web-based tool prototypes with children and parents	Draft initial tool outline and comic storyline/characters based on formative phase research; test and finalize acceptable and relatable tool components and comic content; and resolve tool usability issues identified during testing

The HBM construct of cues to action also guided tool development as it is a strategy to activate readiness for change and stimulate behavior change [56]. Thus, an innovative Web-based interactive tool that includes health messages delivered in a narrative comic format, tailored feedback, and cues to encourage behavior change, guided by the NTT, SCT, and HBM, might be an effective vehicle to promote healthy eating behaviors (see Figure 2).

Child Components

Comic

Children randomized to the experimental group were given access to a 6-chapter interactive nutrition comic titled "Game On" containing health messages focused on F/V and water consumption (see Figure 3). One chapter was made available at the beginning of each week for 6 weeks. Comic content was tailored (to include more information related to either F/V or water) based on responses to initial screening questions (asked at baseline) related to child F/V and water intake, child self-efficacy to increase F/V and water intake, and parent self-efficacy to support child in increasing F/V and water intake.

To ensure acceptability and relatability to our intended population, the comic storyline and its characters were informed by extensive formative research (highlighted in Table 1). Additional details related to how the formative research guided the design and development of the comic are described in another manuscript (currently under review). The comic depicts the story of a seemingly average high school student who discovers he has been tasked with the responsibility of saving the people of his world by battling an evil empire that has restricted access to F/V and water. With help from his friends, he must prepare for his epic battle by eating healthy foods and avoiding energy-dense, sugary foods/drinks. Personality traits, physical features of, and the communication/language used by characters in the comic were designed to be age-appropriate and culturally acceptable to both Latino and black urban children. Furthermore, scenarios in which the characters find themselves (eg, eating snacks in a bodega, racing to catch a subway for school) were intentionally incorporated into the story to model typical daily experiences of our intended population.

Health-related messaging was delivered through multiple mechanisms within the comic. Although the comic was primarily in black and white (the style typically observed in manga comics), health-promoting images related to F/V and water were featured in color for emphasis. In addition, characters modeled both healthy and unhealthy food behaviors, and the resulting benefits or consequences were depicted (in both image and text). Interactive features were also embedded into the comic (see Figure 3, bottom), such as orange-colored tap/click icons that either opened pop-up windows (highlighting health facts, food-related fun facts, or character information, which included favorite healthy foods/beverages) or prompted audio/visual effects to enhance engagement of the tool.

The comic was housed on a home page (see Figure 3, top), which comprised other sections including character profiles (highlighting demographic information for each character and personal fun facts) and trivia questions (combination of story-related and health-promoting questions, released as one per chapter). If all 6 trivia questions were answered correctly, the child received a prize of a downloadable screensaver image.

Goal Setting and Assessment

At the end of each comic chapter, one of the comic characters was shown encouraging the child to select a goal to work on for the week (see Figure 4, top left). Clicking on the link in the message opened a new page where the child was able to choose from 8 tailored goals related to either encouraging increased F/V or water intake (see Figure 4, top center). Goals included ones that were child-focused (eg, "I will eat fruits I like [such as grapes or bananas] as a snack" or "I will drink a glass of water when I wake up each morning") and ones that incorporated the parent (eg, "I will ask my parent to prepare vegetables I like [such as zucchini and tomatoes] for dinner" or "I will ask my parent to drink water with me during meals"). Once selected, a tailored tip was provided to assist the child in achieving that specific goal throughout the week (see Figure 4, top right).

Figure 2. Conceptual framework of *Intervention INC*. BMI: body mass index; HBM: health belief model; NTT: narrative transportation theory; SCT: social cognitive theory.

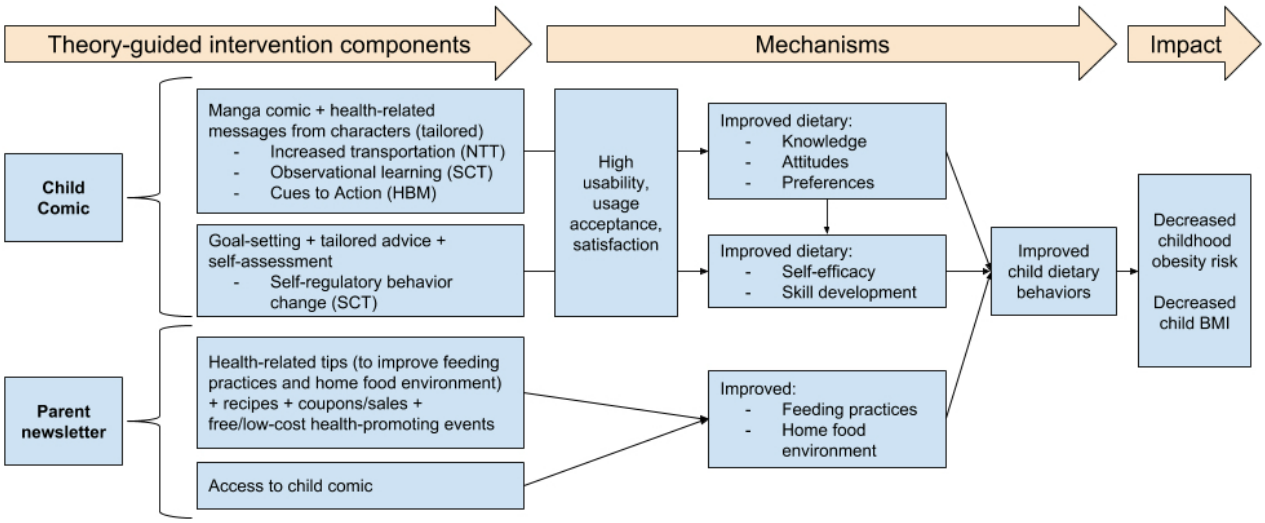
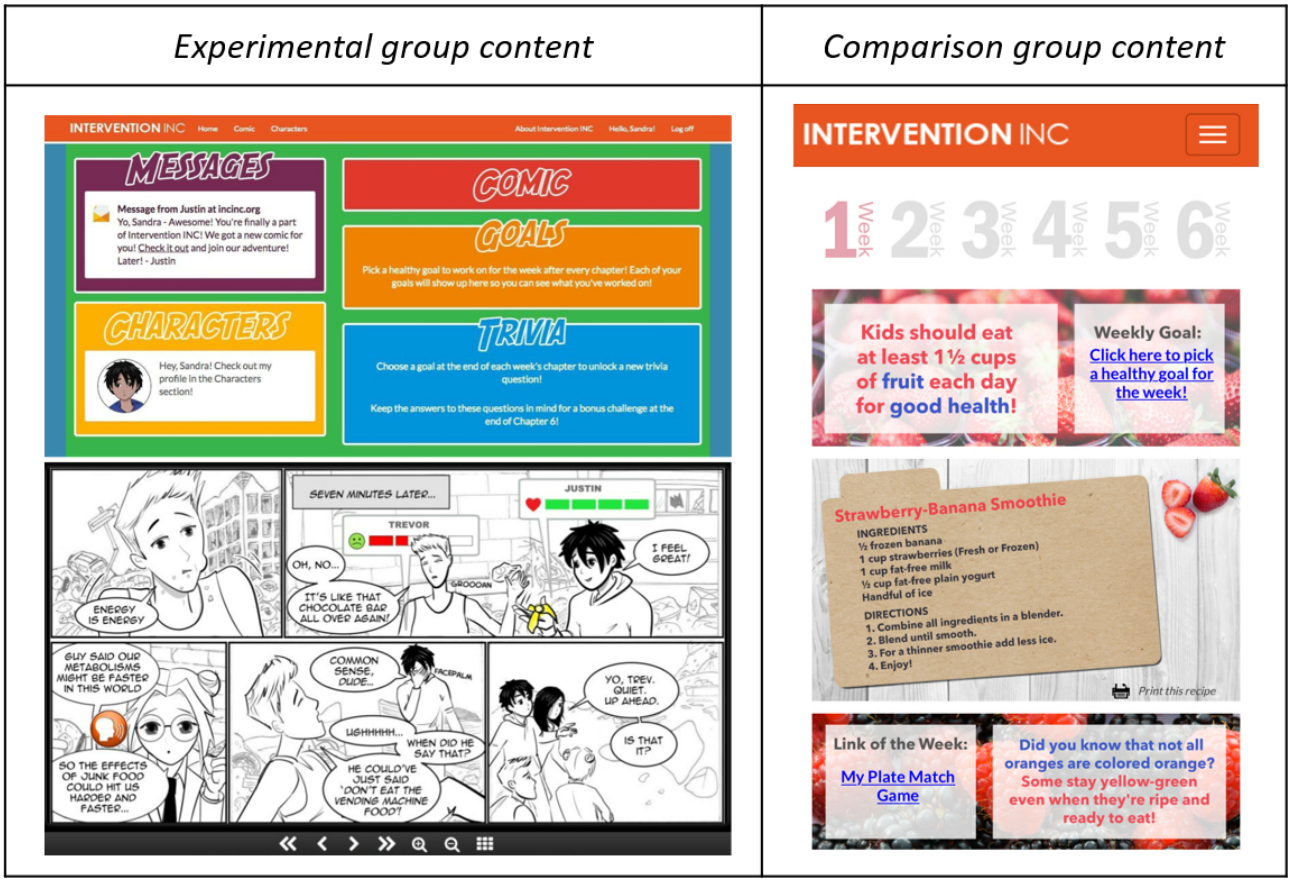


Figure 3. Experimental group (child) website homepage (top left) and snapshot of the comic (bottom left) and comparison group (child) Web-based newsletter example (right).



Before selecting a new goal (at the end of the following week's comic chapter), the child was prompted to self-assess how they did on the goal they chose and focused on for the past week by answering the following question: "How often did you do this in the last week?" (Never, Sometimes, Most of the Time, All the Time), and tailored feedback/encouragement was provided depending on the response chosen (ie, "Congrats! Keep up the good work!" or "Things take time - don't give up!"). If the child selected "Most of the Time" or "All of the Time" in response to the goal assessment question, the child was rewarded with bonus comic content (eg, the backstory for a specific character). The child was then prompted to select another goal to work on for the following week. A total of 5 goals could be selected (no option to select goal at end of the last chapter) and worked on during the intervention period.

Text/Email Messages

A total of 4 messages were delivered to experimental group children each week (total of 23 messages throughout intervention). Messages included announcing the release of a new chapter by a comic character (see Figure 5, left), a reminder to read the comic, and a reminder to select a goal for each week. Messages were delivered via text and/or email based on participant preference identified during the baseline visit.

Parent/Guardian Components

Newsletters

Parents/guardians in the experimental group received 6 Web-based newsletters with similar health messages as their child (see Figure 6, left). Newsletter content comprised healthy recipes, healthy feedings tips for the family, links to coupons to support healthy eating, and links to fun community events (eg, fall and winter festivals). In addition, they were given access to the "Game On" comic and character profiles. Newsletters were translated into Spanish and provided to those parents who expressed a preference for Spanish-language materials.

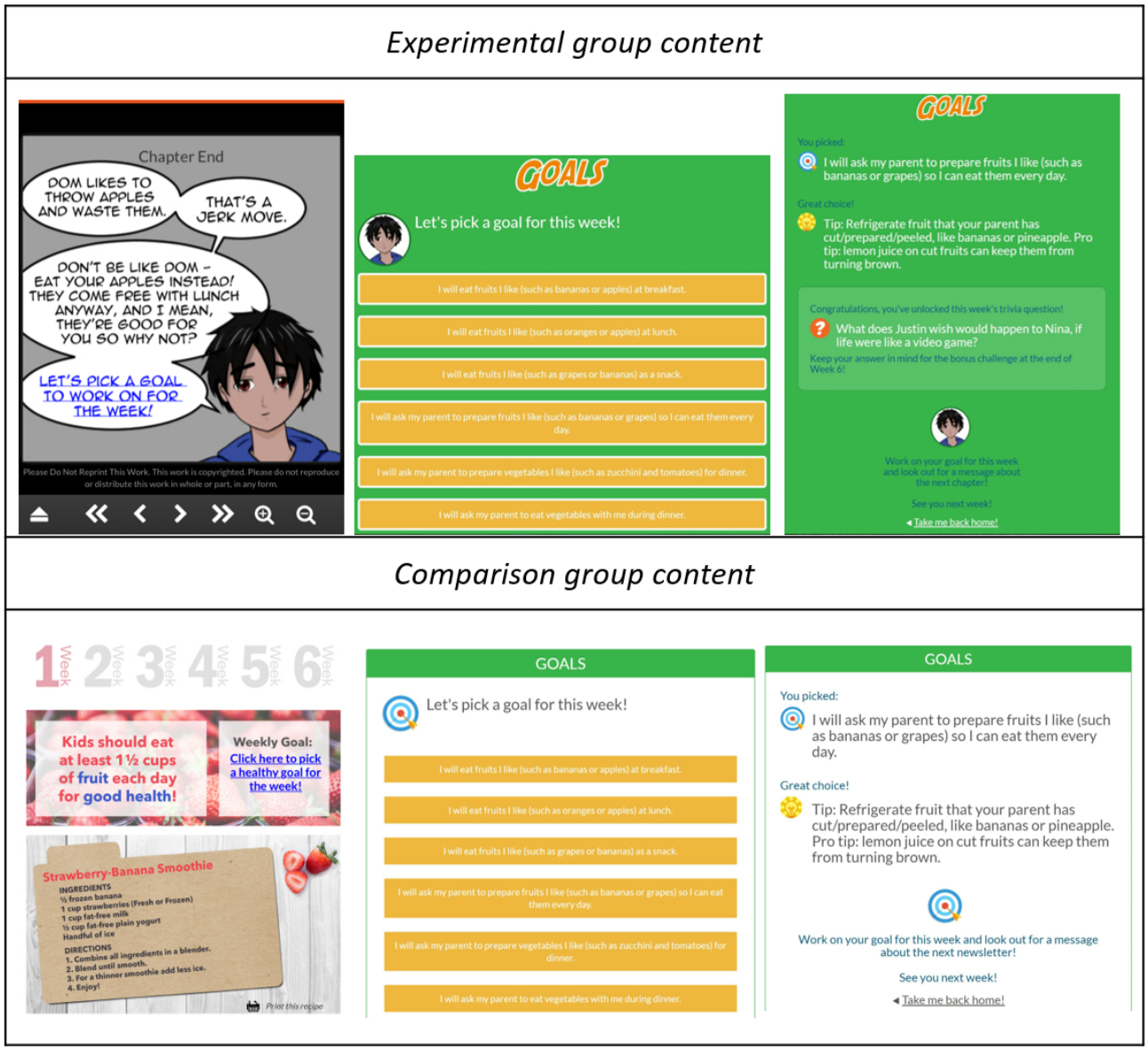
Text/Email Messages

A total of 2 messages were delivered to experimental group parents/guardians (total of 11 messages throughout intervention) each week. Parents/guardians received messages announcing the release of a new newsletter. In addition, they received reminders to encourage their child to read the comic. Messages were delivered via text and/or email based on participant preference identified during baseline. Messages were translated into Spanish and provided to those parents who expressed a preference for Spanish-language materials.

Comparison Group Description

The comparison group had access to Web-based tools similarly hosted on a password-protected website and optimized for use on tablet devices and touch-screen computer/laptop devices. All study participants received training on how to use the website at baseline.

Figure 4. Experimental group (child) goal-setting component (top) with link in the character message at the end of each comic chapter (top left), list of goals (top center), and goal-specific tip (top right) and comparison group (child) goal-setting component (bottom) with link in the Web-based newsletter (bottom left), list of goals (bottom center), and goal-specific tip (bottom right).



Child Components

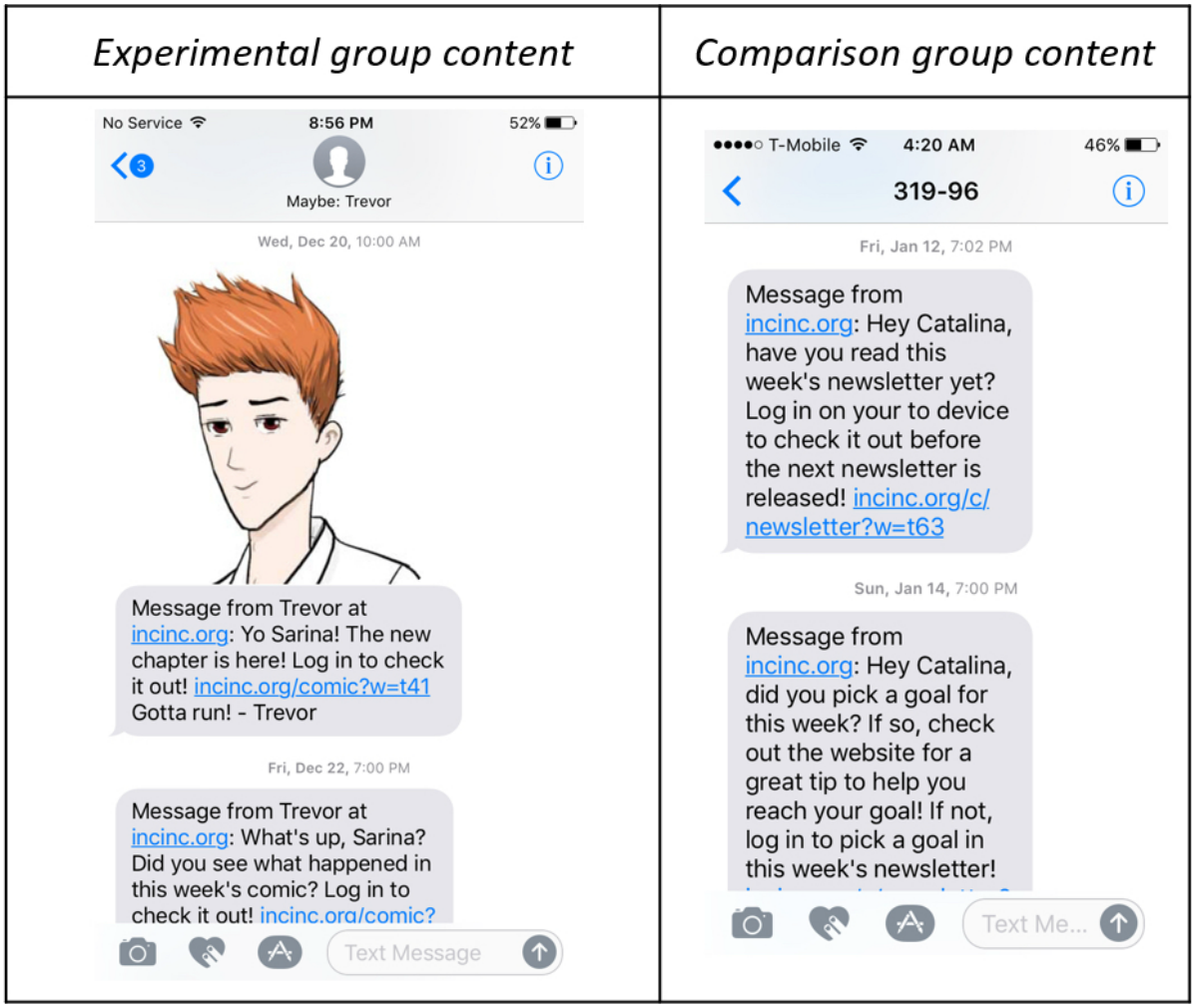
Newsletters

Children randomized to the comparison group received 6 Web-based newsletters with F/V or water information (see Figure 3, right). Similar to the comic, newsletter content was tailored (to include more information related to either F/V or water) based on responses to initial screening questions at baseline related to child F/V and water intake, child self-efficacy to increase F/V and water intake, and parent self-efficacy to support the child in increasing F/V and water intake. Newsletters were housed on a home page, and one was made available at the beginning of each week for 6 weeks. Health-related content for the comparison group was similar to that for the experimental group but was presented in a newsletter (didactic) format. The content comprised healthy eating tips, healthy recipes, diet-related knowledge/facts, health-promoting online games, and a link to selected weekly goals. Of note, comparison group participants were provided access to the "Game On" comic on completion of all data collection in April 2018.

Goal Setting and Assessment

Similar to children in the experimental group, children in the comparison group also had a goal-setting component (see Figure 4, bottom), wherein each week, the child could click the weekly goal link in the newsletter (see Figure 4, bottom left); select from 8 tailored goals to work on, related to either encouraging increased F/V or water intake (see Figure 4, bottom center); receive a tailored tip to provide assistance in achieving that specific goal throughout the week (see Figure 4, bottom right); and self-assess at the end of the week on how they did on the goal over the past week and receive feedback/encouragement. Unlike the goal-setting component in the experimental group, the format in which the goal setting was conducted in the comparison group was non-narrative.

Figure 5. Examples of text messages sent to children in the experimental group (left) and comparison group (right).



Text/Email Messages

A total of 3 messages were delivered to comparison group children each week (total of 17 messages throughout intervention). Messages included announcing the release of a new newsletter, a reminder to read the newsletter, and a reminder to select a goal for each week (see Figure 5, right). Messages were delivered via text and/or email based on participant preference identified during the baseline visit.

Parent/Guardian Components

Newsletters

Parents/guardians of the comparison group received the same 6 Web-based newsletters (in English or Spanish) as that of the parents/guardians in the experimental group. However, parents/guardians in the comparison group were not given access to the "Game On" comic and character profiles (see Figure 6, right).

Text/Email Messages

One message (in English or Spanish) was delivered to comparison group parents/guardians (6 messages throughout intervention) each week announcing the release of a new newsletter. Messages were delivered via text and/or email based on participant preference identified during baseline.

Measures

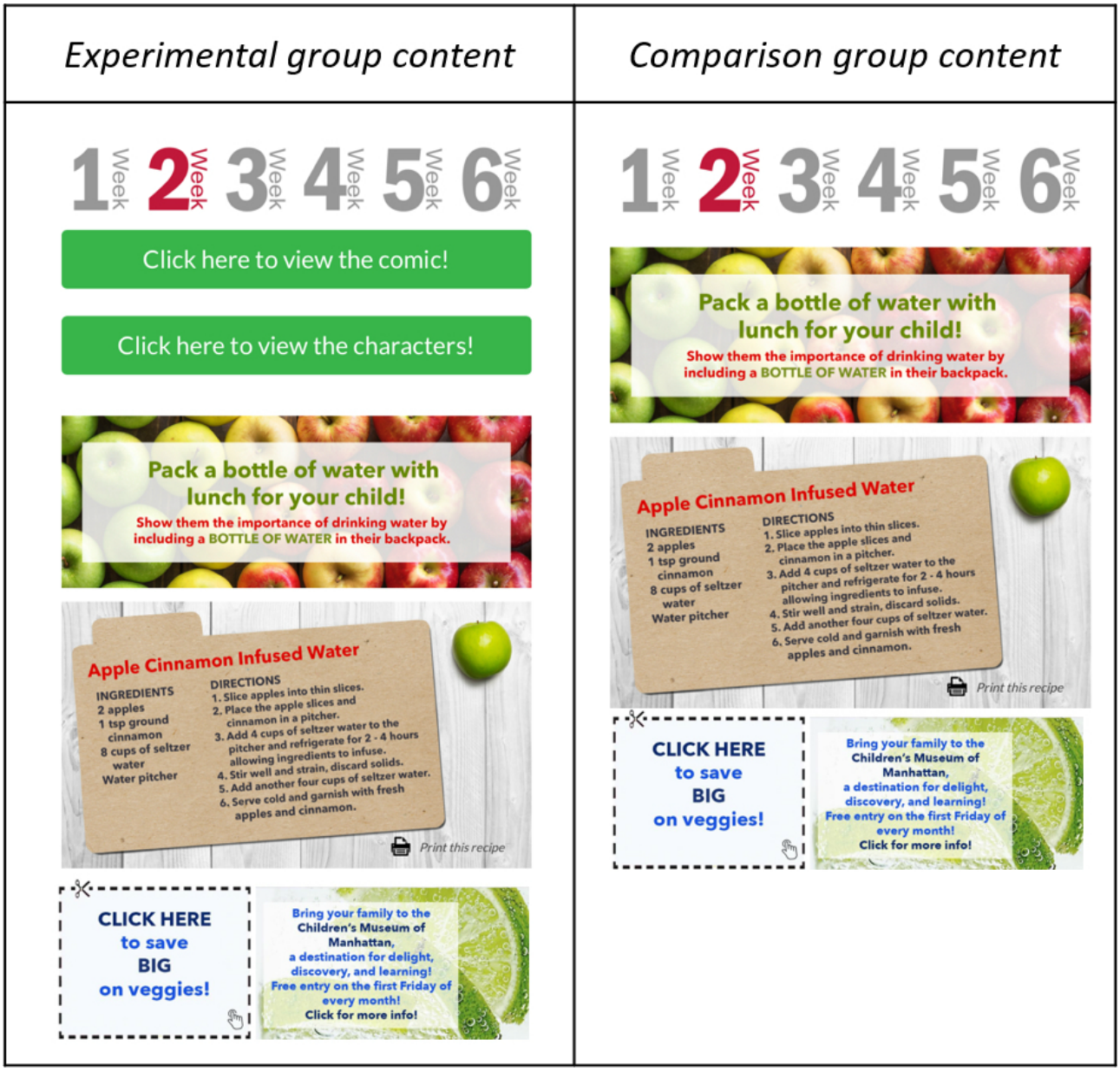
The measures collected are described in Table 2.

Feasibility/Acceptability Measures (Primary Measures)

Usage of Web-Based Tool

A custom-built platform was created to automatically log child and parent user details (created at baseline) and usage details (over 6 weeks of the intervention). User details included username, user type (parent or child), study group (experimental or comparison), type of tailored content (F/V or water), user language (English or Spanish), user email address, user mobile phone number, and start date/time (when username was created at baseline). Usage details included week number of intervention, link clicked, click time, platform used (eg, Mac OS, iPhone OS, Windows 7), and browser used and version (eg, Chrome 38.0, Safari 11.0). For child participants, additional usage data related to goal setting included weekly goal selected, date/time the goal was selected, evaluation at the end of the week (ie, "How often did you do this in the last week?"—Never, Sometimes, Most of the Time, All the Time), and date/time the goal was evaluated.

Figure 6. Examples of Web-based newsletters sent to parents in the experimental group (left) and comparison group (right).



Usability of Web-Based Tool

Questionnaires were administered to the child and parent at several time points throughout the study. Usability was assessed with an adapted version of the System Usability Scale (SUS) [62]; Usefulness, Satisfaction, and Ease-of-use questionnaire (USE) [63]; and a 26-item acceptability/usability measure by Ben-Zeev et al [64] to assess 5 usability domains: usability, usefulness, ease of use, ease of learning, and satisfaction. The child's questionnaire comprised 30 usability questions—10 questions from SUS, 15 from USE, and 5 from the acceptability/usability measure. On the basis of pilot testing with Latino and black children, modifications were made to tailor the questionnaire according to the literacy levels of our intended population. For example, the item "I found the system very cumbersome to use" was replaced with "I found it awkward to use" and "I would imagine most people would learn to use this system very quickly" was changed to "I think most people my age would learn to use it very quickly." The parent questionnaire comprised 9 usability questions—2 questions from SUS, 3 questions from USE, and 4 questions from the acceptability/usability measure. On the basis of pilot testing, 1 item was modified. Similar to the child questionnaire, the item "I found the system very cumbersome to use" was replaced with "I found it awkward to use." As the content of the parent component was presented in a more didactic format compared with that of the child component, fewer usability questions were relevant to include in the parent questionnaire. In addition, usability data in the form of qualitative interviews with child participants (at T2, T3, and T4) and parent participants (at T3 and T4) were collected to supplement quantitative usage and usability questionnaire data.

Table 2. Key measures, data source, and time of assessment. All questionnaire items were either taken from or directly informed by validated questionnaires.

Measures	Data source	Time points				
		T1[a]	T2[b]	T3[c]	T4[d]	O[e]
Feasibility/acceptability measures (primary measures)						
Usage of Web-based tool	Tracking system (internally created)	—[f]	—	—	—	C[g]/P[h]
Usability of Web-based tool	Interview, questionnaire items [62-64]	—	C	C/P	C/P	—
Feasibility of study implementation	Process data (eg, recruitment, attrition) [65,66]	—	—	—	C/P	S[i]
Outcome measures (secondary measures)						
Dietary knowledge and attitudes	Questionnaire items [67,68]	C	C	C	C	—
Dietary intake	Questionnaire items [69,70]	C	C	C	C	—
Anthropometric measures	Digital stadiometer, body composition monitor	C	—	—	C	—
Feeding practices	Questionnaire items [71]	P	—	P	P	—
Home food environment	Questionnaire items [72]	P	—	P	P	—

[a]T1: Time points indicated by baseline.

[b]T2: Time points indicated by midpoint (3 weeks postbaseline).

[c]T3: Time points indicated by endpoint (6 weeks postbaseline).

[d]T4: Time points indicated by follow-up (3 months postintervention).

[e]O: Ongoing throughout intervention period.

[f]Indicates measures that were not collected at specific timepoints.

[g]C: Data collected from child.

[h]P: Data collected from parent/guardian.

[i]S: Data collected from study staff (internal).

Feasibility of Study Implementation

Process data collected throughout the study assessed the feasibility of implementing the study [65,66]. These data included quantitative/qualitative measures of recruitment and retention (ie, enrollment rate, restrictiveness of eligibility criteria, attrition rate), assessment of resource capacity (ie, staff hours needed for recruitment, participant communication approaches), data collection (ie, length of time to complete online questionnaires), and data reliability (ie, study staff adherence to protocol). Satisfaction with study participation was assessed through questionnaire items with child and parent participants at T4 (ie, frequency and format of communication and study visit scheduling with study staff) as well as qualitative observations of child participants at T1 and T4 while completing questionnaires (ie, verbal and nonverbal expressions indicating frustration, boredom, and confusion).

Outcome Measures (Secondary Measures)

Child Dietary Knowledge and Attitudes

Child participants completed a questionnaire related to knowledge, outcome expectations, self-efficacy, behavioral intention, attitudes and preferences regarding behaviors associated with F/V, water, junk food, and sugary drinks. A total of 6 questions addressed knowledge (ie, I should eat 1 cup of fruit each day for good health), 20 questions addressed outcome expectancies (ie, Eating vegetables every day will keep me from getting sick), 9 questions addressed self-efficacy (ie, If I decide to not eat junk food every day, I can do it), 10 questions addressed intention (ie, If my parent offers me water, I will drink it), 15 questions addressed attitudes (ie, I think sugary drinks are cool), and 24 questions addressed preferences (ie, Which of the following fruits do you like or dislike?). A total of 84 questions were informed by and modified from the validated ProChildren questionnaire [67] and the validated Reynolds questionnaire [68]. Modifications to wording were made to ensure questions were appropriate for this study and to adjust for literacy levels of our intended population. A recent study conducted among Latino children also adapted the ProChildren questionnaire to measure children's self-efficacy for eating fruits and vegetables and for consuming water [73].

Child Dietary Intake

Child participants completed a questionnaire that assessed the frequency of consumption of F/V, water, junk food, and sugary drinks during the past 7 days. This 17-item questionnaire comprised 8 questions (6 directly from and 2 informed by) from the validated 2017 Youth Risk Behavior Surveillance System (YRBSS) questionnaire [69], which was created to monitor obesity prevalence and related behaviors, among other priority adolescent health issues. Nationally representative samples of students along with selected large urban school districts are engaged in the data collection process. Other studies conducted specifically with black and Latino children exploring dietary and physical activity behaviors have also utilized items from the YRBSS questionnaire [74,75]. Moreover, 6 items were informed by the validated Beverage and Snack Questionnaire, which was tested with a diverse group of children as approximately 45% were from minority populations [70], and

it was used in a more recent study that evaluated the efficacy of a serious game on low-income urban public school children's dietary behaviors [76]. A total of 3 items were internally created (related to assessing the intake of different types of water).

Child Anthropometric Measures

Height and weight of child participants were measured using standardized methods [77]. Height was measured to the nearest 1/8 inch using a digital stadiometer (SECA 264), with the participant fully erect, without shoes, feet together, head in the Frankfort plane, and at the end of a deep inhalation. Weight and body composition were measured using a body composition monitor (Tanita MC-780U) wearing lightweight clothes and without socks and shoes. Weight was measured to the nearest 0.2 lb. Height and weight were measured in duplicate and recorded. A third measurement was taken if there was any uncertainty on the accuracy of height or weight measurements (eg, if height measurements differed more than 0.5 inch). An average of the measurements was used for the BMI calculations. The Centers for Disease Control and Prevention BMI percentile calculator was used to determine BMI percentage [78]. If needed, the average height was rounded down to the nearest eighth of an inch, and the average weight was rounded down to the nearest quarter pound, to accommodate the calculator's units of measurement.

Parent Feeding Practices

Parent participants completed a questionnaire that asked about multiple parental feeding practices, specifically including 6 questions related to environment (ie, I offer a second helping of vegetables to my child during meals at home), 4 related to involvement in purchasing/preparing food (ie, I allow my child to help prepare fruit and vegetable dishes for family meals), 7 related to encouragement (ie, I encourage my child to drink water drinks [unsweetened] before sugary beverages), 8 related to modeling (ie, I model drinking water for my child even if it is not my favorite), and 2 related to teaching about healthy food practices (ie, I discuss with my child why it's important to eat fruits and vegetables.). The 27-item questionnaire was informed by the validated Comprehensive Feeding Practices Questionnaire [71], which has been used in previous studies with low-income Hispanic parents and African American fathers [79,80].

Home Food Environment

Parent participants completed a questionnaire related to the availability of fruits, vegetables, and water in their home and how often they store fruits, vegetables, and water in a place easily seen by their child. The questionnaire comprised 6 questions and was informed by the validated Home Environment survey [72].

Potential Confounders

Demographic factors such as age, gender, race/ethnicity, and whether the United States was the country of birth for both the child and parent were collected. Additional child measures included grade, technology use, physical activity, sedentary behavior, and perceived health. Parental measures also included marital status, education level, household income, household profile, Supplemental Nutrition Assistance Program participation, child participation in school breakfast and lunch program, and perceived health. These measures were collected at T1.

Data Management

A manual of procedures, including protocols related to data collection and storage, was developed at the outset of the study and refined continuously with input from all study staff. Study staff involved in collecting data were trained in implementing all procedures. Data collection and management procedures were reviewed at study staff meetings throughout the intervention period to ensure that they were followed with fidelity and to also address any issues or barriers to implementation.

Data collected in this study includes both quantitative data (auto-generated website usage data, online questionnaires, and anthropometric measures) and qualitative data (interviews). To ensure generated data are reliable, valid, and usable, the study staff used validated questionnaire items (or questionnaire items informed by validated questionnaires) and best practices for questionnaire, interview, and anthropometric data collection. Quantitative data were downloaded in spreadsheet format at least twice weekly, and qualitative data were downloaded as audio files weekly. All data were uploaded to password-protected institutional servers. Data were checked regularly to ensure the accuracy of data capture. A data dictionary that includes original items, answer choices, scoring/coding of answers, scoring of scales, and examples was created to ensure that all project data are accurately and readily usable and to aid in data analysis.

Data Analysis

Quantitative Data

Usage and usability of the Web-based tool, along with the feasibility of study implementation, will be assessed using descriptive analyses. As usage data are key to understanding technology-based behavioral intervention dose and also how participants engage with the Web-based tool itself [81], patterns of usage by children and parents/guardians will be described/calculated in multiple ways including as a binary variable by week (eg, did child/parent visit the website in week 1), as an ordered variable based on usage over 6 weeks (eg, high use, low use, and minimal use), or as a continuous variable measured as number of times visited over 6 weeks. Previous studies have similarly assessed patterns of usage when analyzing user engagement with a website or app in an intervention [82-85]. Both usage and usability data will also be used to stratify analysis to determine if there are any significant associations between individual demographic characteristics and health-related outcomes. These data will have high relevance for interpretation of outcome data and further inform refinement and enhancement of the intervention.

The changes in study outcomes within and between groups will be examined using mixed-models methodology with repeated assessments (T1, T2, T3, and T4), condition (experimental / comparison), and time by condition interaction. Both within- and between-group effect sizes will be calculated for all study measures to assess the magnitude of intervention effects overall and by potential moderators and inform subsequent larger RCTs.

To control for multiple comparisons, *P* values will be evaluated based on the false discovery rate [86]. All analyses will be conducted using an intent-to-treat approach.

Qualitative Data

Audio files of interviews conducted with children and parents/guardians at T2, T3, and T4 will be transcribed. Inductive and deductive processes will be used to analyze qualitative data collected from interviews with child participants (at T2, T3, and T4) and parent participants (at T3 and T4) as well as qualitative observations (detailed notes) during in-person study sessions at T1 and T4. Using a content analysis approach [87], transcribed audio files and field notes will be coded by at least 2 independent reviewers and reviewed to identify trends and recurring themes, especially related to barriers and facilitators to use and adoption of the *Intervention INC* Web-based tool. A qualitative analysis software will be used to assist with organizing, coding, and analyzing transcripts and notes.

Results

A total of 89 child-parent dyads were enrolled into the study on a rolling basis between August and November 2017. The dyads were randomized to either the experimental (n=44) or comparison (n=45) group. The pilot RCT was concluded as of April 2018, and data analysis is currently underway.

Discussion

Implications and Strengths

The *Intervention INC* Web-based interactive tool was developed to help engage low-income, minority children to change individual dietary behaviors and provide parents information and resources to improve feeding practices and promote a supportive home food environment, with the ultimate goal of reducing childhood obesity risk.

To the best of our knowledge, this is one of the first studies to explore the potential impact of an interactive Web-based tool specifically designed by and for at-risk, minority preadolescents. There is a distinct lack of effective health promotion tools that have been culturally tailored to meet the needs and preferences of populations with disproportionate rates of chronic disease [88], even fewer have been developed for children [18]. Our tool aims to address this as it has been specifically designed for black/African American and Latino children, who are at the greatest risk of childhood obesity. Furthermore, our intervention engages parents who play a significant role in shaping the home food environment and influencing child dietary behaviors [89,90]. It is well documented that sustained engagement of both children and parents in long-term interventions is a major challenge, particularly within at-risk populations [91,92].

Intervention INC is unique, given its innovative narrative and interactive Web-based approach to enhance adoption of the tool with hard-to-reach, at-risk populations. Embedded points of interactivity such as the pop-up features and special effects might further enhance engagement of the tool, thus potentially increasing the exposure of the intervention through additional opportunities to deliver meaningful health information. Assignment to a tailored track was based on initial screening at baseline to assess child F/V and water intake and child/parent self-efficacy related to F/V and water intake. Results of the screening process identified which at-risk behavior (F/V or water intake) was targeted during the intervention.

Notably, user-centered approaches were used throughout formative and development stages of this intervention, including co-development of the storyline and other content with children and parents and the use of multiple usability sessions to inform refinement of the tool. Although several studies have emphasized how usability testing can improve technology-enhanced tools [93-95], few have conducted usability testing methods for health promotion tools with youth users [96-98]. Usability testing is a crucial step in the development of online health tools to ensure that they are accessible, understandable, and useful to end users and are delivered in an efficient, effective, satisfying, and culturally competent manner [99].

Our study has numerous strengths, which include objective measures such as tool usage (process) and BMI (outcome). Importantly, the collection and analysis of detailed usage data allow for the potential to identify mechanisms of change, that is, which components of the *Intervention INC* tool might be contributing to any observed dietary-related changes. Our study has also incorporated multiple strategies to minimize attrition, which include partnering with community organizations, basing the study site within our priority community, recruiting bilingual research team members who come from similar communities as our participants, providing incentives comprising gift cards to local stores (dispersed in increasing amounts) throughout participation period, and sending emails with recipes during the 3-month follow-up period.

Limitations

This pilot study has limitations, which need to be considered. Initial recruitment challenges led to modifications in BMI eligibility criteria. In addition to overweight/obese children, healthy-weight children were also recruited. Not only could changes in BMI criteria dilute any anthropometric changes, but such recruitment challenges will also have implications for a larger scale randomized trial. Participants were recruited on a rolling basis over the course of 3 months; therefore, seasonality might bias various health-related behaviors, and thus our findings. The comparison group received similar health information (in non-narrative form), which may result in differences not being observed between groups. In addition, the comparison group (both child and parent) received 1 less text/email weekly reminder, which may influence tool usage, though this is likely to be minimal. Self-reported data from both the children and parents have been collected, which pose a validity risk, due to intentional/unintentional misreporting. However, our study design allows for children and parents to complete surveys at home as opposed to the study site with staff, which may contribute to decreased social desirability bias.

Conclusions

This study aims to implement an innovative approach to deliver healthy dietary messages and resources to at-risk minority children and their parents. If found to be acceptable, engaging, and feasible, a larger RCT with the *Intervention INC* Web-based comic tool will be conducted to assess its efficacy related to improving child dietary behaviors, child health outcomes, parent feeding practices, and the home food environment.

Acknowledgments

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Authors' Contributions

MML conceived the intervention concept and study design. All authors contributed to the writing of the manuscript and provided critical feedback.

Conflicts of Interest

None declared.

Multimedia Appendix 1

Peer-reviewer report from the Agency for Healthcare Research and Quality.

[PDF File (Adobe PDF File), 105KB - resprot_v7i11e10682_app1.pdf]

References

1. Ogden CL, Carroll MD, Fakhouri TH, Hales CM, Fryar CD, Li X, et al. Prevalence of obesity among youths by household income and education level of head of household - United States 2011-2014. MMWR Morb Mortal Wkly Rep 2018 Feb 16;67(6):186-189 [FREE Full text] [doi: 10.15585/mmwr.mm6706a3] [Medline: 29447142]
2. Skinner AC, Perrin EM, Moss LA, Skelton JA. Cardiometabolic risks and severity of obesity in children and young adults. N Engl J Med 2015 Oct;373(14):1307-1317. [doi: 10.1056/NEJMoa1502821] [Medline: 26422721]
3. Goran MI, Ball GD, Cruz ML. Obesity and risk of type 2 diabetes and cardiovascular disease in children and adolescents. J Clin Endocrinol Metab 2003 Apr;88(4):1417-1427. [doi: 10.1210/jc.2002-021442] [Medline: 12679416]
4. Reilly JJ, Kelly J. Long-term impact of overweight and obesity in childhood and adolescence on morbidity and premature mortality in adulthood: systematic review. Int J Obes 2011 Jul;35(7):891-898. [doi: 10.1038/ijo.2010.222] [Medline: 20975725]
5. Danaei G, Ding EL, Mozaffarian D, Taylor B, Rehm J, Murray CJ, et al. The preventable causes of death in the United States: comparative risk assessment of dietary, lifestyle, and metabolic risk factors. PLoS Med 2009 Apr 28;6(4):e1000058 [FREE Full text] [doi: 10.1371/journal.pmed.1000058] [Medline: 19399161]
6. Freedman DS, Khan LK, Dietz WH, Srinivasan SR, Berenson GS. Relationship of childhood obesity to coronary heart disease risk factors in adulthood: the Bogalusa Heart Study. Pediatrics 2001 Sep;108(3):712-718. [Medline: 11533341]
7. Leung MM, Tripicchio G, Agaronov A, Hou N. Manga comic influences snack selection in Black and Hispanic New York City youth. J Nutr Educ Behav 2014;46(2):142-147. [doi: 10.1016/j.jneb.2013.11.004] [Medline: 24433817]
8. Leung MM, Green MC, Tate DF, Cai J, Wyka K, Ammerman AS. Fight for your right to fruit: psychosocial outcomes of a manga comic promoting fruit consumption in middle-school youth. Health Commun 2017 May;32(5):533-540. [doi: 10.1080/10410236.2016.1211074] [Medline: 27540773]
9. Branscum P, Housley A, Bhochhibhoya A, Hayes L. A formative evaluation of Healthy Heroes: a photo comic book-social cognitive theory based obesity prevention program. J Health Educ Teach 2016;7(1):52-63 [FREE Full text]
10. Lee H, Fawcett J, DeMarco R. Storytelling/narrative theory to address health communication with minority populations. Appl Nurs Res 2016 May;30:58-60. [doi: 10.1016/j.apnr.2015.09.004] [Medline: 27091254]
11. Houston TK, Allison JJ, Sussman M, Horn W, Holt CL, Trobaugh J, et al. Culturally appropriate storytelling to improve blood pressure: a randomized trial. Ann Intern Med 2011 Jan 18;154(2):77-84. [doi: 10.7326/0003-4819-154-2-201101180-00004] [Medline: 21242364]
12. Kreuter MW, Green MC, Cappella JN, Slater MD, Wise ME, Storey D, et al. Narrative communication in cancer prevention and control: a framework to guide research and application. Ann Behav Med 2007 Jun;33(3):221-235. [doi: 10.1080/08836610701357922] [Medline: 17600449]

13. Larkey LK, Lopez AM, Minnal A, Gonzalez J. Storytelling for promoting colorectal cancer screening among underserved Latina women: a randomized pilot study. Cancer Control 2009 Jan;16(1):79-87. [doi: 10.1177/107327480901600112] [Medline: 19078934]
14. Rideout V, Foehr U, Roberts D. Kaiser Family Foundation. 2010. Generation M2: Media in the Lives of 8- to 18-Year-Olds URL: https://www.kff.org/other/poll-finding/report-generation-m2-media-in-the-lives/ [accessed 2018-10-08] [WebCite Cache ID 731CNQW7X]
15. Weihrauch-Blüher S, Koormann S, Brauchmann J, Wiegand S. Electronic media in obesity prevention in childhood and adolescence. Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz 2016 Nov;59(11):1452-1464. [doi: 10.1007/s00103-016-2455-z] [Medline: 27757512]
16. Baranowski T, Frankel L. Let's get technical! Gaming and technology for weight control and health promotion in children. Child Obes 2012 Feb;8(1):34-37. [doi: 10.1089/chi.2011.0103] [Medline: 22799477]
17. Wang Y, Fadhil A, Lange JP, Reiterer H. Arxiv. Towards a Holistic Approach to Designing Theory-based Mobile Health Interventions URL: http://arxiv.org/abs/1712.02548 [accessed 2018-10-03] [WebCite Cache ID 72tZORRKj]
18. Tate EB, Spruijt-Metz D, O'Reilly G, Jordan-Marsh M, Gotsis M, Pentz MA, et al. mHealth approaches to child obesity prevention: successes, unique challenges, and next directions. Transl Behav Med 2013 Dec;3(4):406-415 [FREE Full text] [doi: 10.1007/s13142-013-0222-3] [Medline: 24294329]
19. Tufano JT, Karras BT. Mobile eHealth interventions for obesity: a timely opportunity to leverage convergence trends. J Med Internet Res 2005;7(5):e58 [FREE Full text] [doi: 10.2196/jmir.7.5.e58] [Medline: 16403722]
20. Khaylis A, Yiaslas T, Bergstrom J, Gore-Felton C. A review of efficacious technology-based weight-loss interventions: five key components. Telemed J E Health 2010 Nov;16(9):931-938 [FREE Full text] [doi: 10.1089/tmj.2010.0065] [Medline: 21091286]
21. Flores Mateo G, Granado-Font E, Ferré-Grau C, Montaña-Carreras X. Mobile phone apps to promote weight loss and increase physical activity: a systematic review and meta-analysis. J Med Internet Res 2015;17(11):e253 [FREE Full text] [doi: 10.2196/jmir.4836] [Medline: 26554314]
22. Cullen KW, Thompson D, Chen TA. Outcome evaluation of Family Eats. Health Educ Behav 2017 Dec;44(1):32-40. [doi: 10.1177/1090198116643917] [Medline: 27198535]
23. Chamberland K, Sanchez M, Panahi S, Provencher V, Gagnon J, Drapeau V. The impact of an innovative web-based school nutrition intervention to increase fruits and vegetables and milk and alternatives in adolescents: a clustered randomized trial. Int J Behav Nutr Phys Act 2017 Dec 16;14(1):140 [FREE Full text] [doi: 10.1186/s12966-017-0595-7] [Medline: 29037203]
24. Kaakinen P, Kyngäs H, Kääriäinen M. Technology-based counseling in the management of weight and lifestyles of obese or overweight children and adolescents: a descriptive systematic literature review. Inform Health Soc Care 2018 Mar;43(2):126-141. [doi: 10.1080/17538157.2017.1353997] [Medline: 28829655]
25. Antwi F, Fazylova N, Garcon MC, Lopez L, Rubiano R, Slyer JT. The effectiveness of web-based programs on the reduction of childhood obesity in school-aged children: a systematic review. JBI Libr Syst Rev 2012;10(42 Suppl):1-14. [doi: 10.11124/jbisrir-2012-248] [Medline: 27820152]
26. Brotman LM, Dawson-McClure S, Huang KY, Theise R, Kamboukos D, Wang J, et al. Early childhood family intervention and long-term obesity prevention among high-risk minority youth. Pediatrics 2012 Mar;129(3):e621-e628 [FREE Full text] [doi: 10.1542/peds.2011-1568] [Medline: 22311988]
27. Van Horn L, Obarzanek E, Friedman LA, Gernhofer N, Barton B. Children's adaptations to a fat-reduced diet: the Dietary Intervention Study in Children (DISC). Pediatrics 2005 Jun;115(6):1723-1733. [doi: 10.1542/peds.2004-2392] [Medline: 15930237]
28. Barkin SL, Gesell SB, Po'e EK, Escarfuller J, Tempesti T. Culturally tailored, family-centered, behavioral obesity intervention for Latino-American preschool-aged children. Pediatrics 2012 Sep;130(3):445-456 [FREE Full text] [doi: 10.1542/peds.2011-3762] [Medline: 22869834]
29. Robinson TN, Matheson DM, Kraemer HC, Wilson DM, Obarzanek E, Thompson NS, et al. A randomized controlled trial of culturally tailored dance and reducing screen time to prevent weight gain in low-income African American girls: Stanford GEMS. Arch Pediatr Adolesc Med 2010 Nov;164(11):995-1004 [FREE Full text] [doi: 10.1001/archpediatrics.2010.197] [Medline: 21041592]
30. Falbe J, Cadiz AA, Tantoco NK, Thompson HR, Madsen KA. Active and healthy families: a randomized controlled trial of a culturally tailored obesity intervention for Latino children. Acad Pediatr 2015;15(4):386-395. [doi: 10.1016/j.acap.2015.02.004] [Medline: 25937516]
31. Barrera M, Castro FG, Strycker LA, Toobert DJ. Cultural adaptations of behavioral health interventions: a progress report. J Consult Clin Psychol 2013 Apr;81(2):196-205 [FREE Full text] [doi: 10.1037/a0027085] [Medline: 22289132]
32. Victorson D, Banas J, Smith J, Languido L, Shen E, Gutierrez S, et al. eSalud: designing and implementing culturally competent ehealth research with latino patient populations. Am J Public Health 2014 Dec;104(12):2259-2265. [doi: 10.2105/AJPH.2014.302187] [Medline: 25320901]

33. Kreuter MW, Lukwago SN, Bucholtz RD, Clark EM, Sanders-Thompson V. Achieving cultural appropriateness in health promotion programs: targeted and tailored approaches. Health Educ Behav 2003 Apr;30(2):133-146. [doi: 10.1177/1090198102251021] [Medline: 12693519]
34. Davis RE, Peterson KE, Rothschild SK, Resnicow K. Pushing the envelope for cultural appropriateness: does evidence support cultural tailoring in type 2 diabetes interventions for Mexican American adults? Diabetes Educ 2011;37(2):227-238 [FREE Full text] [doi: 10.1177/0145721710395329] [Medline: 21343599]
35. Hales CM, Carroll MD, Fryar CD, Ogden CL. Prevalence of obesity among adults and youth: United States, 2015-2016. NCHS Data Brief 2017 Dec(288):1-8 [FREE Full text] [Medline: 29155689]
36. Nicklaus S, Boggio V, Chabanet C, Issanchou S. A prospective study of food variety seeking in childhood, adolescence and early adult life. Appetite 2005 Jun;44(3):289-297. [doi: 10.1016/j.appet.2005.01.006] [Medline: 15927730]
37. Birch L, Savage JS, Ventura A. Influences on the development of children's eating behaviours: from infancy to adolescence. Can J Diet Pract Res 2007;68(1):s1-s56 [FREE Full text] [Medline: 19430591]
38. Mikkilä V, Räsänen L, Raitakari OT, Pietinen P, Viikari J. Consistent dietary patterns identified from childhood to adulthood: the cardiovascular risk in Young Finns Study. Br J Nutr 2005 Jun;93(6):923-931. [Medline: 16022763]
39. Demory-Luce D, Morales M, Nicklas T, Baranowski T, Zakeri I, Berenson G. Changes in food group consumption patterns from childhood to young adulthood: the Bogalusa Heart Study. J Am Diet Assoc 2004 Nov;104(11):1684-1691. [doi: 10.1016/j.jada.2004.07.026] [Medline: 15499355]
40. Turner T, Spruijt-Metz D, Wen CK, Hingle MD. Prevention and treatment of pediatric obesity using mobile and wireless technologies: a systematic review. Pediatr Obes 2015 Dec;10(6):403-409. [doi: 10.1111/ijpo.12002] [Medline: 25641770]
41. Hammersley ML, Jones RA, Okely AD. Parent-focused childhood and adolescent overweight and obesity eHealth interventions: a systematic review and meta-analysis. J Med Internet Res 2016 Jul 21;18(7):e203 [FREE Full text] [doi: 10.2196/jmir.5893] [Medline: 27443862]
42. Smith AJ, Skow A, Bodurtha J, Kinra S. Health information technology in screening and treatment of child obesity: a systematic review. Pediatrics 2013 Mar;131(3):e894-e902. [doi: 10.1542/peds.2012-2011] [Medline: 23382447]
43. Lee J, Piao M, Byun A, Kim J. A systematic review and meta-analysis of intervention for pediatric obesity using mobile technology. Stud Health Technol Inform 2016;225:491-494. [Medline: 27332249]
44. Banfield EC, Liu Y, Davis JS, Chang S, Frazier-Wood AC. Poor adherence to US dietary guidelines for children and adolescents in the national health and nutrition examination survey population. J Acad Nutr Diet 2016 Jan;116(1):21-27 [FREE Full text] [doi: 10.1016/j.jand.2015.08.010] [Medline: 26391469]
45. Moss JL, Liu B, Zhu L. Comparing percentages and ranks of adolescent weight-related outcomes among U.S. states: implications for intervention development. Prev Med 2017 Dec;105:109-115. [doi: 10.1016/j.ypmed.2017.09.006] [Medline: 28888823]
46. Kenney EL, Long MW, Cradock AL, Gortmaker SL. Prevalence of inadequate hydration among US children and disparities by gender and race/ethnicity: national health and nutrition examination survey, 2009-2012. Am J Public Health 2015 Aug;105(8):e113-e118. [doi: 10.2105/AJPH.2015.302572] [Medline: 26066941]
47. Lancaster GA, Dodd S, Williamson PR. Design and analysis of pilot studies: recommendations for good practice. J Eval Clin Pract 2004 May;10(2):307-312. [doi: 10.1111/j.2002.384.doc.x] [Medline: 15189396]
48. Denzin NK, Lincoln YS. The SAGE Handbook of Qualitative Research. Thousand Oaks, CA: SAGE Publications; 2011.
49. Saghaei M. QMinim. QMinim Online Minimization URL: http://rct.mui.ac.ir/q/index.php [accessed 2018-10-03] [WebCite Cache ID 72taWpmOm]
50. Cohn N, Taylor-Weiner A, Grossman S. Framing attention in Japanese and American comics: cross-cultural differences in attentional structure. Front Psychol 2012;3:349 [FREE Full text] [doi: 10.3389/fpsyg.2012.00349] [Medline: 23015794]
51. Green MC, Clark JL. Transportation into narrative worlds: implications for entertainment media influences on tobacco use. Addiction 2013 Mar;108(3):477-484. [doi: 10.1111/j.1360-0443.2012.04088.x] [Medline: 22994374]
52. Green MC, Brock TC. In the mind's eye: Transportation-imagery model of narrative persuasion. In: Narrative Impact: Social and Cognitive Foundations. Mahwah, NJ: Lawrence Erlbaum Associates Publishers; 2002:315-341.
53. Lytle L, Achterberg C. Changing the diet of America's children: what works and why? J Nutr Educ 1995 Sep;27(5):250-260. [doi: 10.1016/S0022-3182(12)80793-X]
54. Green MC, Garst J, Brock TC. The power of fiction: determinants and boundaries. In: The Psychology of Entertainment Media: Blurring the Lines between Entertainment and Persuasion. Mahwah, NJ: Lawrence Erlbaum Associates Publishers; 2004:161-176.
55. Cole K, Waldrop J, D'Auria J, Garner H. An integrative research review: effective school-based childhood overweight interventions. J Spec Pediatr Nurs 2006 Jul;11(3):166-177. [doi: 10.1111/j.1744-6155.2006.00061.x] [Medline: 16774527]
56. Glanz K, Rimer BK, Viswanath K. Health Behavior and Health Education: Theory, Research, and Practice. San Francisco, CA: John Wiley & Sons, Incorporated; 2008.
57. Annesi JJ, Walsh SM, Greenwood BL, Mareno N, Unruh-Rewkowski JL. Effects of the Youth Fit 4 Life physical activity/nutrition protocol on body mass index, fitness and targeted social cognitive theory variables in 9- to 12-year-olds during after-school care. J Paediatr Child Health 2017 Apr;53(4):365-373. [doi: 10.1111/jpc.13447] [Medline: 28052570]

58. McAlister AL, Perry CL, Parcel GS. How individuals, environments, and health behavior interact: social cognitive theory. In: Health Behavior and Health Education: Theory, Research, and Practice. 4th Edition. San Francisco, CA: Jossey-Bass; 2008:978.
59. Branscum P, Sharma M, Wang LL, Wilson BR, Rojas-Guyler L. A true challenge for any superhero: an evaluation of a comic book obesity prevention program. Fam Community Health 2013;36(1):63-76. [doi: 10.1097/FCH.0b013e31826d7607] [Medline: 23168347]
60. Thompson D, Bhatt R, Lazarus M, Cullen K, Baranowski J, Baranowski T. A serious video game to increase fruit and vegetable consumption among elementary aged youth (Squire's Quest! II): rationale, design, and methods. JMIR Res Protoc 2012;1(2):e19 [FREE Full text] [doi: 10.2196/resprot.2348] [Medline: 23612366]
61. Thompson D, Baranowski T, Buday R, Baranowski J, Thompson V, Jago R, et al. Serious video games for health how behavioral science guided the development of a serious video game. Simul Gaming 2010 Aug 1;41(4):587-606 [FREE Full text] [doi: 10.1177/1046878108328087] [Medline: 20711522]
62. Brooke J. SUS: A quick and dirty usability scale. J Usability Stud 2013;8(2):29-40 [FREE Full text]
63. Lund A. Measuring usability with the USE Questionnaire. Usability User Exp Newsl STC Usability SIG 2001;8 [FREE Full text]
64. Ben-Zeev D, Brenner CJ, Begale M, Duffecy J, Mohr DC, Mueser KT. Feasibility, acceptability, and preliminary efficacy of a smartphone intervention for schizophrenia. Schizophr Bull 2014 Nov;40(6):1244-1253. [doi: 10.1093/schbul/sbu033] [Medline: 24609454]
65. Bowen DJ, Kreuter M, Spring B, Cofta-Woerpel L, Linnan L, Weiner D, et al. How we design feasibility studies. Am J Prev Med 2009 May;36(5):452-457 [FREE Full text] [doi: 10.1016/j.amepre.2009.02.002] [Medline: 19362699]
66. Tickle-Degnen L. Nuts and bolts of conducting feasibility studies. Am J Occup Ther 2013;67(2):171-176 [FREE Full text] [doi: 10.5014/ajot.2013.006270] [Medline: 23433271]
67. De Bourdeaudhuij I, Klepp KI, Due P, Rodrigo CP, de Almeida M, Wind M, et al. Reliability and validity of a questionnaire to measure personal, social and environmental correlates of fruit and vegetable intake in 10-11-year-old children in five European countries. Public Health Nutr 2005 Apr;8(2):189-200. [Medline: 15877912]
68. Reynolds KD, Yaroch AL, Franklin FA, Maloy J. Testing mediating variables in a school-based nutrition intervention program. Health Psychol 2002 Jan;21(1):51-60. [Medline: 11846345]
69. Youth Risk Behavior Surveillance System, Data, Adolescent and School Health.: CDC URL: https://www.cdc.gov/healthyyouth/data/yrbs/index.htm [WebCite Cache ID 72tbnYeUl]
70. Neuhouser ML, Lilley S, Lund A, Johnson DB. Development and validation of a beverage and snack questionnaire for use in evaluation of school nutrition policies. J Am Diet Assoc 2009 Sep;109(9):1587-1592. [doi: 10.1016/j.jada.2009.06.365] [Medline: 19699839]
71. Melbye EL, Øgaard T, Øverby NC. Validation of the Comprehensive Feeding Practices Questionnaire with parents of 10-to-12-year-olds. BMC Med Res Methodol 2011 Aug 09;11:113 [FREE Full text] [doi: 10.1186/1471-2288-11-113] [Medline: 21827703]
72. Gattshall ML, Shoup JA, Marshall JA, Crane LA, Estabrooks PA. Validation of a survey instrument to assess home environments for physical activity and healthy eating in overweight children. Int J Behav Nutr Phys Act 2008 Jan 11;5:3 [FREE Full text] [doi: 10.1186/1479-5868-5-3] [Medline: 18190709]
73. Wilmoth S, Pan M, Correa L, Martinez E, Mendoza R, Sosa E, et al. A summer obesity prevention program for Hispanic kids and families through vacation bible school: a pilot study. J Child Obes 2018 Feb 16;3(1). [doi: 10.21767/2572-5394.100042]
74. Glover S, Piper CN, Hassan R, Preston G, Wilkinson L, Bowen-Seabrook J, et al. Dietary, physical activity, and lifestyle behaviors of rural African American South Carolina children. J Natl Med Assoc 2011 Apr;103(4):300-304. [Medline: 21805808]
75. Racine EF, Coffman MJ, Chrimes DA, Laditka SB. Evaluation of the Latino food and Fun curriculum for low-income Latina mothers and their children: a pilot study. Hisp Health Care Int 2013;11(1):31-37. [doi: 10.1891/1540-4153.11.1.31] [Medline: 24830482]
76. Majumdar D, Koch PA, Lee H, Contento IR, Islas-Ramos AD, Fu D. "Creature-101": a serious game to promote energy balance-related behaviors among middle school adolescents. Games Health J 2013 Oct;2(5):280-290 [FREE Full text] [doi: 10.1089/g4h.2013.0045] [Medline: 24761326]
77. National Health and Medical Research Council. ClinicalGuidelines.gov. Clinical practice guidelines for the management of overweight and obesity in adults, adolescents and children in Australia URL: https://www.clinicalguidelines.gov.au/portal/2231/clinical-practice-guidelines-management-overweight-and-obesity-adults-adolescents-and [accessed 2018-10-03] [WebCite Cache ID 72tcXuDeY]
78. CDC. BMI Calculator Child and Teen, Healthy Weight URL: https://www.cdc.gov/healthyweight/bmi/calculator.html [accessed 2018-10-03] [WebCite Cache ID 72tcgkXBc]
79. Otterbach L, Mena NZ, Greene G, Redding CA, De Groot A, Tovar A. Community-based childhood obesity prevention intervention for parents improves health behaviors and food parenting practices among Hispanic, low-income parents. BMC Obes 2018;5:11 [FREE Full text] [doi: 10.1186/s40608-018-0188-2] [Medline: 29610670]

80. Harris TS, Ramsey M. Paternal modeling, household availability, and paternal intake as predictors of fruit, vegetable, and sweetened beverage consumption among African American children. Appetite 2015 Feb;85:171-177. [doi: 10.1016/j.appet.2014.11.008] [Medline: 25447009]
81. Heerman WJ, JaKa MM, Berge JM, Trapl ES, Sommer EC, Samuels LR, et al. The dose of behavioral interventions to prevent and treat childhood obesity: a systematic review and meta-regression. Int J Behav Nutr Phys Act 2017 Dec 15;14(1):157 [FREE Full text] [doi: 10.1186/s12966-017-0615-7] [Medline: 29141651]
82. Taki S, Lymer S, Russell CG, Campbell K, Laws R, Ong K, et al. Assessing user engagement of an mHealth intervention: development and implementation of the growing healthy app engagement index. JMIR Mhealth Uhealth 2017 Jun 29;5(6):e89 [FREE Full text] [doi: 10.2196/mhealth.7236] [Medline: 28663164]
83. Tian H, Brimmer DJ, Lin JS, Tumpey AJ, Reeves WC. Web usage data as a means of evaluating public health messaging and outreach. J Med Internet Res 2009;11(4):e52 [FREE Full text] [doi: 10.2196/jmir.1278] [Medline: 20026451]
84. Arendt J, Wagner C. Beyond description: converting web site usage statistics into concrete site improvement ideas. J Web Librariansh 2010;4(1):37-54. [doi: 10.1080/19322900903547414]
85. Glasgow RE, Christiansen SM, Kurz D, King DK, Woolley T, Faber AJ, et al. Engagement in a diabetes self-management website: usage patterns and generalizability of program use. J Med Internet Res 2011;13(1):e9 [FREE Full text] [doi: 10.2196/jmir.1391] [Medline: 21371992]
86. Benjamini Y, Hochberg Y. Controlling the false discovery rate: a practical and powerful approach to multiple testing. J R Stat Soc Series B Methodol 1995;57(1):289-300.
87. Hsieh HF, Shannon SE. Three approaches to qualitative content analysis. Qual Health Res 2005 Nov;15(9):1277-1288. [doi: 10.1177/1049732305276687] [Medline: 16204405]
88. Nguyen B, Kornman KP, Baur LA. A review of electronic interventions for prevention and treatment of overweight and obesity in young people. Obes Rev 2011 May;12(5):e298-e314. [doi: 10.1111/j.1467-789X.2010.00830.x] [Medline: 21348921]
89. Faith MS, Van Horn L, Appel LJ, Burke LE, Carson JA, Franch HA, et al. Evaluating parents and adult caregivers as "agents of change" for treating obese children: evidence for parent behavior change strategies and research gaps: a scientific statement from the American Heart Association. Circulation 2012 Mar 6;125(9):1186-1207 [FREE Full text] [doi: 10.1161/CIR.0b013e31824607ee] [Medline: 22271754]
90. Hoerr SL, Hughes SO, Fisher JO, Nicklas TA, Liu Y, Shewchuk RM. Associations among parental feeding styles and children's food intake in families with limited incomes. Int J Behav Nutr Phys Act 2009 Aug 13;6:55 [FREE Full text] [doi: 10.1186/1479-5868-6-55] [Medline: 19678947]
91. Davison KK, Lawson HA, Coatsworth JD. The Family-centered Action Model of Intervention Layout and Implementation (FAMILI): the example of childhood obesity. Health Promot Pract 2012 Jul;13(4):454-461. [doi: 10.1177/1524839910377966] [Medline: 21632465]
92. Ingoldsby EM. Review of interventions to improve family engagement and retention in parent and child mental health programs. J Child Fam Stud 2010 Oct 01;19(5):629-645 [FREE Full text] [doi: 10.1007/s10826-009-9350-2] [Medline: 20823946]
93. Arvidsson S, Gilljam BM, Nygren J, Ruland CM, Nordby-Bøe T, Svedberg P. Redesign and validation of Sisom, an interactive assessment and communication tool for children with cancer. JMIR Mhealth Uhealth 2016 Jun 24;4(2):e76 [FREE Full text] [doi: 10.2196/mhealth.5715] [Medline: 27343004]
94. Stålberg A, Sandberg A, Söderbäck M, Larsson T. The child's perspective as a guiding principle: young children as co-designers of an interactive application to facilitate participation in healthcare situations. J Biomed Inform 2016 Apr 2;61:149-158. [doi: 10.1016/j.jbi.2016.03.024] [Medline: 27050824]
95. Ruland CM, Starren J, Vatne TM. Participatory design with children in the development of a support system for patient-centered care in pediatric oncology. J Biomed Inform 2008 Aug;41(4):624-635 [FREE Full text] [doi: 10.1016/j.jbi.2007.10.004] [Medline: 18082468]
96. Rakes GC, Rakes TA, Smith LJ. Using visuals to enhance secondary students? Reading comprehension of expository texts. J Adolesc Adult Lit 1995;39:46-54.
97. Khanum MA, Trivedi MC. Arxiv. 2012 Dec. Take Care: A Study on Usability Evaluation Methods for Children URL: http://arxiv.org/abs/1212.0647 [accessed 2018-10-03] [WebCite Cache ID 72tdZFI8c]
98. Andersen MH, Khalid MS, Brooks EI. Considerations and methods for usability testing with children. In: Interactivity, Game Creation, Design, Learning, and Innovation. Cham, Switzerland: Springer; 2016:228-238.
99. Stinson J, McGrath P, Hodnett E, Feldman B, Duffy C, Huber A, et al. Usability testing of an online self-management program for adolescents with juvenile idiopathic arthritis. J Med Internet Res 2010;12(3):e30 [FREE Full text] [doi: 10.2196/jmir.1349] [Medline: 20675293]

Abbreviations

AHRQ: Agency for Healthcare Research and Quality
BMI: body mass index

F/V: fruit/vegetable
HBM: health belief model
INC: Interactive Nutrition Comics for urban, minority preadolescents
mHealth: mobile health
NTT: narrative transportation theory
NYC: New York City
RCT: randomized controlled trial
SCT: social cognitive theory
SUS: System Usability Scale
USE: Usefulness, Satisfaction, and Ease-of-use questionnaire
YRBSS: Youth Risk Behavioral Surveillance

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Protocol

The Ready to Reduce Risk (3R) Study for a Group Educational Intervention With Telephone and Text Messaging Support to Improve Medication Adherence for the Primary Prevention of Cardiovascular Disease: Protocol for a Randomized Controlled Trial

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Abstract

Background: Poor adherence to cardiovascular medications is associated with worse clinical outcomes. Evidence for effective education interventions that address medication adherence for the primary prevention of cardiovascular disease is lacking. The Ready to Reduce Risk (3R) study aims to investigate whether a complex intervention, involving group education plus telephone and text messaging follow-up support, can improve medication adherence and reduce cardiovascular risk.

Objective: This protocol paper details the design and rationale for the development of the 3R intervention and the study methods used.

Methods: This is an open and pragmatic randomized controlled trial with 12 months of follow-up. We recruited participants from primary care and randomly assigned them at a 1:1 frequency, stratified by sex and age, to either a control group (usual care from a general practitioner) or an intervention group involving 2 facilitated group education sessions with telephone and text messaging follow-up support, with a theoretical underpinning and using recognized behavioral change techniques. The primary outcome was medication adherence to statins. The primary measure was an objective, novel, urine-based biochemical measure of medication adherence. We also used the 8-item Morisky Medication Adherence Scale to assess medication adherence. Secondary outcomes were changes in total cholesterol, blood pressure, high-density lipoprotein, total cholesterol to high-density lipoprotein ratio, body mass index, waist to hip ratio, waist circumference, smoking behavior, physical activity, fruit and vegetable intake,

patient activation level, quality of life, health status, health and medication beliefs, and overall cardiovascular disease risk score. We also considered process outcomes relating to acceptability and feasibility of the 3R intervention.

Results: We recruited 212 participants between May 2015 and March 2017. The 12-month follow-up data collection clinics were completed in April 2018, and data analysis will commence once all study data have been collected and verified.

Conclusions: This study will identify a potentially clinically useful and effective educational intervention for the primary prevention of cardiovascular disease. Medication adherence to statins is being assessed using a novel urine assay as an objective measure, in conjunction with other validated measures.

Trial Registration: International Standard Randomized Controlled Trial Number ISRCTN16863160; http://www.isrctn.com/ISRCTN16863160 (Archived by WebCite at http://www.webcitation.org/734PqfdQw)

International Registered Report Identifier (IRRID): DERR1-10.2196/11289

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KEYWORDS

medication adherence; cardiovascular diseases; primary prevention; educational intervention; telephone support; text messaging support

Introduction

Background

Globally, cardiovascular disease (CVD), including heart attacks and stroke, is the leading cause of death. An estimated 17.7 million people died of CVD in 2015, representing 31% of all global deaths [1]. This is a significant burden on society. The overall CVD cost to the UK economy is approximately £19 billion [2]. However, it is estimated that 75% of all premature deaths from CVD are avoidable through effective reduction of modifiable risk factors [3].

International Guidance on Cardiovascular Disease Risk Management for Primary Prevention

Major international guidelines for the primary prevention of CVD provide the latest evidence-based guidance on lifestyle factors (exercise, diet, smoking, weight, and alcohol) and lipid-lowering medication to reduce CVD risk [4-7]. Despite some differences in the detail of the recommendations, there is a general consensus about the benefits of exercise, the cessation of smoking, and the use of statins for people at high risk of CVD [8].

The American Heart Association recommends the prescribing of statins for the primary prevention of CVD for all patients with a serum low-density lipoprotein cholesterol level above 4.9 mmol/L, regardless of their CVD risk profile [6]. In contrast, the European Society of Cardiology is more cautious and states that statins are more frequently required by individuals with low-density lipoprotein cholesterol levels raised to above 4.9 mmol/L but may not be necessary for those with a low CVD risk score (European Society of Cardiology systematic coronary risk estimation <5%) [7]. The latest UK National Institute for Health and Care Excellence guidelines no longer use specific cholesterol targets as markers of CVD risk; instead, they advise atorvastatin 20 mg to be offered as primary prevention in patients younger than 85 years with a 10-year QRISK2 score of more than 10% [4]. The QRISK2 is the updated version of the QRISK CVD risk calculator, which was developed and validated on a UK population and addresses risk issues such as ethnicity and social deprivation [9].

In the United Kingdom, this guidance has been controversial; as such, a low threshold for starting statins would mean that a 65-year-old man would obtain a risk of 10% despite optimal body mass index, optimal cholesterol, and no comorbidities [8]. An article by Abramson et al [10] further fueled the debate over the intolerable adverse effects that are reported by 5% to 10% of patients. Consequently, in the United Kingdom, there has been a lot of negative media coverage regarding the prescribing of statins, which has resulted in many patients stopping their medication [11]. Moreover, medication adherence to CVD-preventive drugs remains a problem in both secondary and primary CVD prevention.

Medication Adherence and Cardiovascular Disease Risk

For patients with CVD, self-reported adherence to CVD medications with a common combination of aspirin, beta-blocker, and a statin was shown to be less than 40% in both isolated and long-term follow-up surveys [12]. Moreover, despite the demonstrated safety and effectiveness of statins for CVD prevention, patient adherence to long-term statin treatment is poor [13-15]. In a recent study of a large cohort of Finnish patients (n=97,575), there was an approximately 30% increase in the risk of any cardiovascular events or death among primary prevention patients who adhered poorly to statins when they were compared with good adherers [16]. However, the evidence also suggests that the use of statins by patients is dynamic, and many patients after long periods of nonadherence will restart their treatment. This is strongly linked to clinical visits, implying that reiteration by general practitioners (GPs) of the role statins play in reducing risk may be beneficial [17].

With statin and antihypertensive treatments (the main medications used in primary CVD prevention), there are often multiple reasons for poor adherence to medication: forgetfulness, a negative attitude toward medication, frustration with poor therapeutic responses, preconceived beliefs regarding health and medication, and a poor understanding of the pros and cons of a prescribed drug. In particular, there is a lack of understanding of the benefit of CVD prevention medication and a fear of drug-related adverse events [18]. The number of barriers to medication adherence stresses the importance of how

health professionals communicate risk and treatment options to patients to promote behavioral change and engage people in self-management.

Poor medication adherence is one of the key reasons why overall CVD risk remains high despite patients being prescribed statins and provided with lifestyle advice by their GPs. Therefore, it is important that patient education addresses this issue and the many misconceptions to do with statins.

Structured Cardiovascular Disease Risk Education

Structured education has been widely advocated as a cost-effective method of promoting self-management and behavior change in individuals with chronic disease [19]. It is an alternative to one-to-one counselling and refers to group-based, patient-centered educational programs that have a clear philosophy; a written curriculum that is underpinned by appropriate learning and health behavior theories; an evidence base; and trained, quality-assessed educators [20].

In the United Kingdom, the Diabetes Education and Self Management for Ongoing and Newly Diagnosed (DESMOND) program for individuals with type 2 diabetes has demonstrated that a structured education program can be delivered within the UK National Health Service (NHS) at a national level and promote behavior change [21]. With the introduction of the NHS Health Checks and new treatment guidelines, there is a growing need for similar interventions to be developed, tested, and implemented to provide a proper pathway for the management of CVD risk.

Study Rationale

This paper details the design and rationale of the Ready to Reduce Risk (3R) study, a randomized controlled trial to evaluate the effectiveness of a complex intervention (the 3R Education Program with follow-up short message service (SMS) text messaging and telephone support) to improve medication adherence and reduce risk in the primary prevention of CVD in high-risk individuals. We describe the development of the 3R intervention and the study methods we used so as to allow for a thorough and robust report of the methodology used to deliver and evaluate this complex intervention prior to analysis and the publication of a results paper.

Methods

Compliance With Standards

We used the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) checklist (Multimedia Appendix 1) [22], in conjunction with the Consolidated Standards of Reporting Trials of Electronic and Mobile Health Applications and Online Telehealth (CONSORT-EHEALTH) checklist (Multimedia Appendix 2) [23], to describe the design of this study to ensure that this trial protocol is well reported.

Study Design

The study was an open, individual, and pragmatic randomized controlled trial recruiting participants from UK general practices (attached to a single study center). We recruited patients identified as being at high risk of CVD for primary prevention (total cholesterol ≥5 mmol/L) and already prescribed statins to reduce this risk. Participants were randomly assigned to either the control group (usual GP care) or the intervention group (3R Group Education Program plus follow-up telephone and SMS text messaging support). For both the control and intervention participants, the GP was informed of a patient's participation in the study but was not made aware of their group allocation. Both groups attended clinic visits at baseline and 12 months so that we could collect outcome data at these time points (Figure 1).

Participants and Recruitment

Eligibility Criteria for Participants

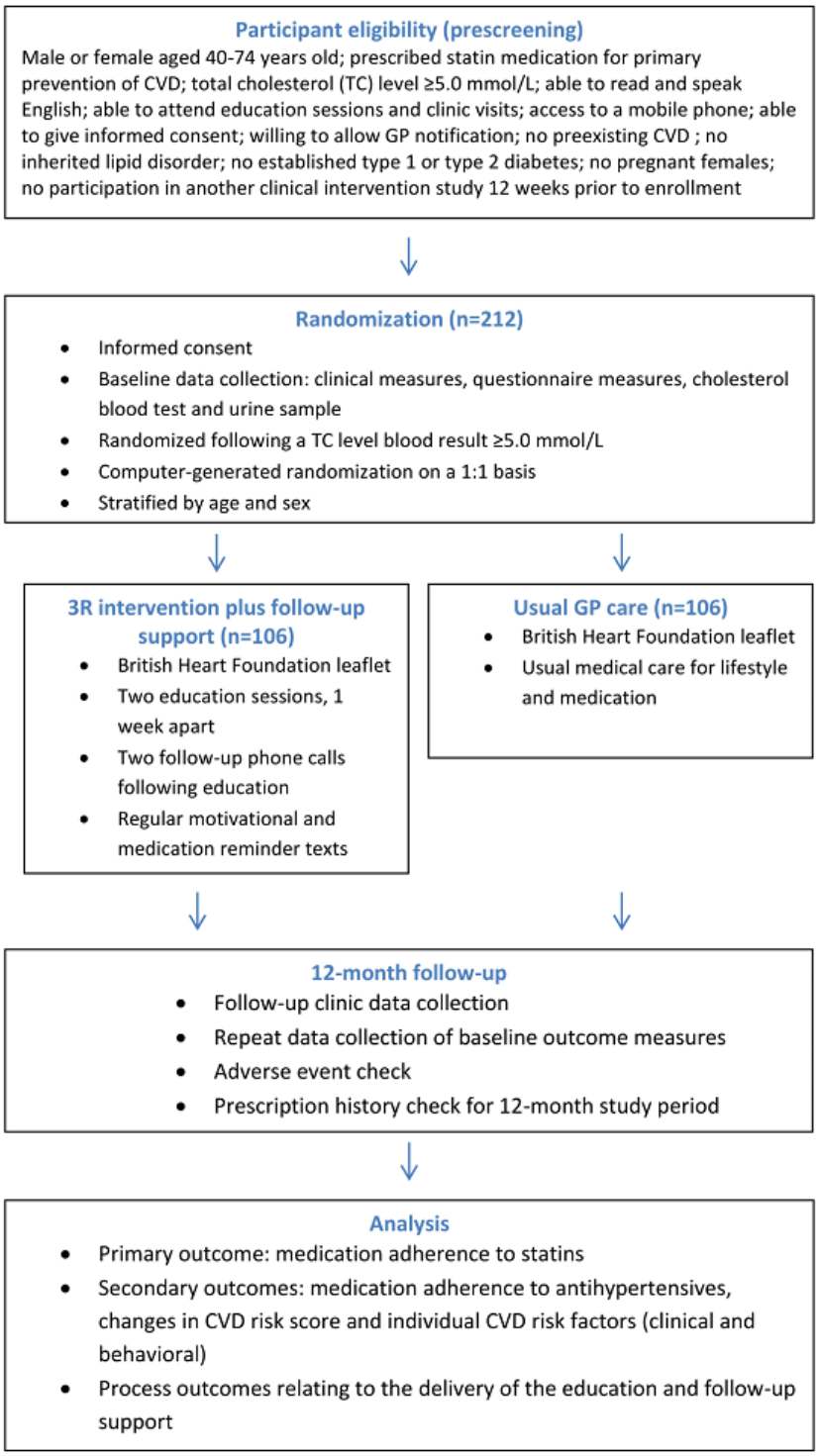
Eligibility criteria were as follow: (1) male or female and aged 40-74 years, inclusive, (2) prescribed a statin medication for primary prevention of CVD that was still active, at least 12 months prior to enrollment, (3) total cholesterol level ≥5.0 mmol/L at enrollment, (4) able to speak and read English to participate effectively in the group education program, (5) willing and able to attend education sessions and clinic visits, (6) access to a mobile phone, (7) willing and able to give informed consent, (8) willing to allow their GP to be notified of participation in the study, (9) no preexisting CVD, (10) no inherited lipid disorder, (11) no established type 1 or type 2 diabetes, (12) no women who were pregnant (self-reported), and (13) no participation in another clinical intervention study in the 12 weeks prior to enrollment.

As we expected there to be participants who had repeat prescriptions for statins but were not taking them as directed, we considered a prescription to be active, for the purpose of the study, if the prescription had been issued at least twice within the previous 2 years. We recruited participants with a total cholesterol level of 5 mmol/L or greater at baseline, based on the assumption that these participants were more likely to be nonadherent to statin medication if their cholesterol levels were higher.

Method of Recruitment

We identified general practices from across Northamptonshire, UK to take part in the study. We developed an automatic Morbidity Query Information Export Syntax (MIQUEST) search (based on the eligibility criteria described above) for the practices to download, from a secure online site, to generate a list of potential participants to be sent invitation packs. MIQUEST is a method that is used to extract data from different types of GP database systems, using a common query language to ensure consistency. Each invitation pack contained an invitation letter, a preliminary study information leaflet, and a reply slip with prepaid envelope. Prior to mailing these packs, a clinical member of the practice staff screened the list to ensure the suitability of patients to take part.

Figure 1. Study design. CVD: cardiovascular disease; GP: general practitioner.



Reply slips (from both positive and negative responders) were returned directly to the research team. We contacted all positive responders to verbally screen and confirm their eligibility for the study. Following this, eligible patients who were interested in taking part were booked to attend an initial data collection clinic. All participants were required to attend 2 data collection clinics: at baseline and at 12 months. The clinics were held in a suitable local venue, usually a community venue. Group clinics (of up to 8 participants at a time) were run by 3 trained study staff, including a qualified nurse. A full patient information sheet was sent with the clinic appointment letter. At the baseline clinic, written informed consent for all participants was taken by a trained research nurse before the collection of any data. All participants were made aware that they could withdraw from the study at any time. For each participant, a blood sample and clinical measurements were taken in accordance with local standard operating procedures, and a urine sample was collected. A hardcopy questionnaire booklet was completed at clinic by each participant. In addition, a hardcopy clinical research form was used to enter all other data collected at the baseline and 12-month time points, including demographic data, medical and medication histories, clinical measurements, blood results, and adverse events. Following clinics, all hardcopy study data collected were treated as confidential and kept securely in locked cabinets. Study data were anonymized and participants were identified by an allocated study number. These hardcopy data were then manually entered onto a validated, secure, and password-protected electronic database to be checked and verified prior to analysis.

Randomization

Following confirmation of an eligible blood result for cholesterol, participants were randomly assigned at a 1:1 frequency by a trained member of the 3R team not involved with data collection, using an online randomization tool (Sealed Envelope Ltd, London, UK). Participants were stratified by age (40-53 years and 54-74 years) and sex before been randomly allocated to either the control or intervention group. If 2 people were taking part from the same household, they were automatically assigned to the same arm to prevent any contamination between groups taking place. We considered contamination between intervention and control participants from the same GP practice to be minimal based on evidence from a systematic review of contamination in trials of education interventions [24]. Although the intervention involved some fact giving, the main objective was motivation for behavior change and knowledge empowerment, which must be directly experienced to be effective and is therefore unlikely to result in contamination.

Following enrollment, blinding of participants was not possible due to the open and pragmatic design of the study. However, we took some steps to reduce bias: data were collected by research nurses not involved in any analysis; GPs were not informed of a participant's group allocation; urine samples were analyzed by laboratory staff blinded to the randomized groups; and, prior to study completion, detailed protocol information was not made available online, which participants could have accessed.

Control Group

The control group continued with their usual GP care with regard to lifestyle and medication advice for the primary prevention of CVD. To ensure that all participants had access to at least some basic knowledge about managing CVD risks, we sent both groups a British Heart Foundation booklet (*Keep Your Heart Healthy*), which contained general information about CVD risk prevention.

Intervention Group

Development of the 3R Education Program and Follow-Up Support

We developed the 3R Education Program in line with UK Medical Research Council recommendations for the development of complex interventions [25,26]. We specifically focused on helping participants develop an increased sense of the role of their behaviors in their long-term health and risk by addressing their perceptions and beliefs surrounding CVD risk and medication adherence. In the absence of one unified model or construct, we used the concept of patient activation [27] and the capability, opportunity, and motivation model, as it encapsulates many theoretical components of behavior change theory [28]. We used the behavior change taxonomy [29] to ensure accurate reporting and to help identify the key active components of behavior change interventions.

An experienced working group of health professionals, led by a psychologist, developed the intervention based on the DESMOND philosophy of empowerment, whereby participants are supported, rather than taught, to discover and work out knowledge to achieve their own health goals [30]. We used several stages (including a literature search and focus groups with potential users) to explore and expand the original idea within the framework of the capability, opportunity, and motivation model [28]. This process informed the content, format, and theoretical basis of the program and was used to draft a curriculum to provide a written structure for the 3R Education Program and to identify the key component behavior change techniques to be used. We evaluated this using an iterative process of testing with potential users, feedback, and modification until we considered the program ready for implementation. We also developed educational, mixed-media resources to support the delivery of the curriculum and to engage participants in the learning activities. In conjunction with the development of the education program, a 2-day training program led by an experienced psychologist was delivered to a group of 6 facilitators to ensure consistent delivery of the curriculum. The newly trained facilitators were given the opportunity to practice delivery of the program before the start of the study.

In addition to the main education program, we developed follow-up support to help sustain any potential positive effects of the education with regard to improvements in medication adherence and other individual CVD risk factors. Continued support to maintain and promote positive health behavioral change has been shown to be effective when provided as brief telephone calls [31], and with SMS text messaging for medication adherence [32,33] and CVD risk factors [34,35]. After reviewing this literature, we considered the best format

for the delivery of the 3R follow-up support to be a combination approach of using both text messages and phone calls to try to sustain the effect of the education.

For the text messages, this process involved using content that had already been robustly developed and validated in the Tobacco, Exercise and Diet Messages (TEXTME) study [36]. These text messages were originally developed for secondary CVD prevention but matched our requirements for primary CVD prevention: (1) general heart health information messages that included facts about CVD and information about medications and risk factors, (2) nutrition messages, (3) physical activity messages, and (4) smoking cessation messages. The message content had been specifically designed using behavioral change techniques, and a whole process of refining and piloting the messages had been applied. We had been impressed by the rigorous methods used to develop these messages and the success that they had achieved with the improvement of low-density lipoprotein cholesterol at 6 months, as well as improvement in other secondary end points (blood pressure, body mass index, smoking, and physical activity) [35]. Prior to use, the TEXTME messages were reviewed and adapted to make the content culturally appropriate for our UK patient cohort by 3 health professionals (a dietician, a nurse research fellow, and a GP). Furthermore, we created some additional medication reminder texts to be delivered in conjunction with the TEXTME texts that were specifically focused on improving medication adherence by prompting people to take their statin medication at a set time.

For the phone calls, we developed a semistructured script and a 1-day training session (involving practice role-play scenarios) using the same framework that we had used for the follow-up calls in the successful Pre‐diabetes Risk Education and Physical Activity Recommendation and Encouragement (PREPARE) study, which sustained the effect of a an educational intervention on glucose regulation at 2 years [31].

Delivery of the 3R Education Program and Follow-Up Support

We invited the intervention group to attend the 3R Education Program and receive the follow-up support (text messages and phone calls). They continued with their usual GP care and were sent a copy of the British Heart Foundation booklet. Textbox 1, Textbox 2, and Textbox 3 detail the different components involved in the delivery of each of the 3 major elements of the intervention and identify the behavioral control techniques [29] or active components involved in each.

Outcomes and Measures

Primary Outcome

The primary outcome was medication adherence to statins at 12 months (Table 1) [37-44]. The primary measure was a urine-based biochemical measure involving a novel assay to test for statin and antihypertensive levels in urine samples. This method has already been used successfully to show poor adherence to antihypertensive medication [45]. Participants were informed that urine samples would be collected to assess the levels of statins and were asked to provide a first morning urine sample (in a standard urine collection tube) prior to clinic. This test uses a high-performance liquid chromatography–tandem mass spectrometry analysis of spot urine samples (2-5 mL) to detect 60 commonly prescribed cardiovascular medications, including statins. The results are reported as binary outcomes (yes or no) and hence are based on the limit of detection of a medication. The limit of detection is in the low nanomolar per liter range for all medications (in-house data). The method has been set up using established laboratory criteria for qualitative assays [46]. The method is robust and reliable and has been developed from techniques used in forensic medicine [47] and in testing for drug abuse in elite sports [48]. We use the test routinely in various cardiovascular clinics, and have set up the first National Centre for Drug Adherence Testing and receive samples from 25 centers across the United Kingdom [49].

Textbox 1. Ready to Reduce Risk (3R) Education Program.

- Setting: local venue (eg, community hall).
- Format: group education (approximately 8 per group; participants were allowed to take a partner or friend) facilitated by a written structured curriculum and mixed-media educational resources (including a free pedometer).
- Frequency: 2 sessions.
- Duration: approximately 2 hours each.
- Facilitators: 2 trained facilitators (at least one was a health care professional).
- Training: 2-day course, self-study, and practice run.
- Monitoring: ad hoc filmed sessions.
- Outline
  - Session 1: explored understanding and beliefs to do with cardiovascular disease risk and how to manage it; showed how to calculate their own risk score using the Joint British Societies calculator; raised awareness of factors that influence risk, how these affect the body, and the role of medication; and explored beliefs about medication adherence.
  - Session 2: increased knowledge and awareness about how to have a healthier lifestyle to reduce cardiovascular disease risk and introduced behavioral control techniques to support activated participants.
- Theories and models: capability, opportunity, and motivation model; patient empowerment; working alliance; patient activation; self-regulation; self-determination; cognitive dissonance; self-efficacy.
- Behavioral control techniques: goal setting (outcome); problem solving; action planning; self-monitoring of outcome(s) of behavior; social support (emotional); social support (practical); information about health consequences; salience of consequences; demonstration of behavior; pros and cons; adding objects to the environment; incompatible beliefs; valued self-identity.

Textbox 2. Follow-up support phone calls after the Ready to Reduce Risk (3R) Education Program.

- Setting: participants were called at home by a member of the 3R study team from a private office and designated study mobile.
- Format: participants received individual calls facilitated by a semistructured script and delivered using a patient-centered approach.
- Frequency: 2 calls at approximately 2 weeks and 6 months.
- Duration: approximately 10-20 minutes each.
- Facilitator: a trained member of the 3R team who was experienced in calling research participants.
- Monitoring: written records of the calls were documented by the facilitator, using a structured template.
- Outline: participants were called at a convenient time and asked some questions about how they were getting on following the 3R Education Program. The facilitator used open questions to elicit information about what had been going well and not so well, and participants were given the opportunity to discuss any pitfalls and ways to overcome these.
- Theories and models: the theoretical basis was the same as that for the 3R Education Program.
- Behavioral control techniques: goal setting (outcome); problem solving; action planning; self-monitoring of outcome(s) of behavior; social support (emotional); social support (practical); information about health consequences; pros and cons; valued self-identity.

Textbox 3. Text messaging follow-up support after the Ready to Reduce Risk (3R) Education Program.

- Setting: 1 week posteducation, participants received text messages to their own mobiles via an independent text messaging service, which is set up to work from the secure study contacts database.
- Format: a series of automated, unidirectional text messages were sent, consisting of medication reminders (eg, "Have you taken your tablets today?"), and motivational and support Tobacco, Exercise and Diet Messages (TEXTME) messages (eg, "Walking up and down a flight of stairs several times is a great strengthening activity.").
- Duration: 44 weeks.
- Frequency:
  - Medication reminders: weeks 1 and 2 (7 texts); weeks 3 and 4 (4 texts); weeks 5-26 (1 text); weeks 27 and 28 (7 texts); weeks 29 and 30 (4 texts); weeks 31-44 (1 texts). (Sent at the same time each evening.)
  - TEXTME messages: 4 texts per week. (Sent on random weekdays at random times.)
- Facilitator: texts were initiated and stopped manually by the 3R team.
- Training: participants received a *3R Follow-On Support* booklet and facilitators received training from their clinical research service (who developed the study database) on how to manage the text messaging support via the database interface.
- Monitoring: all texts sent were logged and monitored to identify any problems.
- Outline: participants could choose between a smokers' and nonsmokers' pathway for the type of texts that they received. A series of texts relating to healthy eating, physical activity, medication, general heart health, and smoking (if chosen) were then delivered as per the 44-week schedule detailed above. Texts could be stopped at any time by the participant, by sending a text to a specified number.
- Theories and models: the theoretical basis of the TEXTME messages is detailed in the protocol paper by Redfern et al [36].
- Behavioral control techniques: reduce prompts and cues (for medication reminders); other behavioral control techniques associated with the TEXTME messages are detailed in Redfern et al [36].

Table 1. Data collection schedule.

Demographic data	Measure	Baseline	12 months
Sex and age	Self-report	✓	N/A[a]
Medical history	Self-report	✓	✓
Medication history	Self-report/GP[b] database	✓	✓
Primary outcome			
Medication adherence to statins	Urine test	✓	✓
Secondary outcomes			
Cardiovascular disease risk score (%)	QRISK2 calculator	✓	✓
TC[c], HDL[d], TC:HDL (mmol/L)	Blood sample	✓	✓
Blood pressure (mm Hg)	Omron monitor	✓	✓
Body mass index (kg/m^2)	Height (cm) and weight (kg)	✓ (height and weight)	✓ (weight only)
Smoking history	Self-report using QRISK2 format	✓	✓
Fruit and vegetable intake	Self-report: 5-a-day Community Evaluation Tool (FACET) [38]	✓	✓
Quality of life	Self-report: 15D (a generic, comprehensive, 15-dimensional, standardized measure of health-related quality of life) [39]	✓	✓
Health status	Self-report: EuroQol 5 dimensions questionnaire (EQ-5D, a standardized instrument for measuring generic health status) [40]	✓	✓
Physical activity	Self-report: International Physical Activity Questionnaire (IPAQ; short form) [41]	✓	✓
Patient activation	Self-report: Patient Activation Measure (PAM, a valid and reliable scale that reflects a developmental model of an individual's readiness for health behavior change) [42]	✓	✓
Medication/Health Beliefs	Self-report: Beliefs about Medicines Questionnaire (BMQ) [43] and the Brief Illness Perception Questionnaire (Brief IPQ) [44]	✓	✓
Medication adherence to statins	Self-report: 8-item Morisky Medication Adherence Scale (MMAS)[f] [37]	✓	✓
Other supporting outcomes[e]			
Prescription history	Record of repeat prescription issues for statins and antihypertensives (if applicable) from the GP database	✓	✓
Adverse events	Self-report and observed from GP database	✓	✓

[a]N/A: not applicable.

[b]GP: general practitioner.

[c]TC: total cholesterol.

[d]HDL: high-density lipoprotein.

[e]For the duration of the study.

[f]Use of the MMAS is protected by US and International copyright laws. Permission for use is required. A license agreement is available from: Donald E Morisky, MMAS Research (MORISKY), 294 Lindura Court, Las Vegas, NV 89138-4632; dmorisky@gmail.com.

In addition, the self-reported 8-item Morisky Medication Adherence Scale (MMAS) was completed at baseline and 12 months. This is an established and validated scale that is commonly used to measure adherence [37,50,51]. At the end of the study, we asked GP practices to provide details for individual participants regarding both statin and antihypertensive (if applicable) prescription issued during the 12 months of the study (Table 1). These data will provide useful supporting information about the pattern of patient medication adherence behavior over the 12-month study period.

Secondary Outcomes

Secondary outcomes were adherence to antihypertensive medications and other anticipated potential effects of the intervention, including a change in overall CVD risk score

measured by the QRISK2 calculator [52], as well as potential changes in the following individual CVD risk factors: total cholesterol, high-density lipoprotein, total cholesterol to high-density lipoprotein ratio, blood pressure, and body mass index. We also observed changes in behavior and lifestyle using validated questionnaire measures: smoking, physical activity, fruit and vegetable intake, patient activation level, well-being, health status, health and medication beliefs, and medication adherence to antihypertensives (for participants prescribed this treatment for high blood pressure). We collected all outcome measures at the baseline and 12-month clinics in line with standard operating procedures and good clinical practice guidelines (Table 1). In addition, we checked for and recorded adverse events at the final visit and whenever a participant was contacted, for the purpose of the study, to monitor health status during the course of the study. Table 1 details all outcome data collected at the specified time points.

Process Outcomes

We also collected process outcomes relating to participant acceptability and fidelity of the education intervention. We used feedback data from the evaluation forms given out following the end of the education sessions to assess participant acceptability in conjunction with retention rates for the 2 sessions. We videotaped 3 sessions, with the participants' permission, to assess the fidelity of the delivered education sessions. Logs were kept to record the initiation, delivery, and any terminations of text messages, and all attempted follow-up support phone calls were recorded.

Sample Size

The primary outcome measure was medication adherence to statins at 12 months. We based the sample size calculation on the percentage of nonadherers by using data from the Investigation of Text Message Reminders on Adherence to Cardiac Treatment (INTERACT) trial [32]. To detect a difference in the proportion of medication adherers (of 16 percentage points in the intervention group at 12 months compared with the usual-care control group—ie, 91% compared with 74%), we required 84 participants per group with 80% power and 5% significance. After allowing for a 20% dropout, we required 105 participants per group, making 210 participants in total. This minimum difference was based on a similar 16 percentage–point increase in adherence to cardiovascular preventive treatment observed in the INTERACT trial [32], which used text messaging as the sole intervention. This was a 6-month follow-up study with a final control group adherence of 75%. We envisaged similar adherence to medication at 12 months' follow-up, following our complex intervention with continued follow-up support via SMS text messaging and phone calls to sustain any initial intervention effect.

The study design was pragmatic and reflected how it would be delivered if it were implemented in practice. The study was designed to mitigate the effects of unbalanced clustering in the intervention group by using a standardized curriculum, a small group of trained facilitators to deliver education and phone calls, a small number of venues, standardized text messages, and standardized phone calls. Moreover, we assessed process outcomes relating to fidelity to allow for clear reporting of any variation that occurred. This was in line with the Medical Research Council guidance for complex interventions [26].

Statistical Methods

For evaluation, we will summarize baseline characteristics of the 2 groups with means, standard deviations, and medians and ranges for continuous variables; and counts and percentages for categorical variables. Logistic regression will assess the difference in medication adherence by group, adjusted for the stratification factors (sex and age) at 12 months. We will assess the primary outcome at the 5% level with 95% confidence intervals. The primary analysis at 12 months will be based on complete data. The analysis of the secondary outcomes will be conducted in a similar manner using the appropriate model type: logistic regression for binary outcomes, linear for continuous outcomes, and ordinal for ordinal outcomes.

We will carry out sensitivity analyses on an intention-to-treat basis and a per-protocol basis to examine robustness of conclusions for missing data and attendance of the program. To adhere to the intention-to-treat principle, we will impute missing outcome data by multiple imputation using the command MI in Stata (StataCorp LLC). We will also conduct analysis by adding the MMAS adherence data where urine adherence data are missing.

Ethics and Dissemination

We will disseminate the results of this study via the usual scientific forums: peer-reviewed publications and presentations at international conferences. At the local level, key stakeholders will be informed of the findings. The study has been administered by the Leicester Diabetes Centre and is overseen by the UK National Institute for Health Research Collaboration for Leadership in Applied Health Research and Care East Midlands Scientific Committee.

Ethics approval was obtained from the NHS Health Research Authority East Midlands-Leicester South Research Ethics Committee (15/EM/0472) prior to the commencement of the study. The trial is registered with the ISRCTN registry (ISRCTN16863160).

Results

We recruited participants from May 2015 to March 2017, and have enrolled and randomly assigned a total of 212 participants. We finished follow-up clinic data collection in April 2018 and will commence the analysis of the results once we have collected and verified all data.

Discussion

Summary

This study aims to identify a potentially clinically useful and effective educational intervention to improve medication adherence to cardiovascular medications for the primary prevention of CVD, to be delivered as an adjunct to primary care.

This protocol paper offers a complete and thorough description of the 3R intervention and study methodology used prior to

analysis and evaluation. A recent systematic review, looking at interventions to improve adherence to statin medication, highlighted that multifaceted interventions had small, positive effects on adherence, but that more methodologically rigorous trials are needed [53]. The 3R study has followed SPIRIT and CONSORT-EHEALTH guidance [22,23] to ensure rigorous methods are used, and publication of a protocol paper, prior to evaluation, allows this complex intervention to be described in the robust manner that is now expected. Due to significant amendments and potential biasing of outcome data from participants accessing information about the intervention, publishing a protocol paper prior to trial completion introduced several potential pitfalls for the reporting of the study. This is now a recognized problem for complex intervention trials that can be avoided by publishing protocols after trial completion [54].

We developed the 3R educational intervention in line with the Medical Research Council guidelines for complex interventions [25,26]. Moreover, we used a taxonomy of behavior change techniques [29] to identify the key active components to ensure more precise reporting of the intervention and to aid future research in this field. Due to the complexity of the 3R intervention, there will have been unavoidable variations in how the intervention was delivered, such as the use of different facilitators and venue settings; however, we monitored all components of the intervention to ensure that, as far as possible, the intervention was delivered as per protocol. We addressed process outcomes relating to patient acceptability and feasibility of the intervention and will carry out a cost-effectiveness analysis if the study proves to be successful.

Conclusions

Medication adherence is a challenging primary outcome to measure, as no “gold standard” measure exists. In the 3R study, we have addressed this challenge by using a new and novel biochemical urine test as the primary measure [45]. Although this is an objective measure, it is essentially a spot-check of medication adherence to statins. There is also a bias with this measure because, ethically, participants have to be informed that their urine is being tested for statins. Therefore, we have also used a self-reported validated questionnaire (MMAS) [37,50,51] and repeat prescription history as supporting outcome measures. However, despite the challenges of this type of research, if it is successful, we hope that the 3R Education Program can be implemented within the primary care framework to improve medication adherence to statins and other CVD medications, and to provide better support for GPs and people at risk of CVD.

Protocol Amendments

We have made the following significant changes to the original protocol. First, we revised the original time windows for conducting follow-up phone calls, as these were too restrictive and not practical. Second, we changed the primary outcome measure to the objective urine-based measure from the MMAS self-reported questionnaire measure. We made this change following additional validation data for the urine measure, which was not available at the start of the study.

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Authors' Contributions

KK conceived the original idea and is the chief investigator; KK, SR, LJG, JLB, and HMD led the overall design of the randomized controlled trial; YD was responsible for the development of the intervention; JLB drafted the manuscript; and all other authors (KK, SR, LJG, HMD, GW, PP, PG, and MD) helped edit and review the manuscript.

Conflicts of Interest

PG and PP were involved in the development of the urine assay test for the detection of statins and antihypertensive medications.

Multimedia Appendix 1

Checklist of recommended items to address in a clinical trial protocol.

[PDF File (Adobe PDF File), 122KB - resprot_v7i11e11289_app1.pdf]

Multimedia Appendix 2

CONSORT-EHEALTH checklist V 1.6.1.

[PDF File (Adobe PDF File), 359KB - resprot_v7i11e11289_app2.pdf]

Multimedia Appendix 3

Peer-review report from CLAHRC-EM.

[PDF File (Adobe PDF File), 159KB - resprot_v7i11e11289_app3.pdf]

References

1. World Health Organization. Fact sheet: cardiovascular diseases (CVDs). 2017 May 17. URL: http://www.who.int/en/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds) [accessed 2018-06-14] [WebCite Cache ID 70ARZhWU7]
2. Townsend N, Wickramasinghe K, Bhatnagar P, Smolina K, Nichols M, Leal J, et al. Coronary Heart Disease Statistics: 2012 Edition. London, UK: British Heart Foundation; 2012.
3. World Health Organization. The challenge of cardiovascular disease - quick statistics. 2018. URL: http://www.euro.who.int/en/health-topics/noncommunicable-diseases/cardiovascular-diseases/data-and-statistics [accessed 2018-06-14] [WebCite Cache ID 70ARxRTCv]
4. National Institute for Health and Care Excellence. Lipid Modification: Cardiovascular Risk Assessment and the Modification of Blood Lipids for the Primary and Secondary Prevention of Cardiovascular Disease. London, UK: NICE; Jul 2014.
5. Eckel RH, Jakicic JM, Ard JD, de Jesus JM, Houston MN, Hubbard VS, et al. 2013 AHA/ACC guideline on lifestyle management to reduce cardiovascular risk: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation 2014 Jun 24;129(25 Suppl 2):S76-S99 [FREE Full text] [doi: 10.1161/01.cir.0000437740.48606.d1] [Medline: 24222015]
6. Stone NJ, Robinson JG, Lichtenstein AH, Bairey MCN, Blum CB, Eckel RH, American College of Cardiology/American Heart Association Task Force on Practice Guidelines. 2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2014 Jul 01;63(25 Pt B):2889-2934 [FREE Full text] [doi: 10.1016/j.jacc.2013.11.002] [Medline: 24239923]
7. Piepoli MF, Hoes AW, Agewall S, Albus C, Brotons C, Catapano AL, ESC Scientific Document Group. 2016 European Guidelines on cardiovascular disease prevention in clinical practice: the Sixth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of 10 societies and by invited experts)Developed with the special contribution of the European Association for Cardiovascular Prevention & Rehabilitation (EACPR). Eur Heart J 2016 Dec 01;37(29):2315-2381 [FREE Full text] [doi: 10.1093/eurheartj/ehw106] [Medline: 27222591]
8. Stewart J, Manmathan G, Wilkinson P. Primary prevention of cardiovascular disease: a review of contemporary guidance and literature. JRSM Cardiovasc Dis 2017;6:2048004016687211 [FREE Full text] [doi: 10.1177/2048004016687211] [Medline: 28286646]
9. Hippisley-Cox J, Coupland C, Vinogradova Y, Robson J, Minhas R, Sheikh A, et al. Predicting cardiovascular risk in England and Wales: prospective derivation and validation of QRISK2. BMJ 2008 Jun 28;336(7659):1475-1482 [FREE Full text] [doi: 10.1136/bmj.39609.449676.25] [Medline: 18573856]
10. Abramson JD, Rosenberg HG, Jewell N, Wright JM. Should people at low risk of cardiovascular disease take a statin? BMJ 2013 Oct 22;347:f6123. [Medline: 24149819]
11. Matthews A, Herrett E, Gasparrini A, Van Staa T, Goldacre B, Smeeth L, et al. Impact of statin related media coverage on use of statins: interrupted time series analysis with UK primary care data. BMJ 2016 Jun 28;353:i3283 [FREE Full text] [Medline: 27353418]
12. Newby LK, LaPointe NMA, Chen AY, Kramer JM, Hammill BG, DeLong ER, et al. Long-term adherence to evidence-based secondary prevention therapies in coronary artery disease. Circulation 2006 Jan 17;113(2):203-212 [FREE Full text] [doi: 10.1161/CIRCULATIONAHA.105.505636] [Medline: 16401776]
13. Caspard H, Chan AK, Walker AM. Compliance with a statin treatment in a usual-care setting: retrospective database analysis over 3 years after treatment initiation in health maintenance organization enrollees with dyslipidemia. Clin Ther 2005 Oct;27(10):1639-1646. [doi: 10.1016/j.clinthera.2005.10.005] [Medline: 16330301]
14. Perreault S, Blais L, Lamarre D, Dragomir A, Berbiche D, Lalonde L, et al. Persistence and determinants of statin therapy among middle-aged patients for primary and secondary prevention. Br J Clin Pharmacol 2005 May;59(5):564-573 [FREE Full text] [doi: 10.1111/j.1365-2125.2005.02355.x] [Medline: 15842555]
15. Mann DM, Allegrante JP, Natarajan S, Halm EA, Charlson M. Predictors of adherence to statins for primary prevention. Cardiovasc Drugs Ther 2007 Aug;21(4):311-316. [doi: 10.1007/s10557-007-6040-4] [Medline: 17665294]
16. Rannanheimo PK, Tiittanen P, Hartikainen J, Helin-Salmivaara A, Huupponen R, Vahtera J, et al. Impact of statin adherence on cardiovascular morbidity and all-cause mortality in the primary prevention of cardiovascular disease: a population-based cohort study in Finland. Value Health 2015 Sep;18(6):896-905 [FREE Full text] [doi: 10.1016/j.jval.2015.06.002] [Medline: 26409618]
17. Brookhart MA, Patrick AR, Schneeweiss S, Avorn J, Dormuth C, Shrank W, et al. Physician follow-up and provider continuity are associated with long-term medication adherence: a study of the dynamics of statin use. Arch Intern Med 2007 Apr 23;167(8):847-852. [doi: 10.1001/archinte.167.8.847] [Medline: 17452550]

18. Casula M, Tragni E, Catapano AL. Adherence to lipid-lowering treatment: the patient perspective. Patient Prefer Adherence 2012;6:805-814 [FREE Full text] [doi: 10.2147/PPA.S29092] [Medline: 23152673]
19. Chatterjee S, Davies MJ, Heller S, Speight J, Snoek FJ, Khunti K. Diabetes structured self-management education programmes: a narrative review and current innovations. Lancet Diabetes Endocrinol 2018 Dec;6(2):130-142. [doi: 10.1016/S2213-8587(17)30239-5] [Medline: 28970034]
20. Department of Health, Diabetes UK. Structured patient education in diabetes: report from the Patient Education Working Group. 2005 Jun 15. URL: http://webarchive.nationalarchives.gov.uk/20130105204013/http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_4113195 [accessed 2018-06-14] [WebCite Cache ID 70ASLiT7l]
21. Davies MJ, Heller S, Skinner TC, Campbell MJ, Carey ME, Cradock S, et al. Effectiveness of the diabetes education and self management for ongoing and newly diagnosed (DESMOND) programme for people with newly diagnosed type 2 diabetes: cluster randomised controlled trial. BMJ 2008 Mar 1;336(7642):491-495 [FREE Full text] [doi: 10.1136/bmj.39474.922025.BE] [Medline: 18276664]
22. Chan A, Tetzlaff JM, Gøtzsche PC, Altman DG, Mann H, Berlin JA, et al. SPIRIT 2013 explanation and elaboration: guidance for protocols of clinical trials. BMJ 2013;346:e7586 [FREE Full text] [Medline: 23303884]
23. Eysenbach G, CONSORT-EHEALTH Group. CONSORT-EHEALTH: improving and standardizing evaluation reports of Web-based and mobile health interventions. J Med Internet Res 2011;13(4):e126 [FREE Full text] [doi: 10.2196/jmir.1923] [Medline: 22209829]
24. Keogh-Brown MR, Bachmann MO, Shepstone L, Hewitt C, Howe A, Ramsay CR, et al. Contamination in trials of educational interventions. Health Technol Assess 2007 Oct;11(43):iii, ix-iii,107 [FREE Full text] [Medline: 17935683]
25. Campbell M, Fitzpatrick R, Haines A, Kinmonth AL, Sandercock P, Spiegelhalter D, et al. Framework for design and evaluation of complex interventions to improve health. BMJ 2000 Sep 16;321(7262):694-696 [FREE Full text] [Medline: 10987780]
26. Craig P, Dieppe P, Macintyre S, Michie S, Nazareth I, Petticrew M, Medical Research Council Guidance. Developing and evaluating complex interventions: the new Medical Research Council guidance. BMJ 2008;337:a1655 [FREE Full text] [Medline: 18824488]
27. Hibbard JH, Stockard J, Mahoney ER, Tusler M. Development of the Patient Activation Measure (PAM): conceptualizing and measuring activation in patients and consumers. Health Serv Res 2004 Aug;39(4 Pt 1):1005-1026 [FREE Full text] [doi: 10.1111/j.1475-6773.2004.00269.x] [Medline: 15230939]
28. Michie S, van Stralen MM, West R. The behaviour change wheel: a new method for characterising and designing behaviour change interventions. Implement Sci 2011;6:42 [FREE Full text] [doi: 10.1186/1748-5908-6-42] [Medline: 21513547]
29. Michie S, Richardson M, Johnston M, Abraham C, Francis J, Hardeman W, et al. The behavior change technique taxonomy (v1) of 93 hierarchically clustered techniques: building an international consensus for the reporting of behavior change interventions. Ann Behav Med 2013 Aug;46(1):81-95. [doi: 10.1007/s12160-013-9486-6] [Medline: 23512568]
30. Feste C, Anderson RM. Empowerment: from philosophy to practice. Patient Educ Couns 1995 Sep;26(1-3):139-144. [Medline: 7494713]
31. Yates T, Davies MJ, Sehmi S, Gorely T, Khunti K. The Pre-diabetes Risk Education and Physical Activity Recommendation and Encouragement (PREPARE) programme study: are improvements in glucose regulation sustained at 2 years? Diabet Med 2011 Oct;28(10):1268-1271. [doi: 10.1111/j.1464-5491.2011.03357.x] [Medline: 21672008]
32. Wald DS, Bestwick JP, Raiman L, Brendell R, Wald NJ. Randomised trial of text messaging on adherence to cardiovascular preventive treatment (INTERACT trial). PLoS One 2014;9(12):e114268 [FREE Full text] [doi: 10.1371/journal.pone.0114268] [Medline: 25479285]
33. Park LG, Howie-Esquivel J, Chung ML, Dracup K. A text messaging intervention to promote medication adherence for patients with coronary heart disease: a randomized controlled trial. Patient Educ Couns 2014 Feb;94(2):261-268. [doi: 10.1016/j.pec.2013.10.027] [Medline: 24321403]
34. Free C, Knight R, Robertson S, Whittaker R, Edwards P, Zhou W, et al. Smoking cessation support delivered via mobile phone text messaging (txt2stop): a single-blind, randomised trial. Lancet 2011 Jul 2;378(9785):49-55 [FREE Full text] [doi: 10.1016/S0140-6736(11)60701-0] [Medline: 21722952]
35. Chow CK, Redfern J, Hillis GS, Thakkar J, Santo K, Hackett ML, et al. Effect of lifestyle-focused text messaging on risk factor modification in patients with coronary heart disease: a randomized clinical trial. JAMA 2015;314(12):1255-1263. [doi: 10.1001/jama.2015.10945] [Medline: 26393848]
36. Redfern J, Thiagalingam A, Jan S, Whittaker R, Hackett ML, Mooney J, et al. Development of a set of mobile phone text messages designed for prevention of recurrent cardiovascular events. Eur J Prev Cardiol 2014 Apr;21(4):492-499. [doi: 10.1177/2047487312449416] [Medline: 22605787]
37. Morisky DE, Ang A, Krousel-Wood M, Ward HJ. Predictive validity of a medication adherence measure in an outpatient setting. J Clin Hypertens (Greenwich) 2008 May;10(5):348-354 [FREE Full text] [Medline: 18453793]
38. Ashfield-Watt PAL, Welch AA, Godward S, Bingham SA. Effect of a pilot community intervention on fruit and vegetable intakes: use of FACET (Five-a-day Community Evaluation Tool). Public Health Nutr 2007 Jul;10(7):671-680. [doi: 10.1017/S1368980007382517] [Medline: 17381948]

39. Sintonen H. The 15D instrument of health-related quality of life: properties and applications. Ann Med 2001 Jul;33(5):328-336. [Medline: 11491191]
40. Dyer MTD, Goldsmith KA, Sharples LS, Buxton MJ. A review of health utilities using the EQ-5D in studies of cardiovascular disease. Health Qual Life Outcomes 2010 Jan 28;8:13 [FREE Full text] [doi: 10.1186/1477-7525-8-13] [Medline: 20109189]
41. Craig CL, Marshall AL, Sjöström M, Bauman AE, Booth ML, Ainsworth BE, et al. International physical activity questionnaire: 12-country reliability and validity. Med Sci Sports Exerc 2003 Aug;35(8):1381-1395. [doi: 10.1249/01.MSS.0000078924.61453.FB] [Medline: 12900694]
42. Hibbard JH, Mahoney ER, Stockard J, Tusler M. Development and testing of a short form of the patient activation measure. Health Serv Res 2005 Dec;40(6 Pt 1):1918-1930 [FREE Full text] [doi: 10.1111/j.1475-6773.2005.00438.x] [Medline: 16336556]
43. Horne R, Weinman J, Hankins M. The beliefs about medicines questionnaire: the development and evaluation of a new method for assessing the cognitive representation of medication. Psychol Health 1999 Jan;14(1):1-24. [doi: 10.1080/08870449908407311]
44. Broadbent E, Petrie KJ, Main J, Weinman J. The brief illness perception questionnaire. J Psychosom Res 2006 Jun;60(6):631-637. [doi: 10.1016/j.jpsychores.2005.10.020] [Medline: 16731240]
45. Tomaszewski M, White C, Patel P, Masca N, Damani R, Hepworth J, et al. High rates of non-adherence to antihypertensive treatment revealed by high-performance liquid chromatography-tandem mass spectrometry (HP LC-MS/MS) urine analysis. Heart 2014 Jun;100(11):855-861 [FREE Full text] [doi: 10.1136/heartjnl-2013-305063] [Medline: 24694797]
46. Scientific Working Group for Forensic Toxicology. Scientific Working Group for Forensic Toxicology (SWGTOX) standard practices for method validation in forensic toxicology. J Anal Toxicol 2013 Sep;37(7):452-474. [doi: 10.1093/jat/bkt054] [Medline: 23934984]
47. Fitzgerald RL, Rivera JD, Herold DA. Broad spectrum drug identification directly from urine, using liquid chromatography-tandem mass spectrometry. Clin Chem 1999 Aug;45(8 Pt 1):1224-1234 [FREE Full text] [Medline: 10430788]
48. World Anti-Doping Agency. Minimum criteria for chromatographic mass spectrometric confirmation of the identity of analytes for doping control purpose (TD2015IDCR). 2015. URL: https://www.wada-ama.org/sites [accessed 2018-08-06] [WebCite Cache ID 71T0PMv7m]
49. University Hospitals of Leicester NHS Trust. National Centre for Adherence Testing (NCAT). 2011. URL: https://www.leicestershospitals.nhs.uk/aboutus/departments-services/pathology/clinical-biochemistry/national-centre-for-drug-adherence-testing-ncat/ [accessed 2018-08-06] [WebCite Cache ID 71T0y35lM]
50. Berlowitz DR, Foy CG, Kazis LE, Bolin LP, Conroy MB, Fitzpatrick P, SPRINT Research Group. Effect of Intensive Blood-Pressure Treatment on Patient-Reported Outcomes. N Engl J Med 2017 Dec 24;377(8):733-744 [FREE Full text] [doi: 10.1056/NEJMoa1611179] [Medline: 28834483]
51. Morisky DE, DiMatteo MR. Improving the measurement of self-reported medication nonadherence: Final response. Journal of Clinical Epidemiology 2011 Mar;64(3):262-263. [doi: 10.1016/j.jclinepi.2010.09.010]
52. ClinRisk Ltd. Welcome to the QRISK®2-2016 cardiovascular disease risk calculator. 2016. URL: https://qrisk.org/2016/index.php [accessed 2018-06-18] [WebCite Cache ID 70GW7ShEN]
53. Rash JA, Campbell DJT, Tonelli M, Campbell TS. A systematic review of interventions to improve adherence to statin medication: what do we know about what works? Prev Med 2016 Dec;90:155-169. [doi: 10.1016/j.ypmed.2016.07.006] [Medline: 27413005]
54. Basu AP, Pearse JE, Rapley T. Publishing protocols for trials of complex interventions before trial completion - potential pitfalls, solutions and the need for public debate. Trials 2017 Dec 09;18(1):5 [FREE Full text] [doi: 10.1186/s13063-016-1757-7] [Medline: 28069042]

Abbreviations

3R: Ready to Reduce Risk
CONSORT-EHEALTH: Consolidated Standards of Reporting Trials of Electronic and Mobile Health Applications and Online Telehealth
CVD: cardiovascular disease
DESMOND: Diabetes Education and Self Management for Ongoing and Newly Diagnosed
GP: general practitioner
INTERACT: Investigation of Text Message Reminders on Adherence to Cardiac Treatment
MIQUEST: Morbidity Query Information Export Syntax
MMAS: 8-item Morisky Medication Adherence Scale
NHS: National Health Service
PREPARE: Pre‐diabetes Risk Education and Physical Activity Recommendation and Encouragement
SMS: short message service
SPIRIT: Standard Protocol Items: Recommendations for Interventional Trials

TEXTME: Tobacco, Exercise and Diet Messages

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Protocol

Improving Self-Management Skills Among People With Spinal Cord Injury: Protocol for a Mixed-Methods Study

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Abstract

Background: Most people with spinal cord injury will develop secondary complications with potentially devastating consequences. Self-management is a key prevention strategy for averting the development of secondary complications and their recurrence. Several studies have shown that self-management programs improve self-management behaviors and health outcomes in individuals living with chronic conditions such as asthma, diabetes, hypertension, and arthritis. Given the burgeoning health care costs related to secondary complications, we developed an alternative electronic health–based implementation to facilitate the development of self-management skills among people with spinal cord injury.

Objective: This study aims to evaluate the efficacy of a self-management app in spinal cord injury populations. The primary outcome is attainment of self-selected, self-management goals. Secondary outcomes include increases in general and self-management self-efficacy and reductions in self-reported health events, health care utilization, and secondary complications related to spinal cord injury. This study also aims to explore how the intervention was implemented and how the app was experienced by end users.

Methods: This study will employ a mix of qualitative and quantitative methods. The quantitative portion of our study will involve a rater-blinded, randomized controlled trial with a stepped wedge design (ie, delayed intervention control group). The primary outcome is successful goal attainment, and secondary outcomes include increases in self-efficacy and reductions in self-reported health events, health care utilization, and secondary conditions related to spinal cord injury. The qualitative portion will consist of semistructured interviews with a subsample of the participants.

Results: We expect that the mobile self-management app will help people with spinal cord injury to attain their self-management goals, improve their self-efficacy, reduce secondary complications, and decrease health care utilization.

Conclusions: If the results are positive, this study will produce credible new knowledge describing multiple outcomes that people with spinal cord injury realize from an app-based self-management intervention and support its implementation in clinical practice.

Trial Registration: ClinicalTrials.gov NCT03140501; http://clinicaltrials.gov/ct2/show/NCT03140501 (Archived by WebCite at http://www.webcitation.org/73Gw0ZlWZ)

International Registered Report Identifier (IRRID): PRR1-10.2196/11069

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KEYWORDS

self-management; spinal cord injury; eHealth; mHealth

Introduction

Background

Damage to the spinal cord following injury can cause sensory, motor, and autonomic impairments that lead to serious and sometimes fatal secondary complications. The prevalence of spinal cord injury in the United States is estimated at 906 per million [1]. Most spinal cord injuries in young adults are attributable to traffic accidents and sports injuries [2], whereas the most common cause of spinal cord injury in older adults is falls [3].

Most people with spinal cord injury will develop secondary complications [4]. For example, during a yearly medical check-up, more than 95% of people with spinal cord injury reported experiencing at least 1 secondary complication associated with their spinal cord injury and 58% reported experiencing 3 or more complications [5]. Some of the most common secondary complications in community-dwelling individuals with spinal cord injury include autonomic dysreflexia, depression, renal problems, and pressure ulcers [6,7].

Secondary complications associated with spinal cord injury can have devastating and costly consequences. For example, individuals experiencing pressure ulcers are often prescribed prolonged bed rest, which can prevent them from participating in community activities [8]. This may result in a negative feedback loop as social isolation can lead to depression, and physical inactivity may lead to weight gain and deconditioning. In extreme cases, pressure ulcers may be fatal if the wound becomes infected with an antibacterial-resistant microorganism [9]. It generally takes about 23 days to heal a pressure ulcer with a direct cost of US $1971 for a stage I (shallow) ulcer and US $19,554 for a stage IV (deep) ulcer [10,11]. It has been estimated that, on average, pressure ulcer complications can add US $43,180 to a hospital stay in the United States [12].

Self-management is a key prevention strategy for averting the development and recurrence of secondary complications [13]. Self-management has been defined as “the individual’s ability to manage the symptoms, treatment, physical and psychological consequences and lifestyle changes inherent in living with a chronic condition” [14]. Self-management programs are aimed at increasing one’s problem-solving and decision-making skills [15]. Interventions to improve self-management are typically informed by social cognitive theory, which has 4 main tenets [16]: self-observation, self-evaluation, self-reaction, and self-efficacy (ie, belief in one’s ability to perform tasks and obtain goals) [16]. According to this theory, self-efficacy can be fostered via experiences of mastery, social modeling, social persuasion, and positive interpretation of physiological reactions [16]. This suggests that learning will be most effective when individuals are given tasks that are appropriate to their experience level, when they are relaxed and confident, and when they are encouraged to achieve the desired outcome [16,17].

Self-management may be an important strategy to improve health outcomes for individuals living with chronic conditions such as spinal cord injury. Several studies have shown that self-management programs improve self-management behaviors and health outcomes in individuals living with chronic conditions such as asthma, diabetes, hypertension, and arthritis [14,18,19]. For example, Barlow et al found that self-management interventions tailored for specific chronic conditions increased self-management behaviors such as monitoring blood glucose in diabetes, managing medication and symptoms in asthma, and managing psychosocial consequences and lifestyle changes in arthritis [11].

With rising health care costs and a shortage of qualified personnel for in-person interventions, more economical ways to teach self-management interventions are being explored, such as the use of eHealth interventions [20]. eHealth interventions may be advantageous over traditional approaches because they (1) are accessible to more people including those who live outside of large urban centers, (2) can be delivered simultaneously to a larger number of individuals, and (3) may be more cost-effective than the traditional face-to-face self-management interventions [21,22]. Evidence from studies involving individuals with diabetes and cigarette smokers show that the most effective technology-based self-management interventions are adaptable and specifically tailored to the end users [23,24]. Azar et al demonstrated that periodic and sustained engagement of the individual is crucial to support lasting behavioral change when using a mobile phone app for weight management [25]. A meta-analysis of the effectiveness of Web-based interventions over non-Web-based interventions for chronic disease management reported increases in knowledge of the condition, participation in health care, maintenance of behavioral changes, and slower health decline of older participants [22]. More recent studies on technology-based interventions corroborate these early findings. For example, eHealth self-management interventions involving Web-based self-monitoring of personal health have been found to improve diabetes management [25-28].

Despite the potential benefits of self-management strategies among people with spinal cord injury, we were able to identify little experimental research that has been conducted in this area. A study on a self-management program for people with indwelling urinary catheters found that participants who used

these strategies decreased the frequency of complications associated with catheters [29]. A scoping review of technological interventions that support self-management of pressure ulcer (eg, computer-based educational technologies and telemedicine programs) found that these technologies demonstrated low-to-moderate effectiveness in reducing risk factors associated with pressure ulcer [30].

We have developed a mobile app designed to facilitate self-management behavior and skill development following spinal cord injury in the inpatient rehabilitation and early community reintegration. This broad-based, mobile self-management app was developed with the input of key stakeholders including people with spinal cord injury and their formal and informal caregivers [31].

Study Objectives

The overarching objective of the study is to evaluate the efficacy of a self-management intervention that features the use of a self-management app among community-dwelling individuals with spinal cord injury who were discharged at least 12 months after inpatient rehabilitation. The primary outcome is attainment of self-selected, self-management goals. Secondary outcomes include increases in general and self-management self-efficacy and reductions in self-reported health outcomes, health care utilization, and secondary complications related to spinal cord injury. We will also examine how the intervention was implemented and how the app was experienced by end users.

We hypothesize that community-dwelling individuals with spinal cord injury who receive our self-management intervention, which features a self-management app, will have significantly better attainment of self-selected, self-management goals than those in the delayed control group.

Ethics Approval

Ethical approval was obtained from the University of British Columbia's Behavioral Research Ethics Board and the Vancouver Coastal Health Research Institute. Furthermore, the study has been prospectively registered before the first patient was enrolled in the study.

Methods

Study Design

This study will employ a mixture of qualitative and quantitative methods (Figure 1) [32]. The quantitative portion of the study will comprise a rater-blinded, randomized controlled trial with a stepped wedge design (ie, delayed intervention control group) [33]. This study design has been chosen over other study designs such as a randomized crossover controlled trial due to limitations in preventing carryover effect once participants have been exposed to the mobile app. The concern of potential carryover effect does not exist with a delayed intervention randomized controlled trial. A delayed intervention randomized controlled trial consists of 2 phases. In the first phase (first 3 months), participants are randomized to either have access to the app or not have access to the app (at this time point, they will serve as a control group that has received no intervention). This duration will allow for the effects of the self-management apps on our study outcomes (ie, self-management goals and improving participant self-efficacy) to be fully observed. In the second phase, all participants will have access to the mobile app for the remainder of the study. With this group, we will be able to see if the initial findings are replicated.

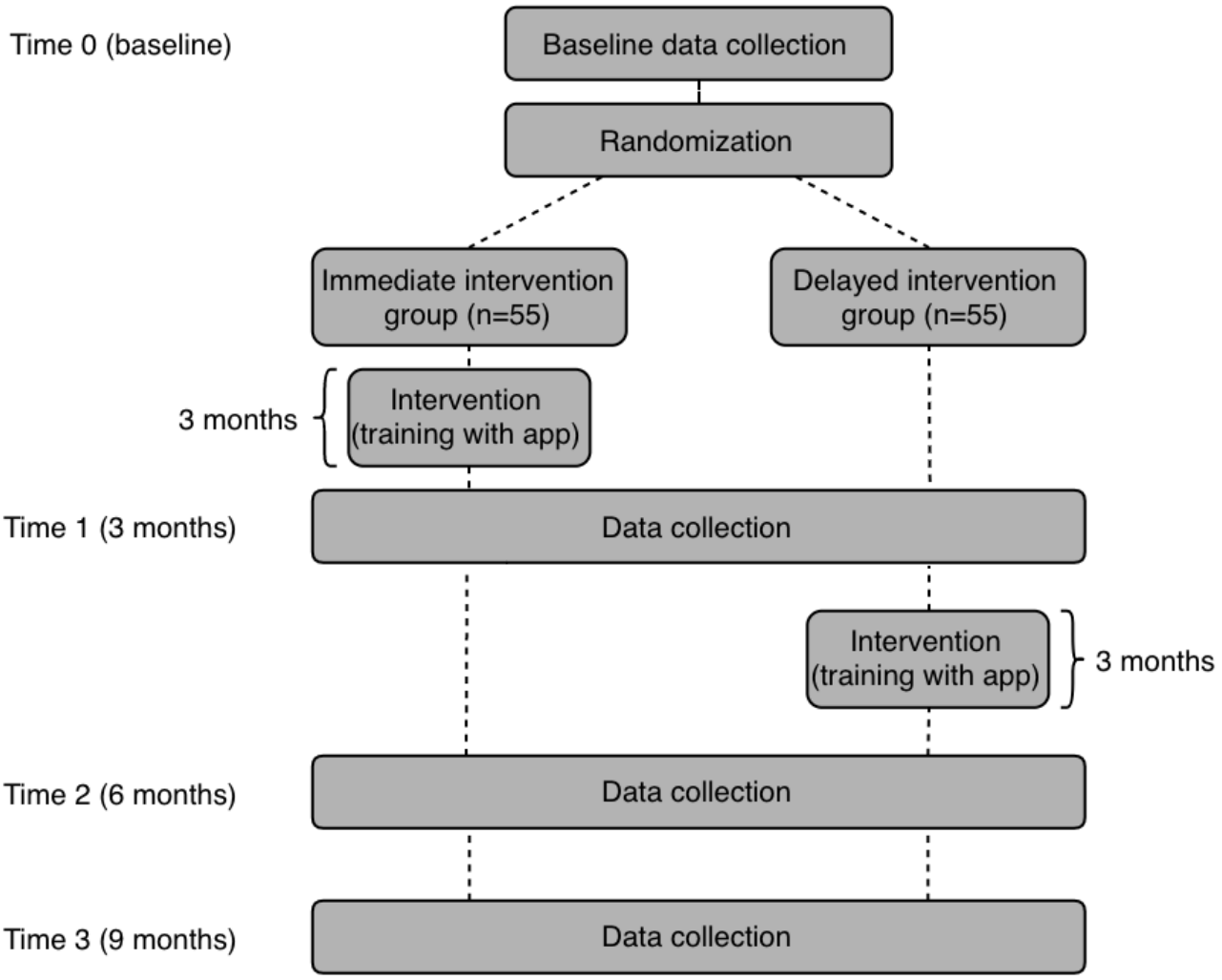
The qualitative portion will comprise semistructured interviews with a subsample of 1 in every 4 study participants. Embedding qualitative methods in randomized controlled trials has been suggested as a form of process evaluation [34,35]. Multiple methods will allow for data triangulation and increase the credibility of our findings [36]. This study will be documented according to the Consolidated Standards of Reporting Trials guidelines [37].

Subject Recruitment

To be included in the study, participants need to (1) be living in the community, (2) have internet access, (3) be living in the community for at least 1 year after their injury, and (4) be able to provide their own consent. From our previous feasibility study, we know that most patients have either a tablet or access to a computer; however, we will purchase some tablets (n=10) for participants to borrow to be as inclusive as possible. We are currently working on making the app accessible via voice activation; however, we may need to exclude those who are unable to use either a computer or mobile device because of limited hand function. We anticipate including participants with spinal cord injury who have experienced a variety of different injury mechanisms and degrees of neurological impairment. Participants will be excluded if they (1) have previously used a self-management app focused on spinal cord injury, (2) are unable to communicate in English, or (3) have cognitive impairments that are likely to prevent them from reliably completing the study questionnaires, as identified using the 6-item cognitive impairment test (6-CIT; see procedures).

We will recruit participants from across the United States and Canada. We will connect and collaborate with other rehabilitation centers in the United States and Canada to facilitate recruitment through a variety of sources. Electronic means will include a study website that we will develop, a local rehabilitation institute's website, e-blasts, and social media (eg, Facebook, Twitter). Participants will also be recruited by a local, spinal cord injury–focused, nonprofit organization's peer recruitment coordinator through spinal cord injury support groups, via letters sent to former patients of a local rehabilitation center who meet the inclusion criteria, and previous research participants with spinal cord injuries who have given permission to be contacted about future research studies, via newspaper and newsletter advertisements. We will contact interested, potential participants by email or phone to confirm their eligibility. We will formally enroll eligible participants by obtaining their informed consent to participate. The risk to the safety of participants involved in the trial is minimal as the app is an alternative way to facilitate the development of self-management skills, an approach that has not been found to be detrimental in other populations. No adverse effects have been documented during pilot testing.

Figure 1. Study design.



Intervention

This individually tailored intervention will involve the use of a mobile app called "SCI Health Storylines" accompanied by 5 to 6 in-person, telephone, or Skype contacts that will occur over a 3-month period. At the beginning of the intervention, there will be 1 to 2 orientation sessions in which the principles of self-management will be reviewed; app-specific, self-management goals will be identified; features of the self-management app will be explained; and any access issues will be resolved. Over the first month, there will be 2 brief follow-up contacts, via telephone or Skype, to review any questions or issues participants are having with the app. During the last 2 months of the intervention, there will be monthly contacts to address the same issues.

SCI Health Storylines focuses on specific elements common to the management of spinal cord injury and uses key concepts such as goal setting and tracking of confidence in one's ability to self-manage their condition [16]. We created tools to address the main self-management topics for individuals with spinal cord injury including bowel and bladder management, skin management, spasticity management, daily exercise, as well as more acute topics including urinary tract infections and autonomic dysreflexia. For each topic, the app prompts the user to set specific targets or goals and then allows the individual to journal their progress and self-management confidence. Generic (non-spinal cord injury specific) tools address other areas including medications and mood. The app is versatile and provides various options in how one wishes to track their self-management progress. For example, someone may select to enter their urine volumes after each catheterization, whereas others may opt to enter it at the end of the day.

Treatment fidelity will be promoted by providing in-depth training to the study interventionist. Treatment fidelity will be monitored by having the interventionists document elements of the intervention that they complete during each contact and by having the principal investigator or research coordinator monitor 5% of contact sessions throughout the research process. The benefits of such a client-patient-centered approach to care have been documented in similar settings and include increased adherence [38], improved clinical outcomes [39], improved communication between the client and provider, greater client satisfaction [38,39], and potentially increased cost-effectiveness [40].

Primary Outcome Measure: Goal Attainment Scaling

Our primary outcome measure, goal attainment scaling, is a promising approach for evaluating psychosocial interventions in community settings (Table 1) [41]. This patient-centered measure will be used to identify self-management goals that

participants want to achieve [42]. Goal attainment scaling has successfully been used to evaluate self-management goals in other clinical populations [43,44]. Goal attainment scaling is known to be sensitive and responsive to treatment and is ideal to use when no standardized measure accurately represents the goals and ideals of all participants [45]. With goal attainment scaling, objective outcomes are identified, which indicate degrees of attainment of participant-selected goals on a 5-point scale ranging from −2 to +2, where −2 is a much worse than expected outcome, 0 represents attaining the goal (the anticipated outcome), and 2 represents a much better than expected outcome; the aggregate T scores are then calculated. Test-retest reliability in nonclassroom educational study showed near-perfect correlation of goal attainment scaling when taken 3 days apart for 5 student-selected goals (Goal 1, r=1.000; Goal 2, r=.957; Goal 3, r=.953; Goal 4, r=.969; Goal 5, r=.749; P<.001) [46]. Goal attainment scaling has been found to be more sensitive than both the functional independence measure and the Barthel index [47] because standardized measures may not detect a change even when a goal is accomplished [48]. The minimal clinically important change for goal attainment scale is 10, based on the linear T score [49], which represents a change in score from the anticipated values.

To ensure that goals are measurable and outcomes are realistic, study personnel will be trained by 1 of the coauthors with experience using the measure to administer it in an objective manner [50]. Before beginning the intervention, participants will set approximately 6 self-management and app-related goals (minimum of 3) with a one-on-one remote trainer who is skilled in goal setting. The remote trainer will ensure that goals are specific, measurable, attainable (over a 3-month timeline), realistic, and defined in time (ie, SMART). Participants will weigh the goals by their relative importance [45]. As the degree of impairment of goals can depend on the degree of the spinal cord injury, this measure will not investigate the type or difficulty levels of self-selected goals. This measure will evaluate whether participants found they were able to achieve their individually tailored goals over the course of the intervention.

In addition, the question “How confident are you that you can achieve these goals?” has been added to the goal attainment scale to examine the self-efficacy of the participants. We have also added the question “How committed are you to achieving this goal?” to the goal attainment scale to examine participants’ goal striving and self-regulation, as this is related to self-efficacy.

Secondary Outcome Measures

Self-Efficacy for Managing Chronic Disease Scale

The self-efficacy for managing chronic disease scale is designed to evaluate confidence in managing long-term disease [51,52]. It has been used extensively in many different populations including people with spinal cord injury to evaluate self-management interventions [53,54]. Each of the 6 items is rated on a scale of 1-10 (with 1 indicating “not at all confident” and 10 indicating “totally confident”), and an average score is calculated [52]. Lorig et al found that the scale was sensitive to their chronic disease self-management intervention [19]. Test-retest reliability was 0.72, and the minimal detectable change was found to be 2.25 among individuals with Parkinson disease [55].

Spinal Cord Injury Secondary Conditions Scale

The spinal cord injury secondary conditions scale targets secondary conditions related to spinal cord injury that have both direct and indirect impacts on health. The 16-item scale uses a 4-point ordinal scale (0-3) ranging from “no problem” to “significant problem,” with the total score ranging from 0-49. The test-retest reliability spinal cord injury secondary conditions scale has been measured at 5 different time points (at baseline, immediately post intervention, 4,8, and 12 months post intervention) and compared across each combination of time points. Findings from the study reveal that the spinal cord injury secondary conditions scale has adequate test-retest reliability between baseline and immediately post intervention (3 weeks after baseline; r=.698) [56]. Furthermore, this scale correlates highly with the 12-item Short-Form Health Survey (SF-12; Spearman P values range from .32 to .64) [56].

Self-Reported Health Care Utilization

Health care utilization will be measured by having participants record visits to see a physician, visits to hospital emergency departments, number of hospitalizations, and the number of nights spent in hospital [19]. Although there may be recall issues within self-reported health care utilization, it has been found to be highly correlated with days in hospital (r=.83) [13]. Participants will complete a weekly journal to help improve the accuracy of the report.

Table 1. Example of goal-attainment scaling for a person with autonomic dysreflexia.

Achieved (−2 to +2)	Behavioral statement of expected outcomes (over the course of 1 week)
Yes	
Much better (+2)	Participant experiences 0 episodes of autonomic dysreflexia
A little better (+1)	Participant experiences 1-3 episodes of autonomic dysreflexia
As expected (0)	Participant experiences 4-5 episodes of autonomic dysreflexia
No	
Same as baseline (−1)	Participant experiences 6 episodes of autonomic dysreflexia
Worse (−2)	Participant experiences more than 6 episodes of autonomic dysreflexia

Self-Reported "Health Events" (Related to Self-Management of Spinal Cord Injury)

Participants will be asked to complete a weekly journal to document specific health events related to the key components of the self-management app (eg, urinary tract infections, episodes of autonomic dysreflexia, and pressure ulcers).

Health-Related Quality of Life

To measure general health status, health changes, and economic impact, participants will be asked to complete the EuroQol 5 Dimension 5 Level (EQ-5D-5L) survey. The EQ-5D-5L consists of 5 health-related dimensions including mobility, self-care, usual activities, pain or discomfort, and anxiety or depression [57]. Each of these dimensions contains 5 response items (no issue, slight issue, moderate issue, severe issue, and extreme issue). The response items (1-5) have no mathematical scoring system and cannot be interpreted as values on a cardinal scale. In addition, participants will also indicate their overall health status on a scale from 0 to 100 [57]. For test-retest reliability, minimal difference was found between administrations (0 and 14 days) of the measure in each of the 5 health dimensions with interclass coefficient scores ranging between .61 and .77 [58]. Furthermore, the scale correlates highly with the physical and mental component summary scores of the SF-12 (Spearman *P* values range from .41 to .67) [58].

App Usage

To understand the uptake of the intervention, basic analytics relating to the usage of the app will be evaluated, including the time spent logged into the app, the number of times logged into the app, and the specific features used within the app. This information will enable us to describe the uptake of the intervention and will complement the data obtained from the semistructured interviews.

Descriptive Information

Descriptive data will be collected about the participant's sociodemographic characteristics such as age, sex, level of education, ethnic origin, language, marital status, type of dwelling, spinal cord injury etiology (traumatic or nontraumatic), lesion level, American Spinal Injury Association Impairment Scale, Spinal Cord Independence Measure 3 [59], and time since injury. In addition, the amount of informal and formal caregiving received (if any) will be recorded, and social support will be identified with the Interpersonal Support Evaluation List short form [60] and the Health Care Climate Questionnaire [61]. The method by which a patient can use the app will also be recorded (eg, manually, with a mouth stylus, and with the assistance of a caregiver). To assess the app's overall quality across 4 dimensions (engagement, functionality, aesthetics, and information), participants will complete the Mobile Application Rating Scale [62]. We will also collect information on the amount of physical activity—at mild, moderate, and heavy intensity—the participants have performed over the previous 7 days using the Leisure Time Physical Activity Questionnaire for People with Spinal Cord Injury [63]. Finally, we will determine participants' readiness to adopt new technologies using the technology readiness index [64].

Adherence

Adherence data will consist of the numbers of goal attainment–focused orientation sessions participants complete with the interventionist, the length of each session, and participants' app usage. Specific data participants enter into the app will also be recorded to further describe app usage patterns. This information will allow us to describe the uptake of the experimental intervention and which aspects of self-management participants specifically focus on. This information will complement the data collected from semistructured interviews.

Treatment Fidelity

To ensure treatment fidelity, we will follow the strategies and guidelines outlined by Lenker et al and Borrelli et al [65,66]. The experimental intervention will be conducted by interventionists trained by the principal investigator to use the same standardized approach and materials as described in a treatment manual. Interventionists will follow and complete a checklist to note the completion of each step in the study protocol. Throughout the study, interventionists will also be observed performing the intervention by the principal investigator to ensure adherence with the study protocols.

Procedures

We will use a Web-based randomization program that will be managed by the project manager. Participants will be randomized to receive the intervention either immediately after baseline data are collected or after a 3-month delay via a randomization service (Figure 2). Participants in both groups will be asked to refrain from using any other self-management apps for the duration of the study. Three months into the intervention (T1), we will compare the outcomes from the immediate intervention group with those from the delayed intervention group. Participant outcomes at 6 months (T2) and 9 months (T3) into the intervention will allow us to determine how well outcomes are maintained in the immediate intervention group, if the effects of the intervention are replicated in the delayed intervention group, and to determine longer-term effects of the intervention.

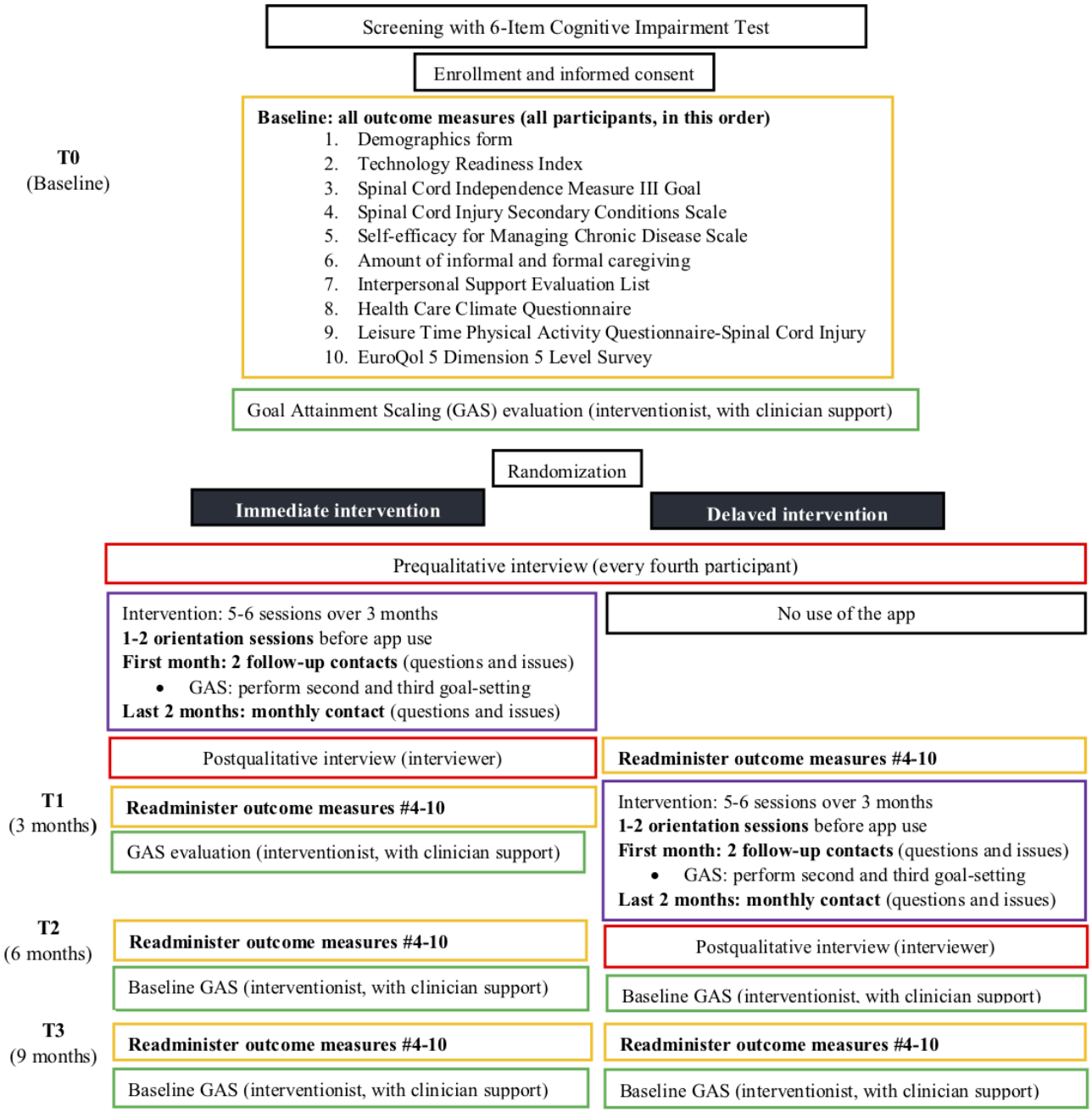
Potential participants will be screened using the 6-CIT [67]. If participants score above the inverse cut-off score of 7, they will be excluded from the study. After screening, informed consent will be obtained, and sociodemographic data and baseline measures will be collected from all participants. Data will be collected for participants at baseline (T0), at 3 months (T1), at 6 months (T2), and at 9 months (T3). Participants will be given the option of completing the questionnaires themselves through a link supplied by the Qualtrics Survey Platform (Qualtrics, Provo, Utah, United States of America) or over the phone, through a rater (research assistant). To protect participant privacy, we will use H.264 encryption on the mobile device and on mobile app servers.

T1 will be considered the primary end point for the intervention, but T3 will be considered the final end point for the study. As it is not possible to blind the participants, the interventionist, or the qualitative interviewer, a single blind study design will be employed in which data collectors are blinded to participants' group allocation. The delayed intervention group will complete

the baseline measures at the same time but will delay the intervention by 3 months. For the delayed intervention group, T1 will occur before the intervention and T2 will occur immediately following the intervention. Figure 2 provides a detailed overview of the study procedures.

Data collection for all participants will take between 5.5 and 7.5 hours. Time spent doing the intervention will vary depending on app usage, which should range from 10 hours (for those using the app for only a few minutes per day) to more than 60 hours (for those in the immediate intervention group who use the app for 30 min per day). Therefore, the total time commitment will range from 15.5 to 67.5 hours, depending on the desired app usage of the participant.

Figure 2. Detailed overview of the study procedures.



Qualitative Interviews

When attempting to interpret research findings, researchers often report personal retrospective impressions about the intervention. The quality of this research material is debatable, as it typically is not methodically collected [68]. To better understand how the self-management intervention was experienced by participants and administered by clinicians, a series of 2 qualitative semistructured interviews will be conducted at baseline (T0) and following the intervention (T1 for the immediate intervention group and T2 for the delayed intervention group) with a subsample of study participants.

These qualitative methods will help facilitate a deeper understanding of the quantitative findings, especially if they are divergent between participants [69], and will not interfere with the intervention or with the acquisition of quantitative data. At baseline, participants will be asked questions about (1) their current self-management strategies living with spinal cord injury, (2) their experiences (including challenges) with self-management, and (3) their expectations of the intervention. After the intervention, we will explore how the intervention was experienced by participants and will identify barriers and facilitators to improve intervention implementation in the future. This will include questions about (1) their overall impression of the intervention they received, (2) things they liked and disliked about the intervention, (3) how the intervention could be improved, and (4) recommendations for implementation. The preliminary interview guide is provided in Textbox 1.

The qualitative portion of the study will be conducted primarily by a single research assistant to limit the potential effects of change in characteristics and settings found with involving too many interviewers. The research assistant will know each participant's group allocation (delayed or immediate). This will allow for the qualitative interviews to be corroborated with the quantitative results. If the interviewer is not available to perform interviews, a replacement interviewer will be available to conduct qualitative interviews. To help build consistency between both interviewers, a semistructured interview guide will help both interviewers focus on their discussion. Furthermore, each interviewer will have undergone a practice session with the principal investigator to ensure they have received proper and equivalent training in conducting one-on-one interviews. Each interviewer's first 2 to 3 interview sessions will be observed by the principal investigator to provide constructive feedback and ensure consistency.

Qualitative interviews will be voice-recorded using a digital recorder and transcribed verbatim by a research assistant. After being transcribed, the transcripts will be reviewed while listening to the recorded audio file to ensure accuracy. Interview field notes that describe the nonverbal behavior and impressions of participants, and the influence of the interviewer on data collection [70], will also be recorded.

Sample Size

To calculate the sample size for the delayed intervention randomized controlled trial portion of the study, we used the formula described by Diggle et al with T1 as the primary end point for the intervention [69]. The sample size was based on an estimated effect size of 0.58 (Cohen *d*) from a previous intervention study that used goal attainment scaling as an outcome measure [50]. With an assumed correlation of .7 between T0 and T1, the required sample size is 46 participants per group (92 in total). Given a possible dropout and premature withdrawal rate of 20%, a sample of 110 participants will be recruited [71]. Our goal is to reach the target sample size in approximately 2 years. If our target sample size cannot be reached within this time frame, we will continue to recruit individuals until our target sample size can be reached.

For our qualitative analysis, we will use sequential sampling and interview every fourth participant in the study in each group (immediate intervention and delayed intervention). This will enable us to get a robust representative sample of participants that should be large enough to achieve data saturation [72,73].

Quantitative Data Analysis

A generalized linear mixed-effect model (GLMM) will be used to assess the association between treatment (immediate intervention vs delayed intervention) and primary and secondary outcomes. GLMM has a number of advantages over other approaches to analyzing longitudinal data, as cases with missing data are not excluded, and so, no imputation is required; it can also handle unbalanced time points while incorporating all data [74,75]. Secondary outcome analyses will be considered exploratory, given the likelihood for increased type 1 errors that result from multiple statistical comparisons. All statistical analysis will be completed with IBM SPSS Statistics Version 22 [76].

Treatment Fidelity Analysis

The percentage of intervention protocol items completed for each subject will be calculated for each participant to determine the treatment fidelity. These quantitative data will be supplemented with data from the qualitative portion of the study.

Qualitative Data Analysis

A thematic analysis will be conducted on the qualitative data using the 5-step process outlined by Braun and Clark [77]. The data analysis will be performed using NVivo 10 (QRS International, Victoria, Australia). As an additional means to monitor treatment fidelity, a content analysis will be performed. Results from the treatment reflections and qualitative interviews will be compared with the quantitative results to identify divergent and complementary findings. Qualitative data will also be compared with quantitative data for individual participants.

Textbox 1. Interview guide.

Baseline

- How would you describe your health currently?
- How do you currently manage your health (ie, living with a spinal cord injury)?
- How satisfied are you with the way you currently manage your health?
- What, if any, self-management challenges do you currently experience?
- What are your self-management goals?
- How do you feel about using a mobile self-management health app for your self-management?
- What, if any, worries or concerns do you have about using the self-management app?
- How do you imagine the self-management app will change your daily life?
- What are you hoping to learn from participating in this study?

After the intervention

- What did you think about the mobile self-management health app?
- How easy was the app for you to use?
- How, if at all, did the app help you attain your self-management goals? a. What were the challenges?
- How confident were you at achieving your goals?
- How, if at all, did the app help manage your secondary complications from your spinal cord injury?
- What was your favorite “tool” and why?
- What was your least favorite “tool” and why?
- What was your overall impression of the intervention you received?
- Which aspects of the intervention did you find most helpful?
- What did you think about how much time was required? a. For example, for learning to use the app, for recording your updates?
- What did you think about the timing of the intervention?
- How much impact, if any, on achieving your self-management goals do you attribute to the self-management app?
- How much impact, if any, on achieving your self-management goals do you attribute to other factors?
- What, if any, benefits did you experience from the intervention?
- Were there any problems that you encountered? a. If yes: Do you have any suggestions for solving the problems?
- How would you describe your health now?
- Do you have any additional comments you would like to add?

Soundness of the Research

A randomized controlled trial is the best way to evaluate the efficacy of a clinical intervention [78]. Given our inability to blind participants to the intervention they will receive, we will implement single blinding, in which raters are blinded to participants’ group allocation. For the qualitative data, we will use reflexivity, triangulation, and member checking to help ensure the trustworthiness of the analyses and findings [79]. We will make interview notes and memos to serve as reflexive tools [77]. This will also help to detail the analytic processes. Multiple data sources and methods of collection will be used for data triangulation, thus increasing the credibility of the findings [36]. Member checking will also be conducted to allow participants the opportunity to review the preliminary study findings and provide feedback about the conclusions made from the data.

Limitations

Although we intend to recruit individuals with a variety of different spinal cord injuries, including individuals with high and low tetraplegia, we do not currently have the resources to create an app with voice activation. In our pilot study, some participants used a mouth stylus or relied on caregivers to enter information into the app. Furthermore, individuals with high tetraplegia will be able to use a large-sized tablet or mobile phone for performing daily tasks on the self-management app with little difficulty.

Another limitation of this study is our ability to determine the active ingredients of the intervention. We can evaluate this to some extent because we track app usage. We will be able to perform a subanalysis to explore whether adherence is related to primary or secondary outcomes. Furthermore, we will ask participants to comment on how much they feel the app is responsible for achieving their primary and secondary outcomes

during qualitative interviews. However, we will not be able to determine the relative contribution of different aspects of the intervention on participants' outcomes.

Results

Anticipated Results

By encouraging individuals with spinal cord injury to adopt positive health behaviors and promoting their autonomy, we intend to demonstrate that SCI Health Storylines can help people with spinal cord injury attain their self-management goals, improve their self-efficacy, reduce secondary complications, and decrease health care utilization.

Study Timeline

A 3-year study timeline is presented in Table 2. In the first 6 months (Q4 2017 and Q1 2018), we obtained research ethics and hired and trained research staff (health professionals who will administer the intervention and research assistants who will collect the data). We will now recruit and collect data over the next 24 months. We will analyze the data and conduct knowledge translation projects over the last 6 months of the study.

Table 2. Project timeline.

Item	2017	2018				2019				2020		
	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3
Obtain research ethics	✓											
Hire and train staff	✓	✓										
Hire and train health professionals	✓	✓										
Recruit participants		✓	✓	✓	✓	✓	✓	✓	✓			
Provision of interventions		✓	✓	✓	✓	✓	✓	✓	✓			
Data collection		✓	✓	✓	✓	✓	✓	✓	✓	✓		
Quantitative data analysis										✓	✓	
Qualitative data analysis				✓	✓	✓	✓	✓	✓	✓	✓	
Knowledge translation									✓	✓	✓	✓

Discussion

Self-management apps have been shown to enhance self-management of chronic conditions such as diabetes and asthma [11,15,16]. As yet, no research has been conducted to determine if this is true for people with spinal cord injury. Having an effective self-management app that is generic (ie, can be used to promote self-management in a variety of areas) and not resource-intense (ie, it is self-directed and does not have extensive formalized involvement of peer mentors and health care professionals) would be extremely beneficial as it would enable people with spinal cord injury to learn the fundamental skills of self-management more independently (eg, goal setting, problem solving, symptom tracking and management, skill development, and self-efficacy) as a form of secondary prevention [80].

If the results are positive, this study will produce credible new knowledge describing multiple outcomes that people with spinal cord injury realize from an app-based self-management intervention. Ultimately, reducing secondary complications will greatly improve the quality of life of people with spinal cord injuries and will reduce health care costs.

Acknowledgments

Funding for the research study was provided by a Craig H Nielsen Foundation grant (Grant no. 44087). The authors wish to acknowledge Self Care Catalysts for providing access to their mobile app platform for research purposes throughout the study. At present, Self Care Catalysts provides free public access to the SCI Health Storylines mobile app on the Google Play Store (Android) and over the Web.

Conflicts of Interest

The authors WBM, GS, MM, PBM, and BS report no real or perceived conflicts of interest. JA has a conflict of interest as he works as a research and development officer for Self Care Catalysts, a company that may benefit from the research on this mobile app. Conflict of interest will be mitigated by Self Catalysts (including JA) having no access to any research data, which will remain on the University of British Columbia premises. JA will not be involved in the analysis of collected data but will be involved in reviewing future manuscripts on this study.

Multimedia Appendix 1

Craig H. Nielsen Foundation peer-review comments.

[PDF File (Adobe PDF File), 35KB - resprot_v7i11e11069_app1.pdf]

References

1. Singh A, Tetreault L, Kalsi-Ryan S, Nouri A, Fehlings MG. Global prevalence and incidence of traumatic spinal cord injury. Clin Epidemiol 2014;6:309-331 [FREE Full text] [doi: 10.2147/CLEP.S68889] [Medline: 25278785]
2. Aghayan H, Arjmand B, Yaghoubi M, Moradi-Lakeh M, Kashani H, Shokraneh F. Clinical outcome of autologous mononuclear cells transplantation for spinal cord injury: a systematic review and meta-analysis. Med J Islam Repub Iran 2014;28:112 [FREE Full text] [Medline: 25678991]
3. Sabapathy V, Tharion G, Kumar S. Cell therapy augments functional recovery subsequent to spinal cord injury under experimental conditions. Stem Cells Int 2015;2015:132172 [FREE Full text] [doi: 10.1155/2015/132172] [Medline: 26240569]
4. Noreau L, Proulx P, Gagnon L, Drolet M, Laramée MT. Secondary impairments after spinal cord injury: a population-based study. Am J Phys Med Rehabil 2000;79(6):526-535. [doi: 10.1097/00002060-200011000-00009] [Medline: 11083303]
5. Anson CA, Shepherd C. Incidence of secondary complications in spinal cord injury. Int J Rehabil Res 1996 Mar;19(1):55-66. [doi: 10.1097/00004356-199603000-00006] [Medline: 8730544]
6. McKinley WO, Jackson AB, Cardenas DD, DeVivo MJ. Long-term medical complications after traumatic spinal cord injury: a regional model systems analysis. Arch Phys Med Rehabil 1999 Nov;80(11):1402-1410. [doi: 10.1016/S0003-9993(99)90251-4] [Medline: 10569434]
7. Dryden DM, Saunders LD, Rowe BH, May LA, Yiannakoulias N, Svenson LW, et al. Depression following traumatic spinal cord injury. Neuroepidemiology 2005;25(2):55-61. [doi: 10.1159/000086284] [Medline: 15947491]
8. Savic G, Charlifue S, Glass C, Soni BM, Gerhart KA, Jamous MA. British Ageing with SCI study: changes in physical and psychosocial outcomes over time. Top Spinal Cord Inj Rehabil 2010 Jan;15(3):41-53. [doi: 10.1310/sci1503-41]
9. Sibbald R, Chapman P, Contreras-Ruiz J. The role of bacteria in pressure ulcers. In: Romanelli M, Clark M, Cherry G, Colin D, Defloor T, editors. Science and Practice of Pressure Ulcer Management. London: Springer-Verlag; 2006:139-162.
10. Palese A, Luisa S, Ilenia P, Laquintana D, Stinco G, Di Giulio P, PARI-ETLD Group. What is the healing time of stage II pressure ulcers? Findings from a secondary analysis. Adv Skin Wound Care 2015 Feb;28(2):69-75. [doi: 10.1097/01.ASW.0000459964.49436.ce] [Medline: 25608012]
11. Azimian J, Dehghan Nayeri N, Pourkhaleghi E, Ansari M. Transdermal wound oxygen therapy on pressure ulcer healing: a single-blind multi-center randomized controlled trial. Iran Red Crescent Med J 2015 Nov;17(11):e20211 [FREE Full text] [doi: 10.5812/ircmj.20211] [Medline: 26734476]
12. Moore ZE, Webster J, Samuriwo R. Wound-care teams for preventing and treating pressure ulcers. Cochrane Database Syst Rev 2015 Sep 16(9):CD011011. [doi: 10.1002/14651858.CD011011.pub2] [Medline: 26373268]
13. Lorig KR, Sobel DS, Stewart AL, Brown Jr BW, Bandura A, Ritter P, et al. Evidence suggesting that a chronic disease self-management program can improve health status while reducing hospitalization: a randomized trial. Med Care 1999 Jan;37(1):5-14. [Medline: 10413387]
14. Barlow J, Wright C, Sheasby J, Turner A, Hainsworth J. Self-management approaches for people with chronic conditions: a review. Patient Educ Couns 2002;48(2):177-187. [doi: 10.1016/S0738-3991(02)00032-0] [Medline: 12401421]
15. Hirsche RC, Williams B, Jones A, Manns P. Chronic disease self-management for individuals with stroke, multiple sclerosis and spinal cord injury. Disabil Rehabil 2011;33(13-14):1136-1146. [doi: 10.3109/09638288.2010.523103] [Medline: 20919875]
16. Redmond BF. Wikispaces.psu. 2016. Self-Efficacy and Social Cognitive Theories URL: https://wikispaces.psu.edu/display/PSYCH484/7.+Self-Efficacy+and+Social+Cognitive+Theories [accessed 2018-10-15] [WebCite Cache ID 73CKGE86u]
17. McAlister AL, Perry CL, Parcel GS. How individuals, environments, and health behaviors interact: social cognitive theory. In: Glanz K, Rimer BK, Viswanath K, editors. Health Behavior and Health Education: Theory, Research, and Practice. San Francisco, CA: Jossey-Bass; 2008:169-188.
18. de Jongh T, Gurol-Urganci I, Vodopivec-Jamsek V, Car J, Atun R. Mobile phone messaging for facilitating self-management of long-term illnesses. Cochrane Database Syst Rev 2012 Dec 12;12:CD007459. [doi: 10.1002/14651858.CD007459.pub2] [Medline: 23235644]
19. Wangberg SC. An internet-based diabetes self-care intervention tailored to self-efficacy. Health Educ Res 2008 Feb;23(1):170-179. [doi: 10.1093/her/cym014] [Medline: 17412717]
20. Lewis TL, Boissaud-Cooke MA, Aungst TD, Eysenbach G. Consensus on use of the term “App” versus “Application” for reporting of mHealth research. J Med Internet Res 2014 Jul 17;16(7):e174 [FREE Full text] [doi: 10.2196/jmir.3460] [Medline: 25033233]
21. Lorig KR, Ritter PL, Laurent DD, Plant K. Internet-based chronic disease self-management: a randomized trial. Med Care 2006 Nov;44(11):964-971. [doi: 10.1097/01.mlr.0000233678.80203.c1] [Medline: 17063127]

22. Wantland DJ, Portillo CJ, Holzemer WL, Slaughter R, McGhee EM. The effectiveness of web-based vs non-web-based interventions: a meta-analysis of behavioral change outcomes. J Med Internet Res 2004 Nov 10;6(4):e40 [FREE Full text] [doi: 10.2196/jmir.6.4.e40] [Medline: 15631964]
23. Heron KE, Smyth JM. Ecological momentary interventions: incorporating mobile technology into psychosocial and health behaviour treatments. Br J Health Psychol 2010;15(1):1-39 [FREE Full text] [doi: 10.1348/135910709X466063] [Medline: 19646331]
24. Horan PP, Yarborough MC, Besigel G, Carlson DR. Computer-assisted self-control of diabetes by adolescents. Diabetes Educ 1990;16(3):205-211. [doi: 10.1177/014572179001600311] [Medline: 2185006]
25. Quinn CC, Shardell MD, Terrin ML, Barr EA, Ballew SH, Gruber-Baldini AL. Cluster-randomized trial of a mobile phone personalized behavioral intervention for blood glucose control. Diabetes Care 2011;34(9):1934-1942 [FREE Full text] [doi: 10.2337/dc11-0366] [Medline: 21788632]
26. Bell AM, Fonda SJ, Walker MS, Schmidt V, Vigersky RA. Mobile phone-based video messages for diabetes self-care support. J Diabetes Sci Technol 2012;6(2):310-319 [FREE Full text] [doi: 10.1177/193229681200600214] [Medline: 22538140]
27. Shetty AS, Chamukuttan S, Nanditha A, Raj RK, Ramachandran A. Reinforcement of adherence to prescription recommendations in Asian Indian diabetes patients using short message service (SMS)--a pilot study. J Assoc Physicians India 2011 Nov;59:711-714. [Medline: 22616337]
28. Zolfaghari M, Mousavifar SA, Pedram S, Haghani H. The impact of nurse short message services and telephone follow-ups on diabetic adherence: which one is more effective? J Clin Nurs 2012;21(13-14):1922-1931. [doi: 10.1111/j.1365-2702.2011.03951.x] [Medline: 22239205]
29. Wilde MH, McMahon JM, McDonald MV, Tang W, Wang W, Brasch J, et al. Self-management intervention for long-term indwelling urinary catheter users: randomized clinical trial. Nurs Res 2015;64(1):24-34 [FREE Full text] [doi: 10.1097/NNR.0000000000000071] [Medline: 25502058]
30. Tung JY, Stead B, Mann W, Pham B, Popovic MR. Assistive technologies for self-managed pressure ulcer prevention in spinal cord injury: a scoping review. J Rehabil Res Dev 2015;52(2):131-146 [FREE Full text] [doi: 10.1682/JRRD.2014.02.0064] [Medline: 26237111]
31. Mortenson WB, Sawatzky B, Mahsa S, Adams J, Mills P. Development of an App to Improve Self-management Skills among People with Spinal Cord Injury. 2016 Presented at: Praxis 2016; April 25, 2016; Vancouver.
32. Creswell J, Clark V. Designing and Conducting Mixed-Methods Research. Thousand Oaks, CA: Sage Publications; 2006.
33. Brown CA, Lilford RJ. The stepped wedge trial design: a systematic review. BMC Med Res Methodol 2006 Nov 08;6:54 [FREE Full text] [doi: 10.1186/1471-2288-6-54] [Medline: 17092344]
34. Oakley A, Strange V, Bonell C, Allen E, Stephenson J, RIPPLE Study Team. Process evaluation in randomised controlled trials of complex interventions. Br Med J 2006 Feb 18;332(7538):413-416 [FREE Full text] [doi: 10.1136/bmj.332.7538.413] [Medline: 16484270]
35. Martin Ginis KA, Phang SH, Latimer AE, Arbour-Nicitopoulos KP, Lewin S, Glenton C, et al. Use of qualitative methods alongside randomised controlled trials of complex healthcare interventions: methodological study. Br Med J 2009;339:b3496 [FREE Full text] [doi: 10.1136/bmj.b3496] [Medline: 19744976]
36. Streubert H, Carpenter D. Triangulation as a qualitative research strategy. In: Qualitative Research in Nursing: Advancing the Humanistic Imperative. Philadelphia: Lippincott Williams and Wilkins; 2003.
37. Schulz KF, Altman DG, Moher D, CONSORT Group. CONSORT 2010 Statement: updated guidelines for reporting parallel group randomised trials. BMC Med 2010 Mar 24;8:18 [FREE Full text] [doi: 10.1186/1741-7015-8-18] [Medline: 20334633]
38. Robinson JH, Callister LC, Berry JA, Dearing KA. Patient-centered care and adherence: definitions and applications to improve outcomes. J Am Acad Nurse Pract 2008 Dec;20(12):600-607. [doi: 10.1111/j.1745-7599.2008.00360.x] [Medline: 19120591]
39. Cott CA, Teare G, McGilton KS, Lineker S. Reliability and construct validity of the client-centred rehabilitation questionnaire. Disabil Rehabil 2006 Nov 30;28(22):1387-1397. [doi: 10.1080/09638280600638398] [Medline: 17071570]
40. Stewart M, Brown JB, Donner A, McWhinney IR, Oates J, Weston WW, et al. The impact of patient-centered care on outcomes. J Fam Pract 2000 Sep;49(9):796-804. [Medline: 11032203]
41. Ruble L, McGrew JH, Toland MD. Goal attainment scaling as an outcome measure in randomized controlled trials of psychosocial interventions in autism. J Autism Dev Disord 2012 Sep;42(9):1974-1983 [FREE Full text] [doi: 10.1007/s10803-012-1446-7] [Medline: 22271197]
42. Kiresuk TJ, Sherman RE. Goal attainment scaling: a general method for evaluating comprehensive community mental health programs. Community Ment Health J 1968 Dec;4(6):443-453. [doi: 10.1007/BF01530764] [Medline: 24185570]
43. Higano K, Shibayama T, Ichikawa M, Motomura M, Shimano H, Kawakami Y, et al. The effects of telenursing with goal attainment scaling in diabetic patients: a case report. Int J Nurs Clin Pract 2015 Feb 18;2:117. [doi: 10.15344/2394-4978/2015/117]
44. Anderson AR, Christison-Lagay J, Procter-Gray E. Self-management goal setting in a community health center: the impact of goal attainment on diabetes outcomes. Diabetes Spectr 2010 May 13;23(2):97-105. [doi: 10.2337/diaspect.23.2.97]

45. Turner-Stokes L, Baguley IJ, De Graaff S, Katrak P, Davies L, McCrory P, et al. Goal attainment scaling in the evaluation of treatment of upper limb spasticity with botulinum toxin: a secondary analysis from a double-blind placebo-controlled randomized clinical trial. J Rehabil Med 2010 Jan;42(1):81-89 [FREE Full text] [doi: 10.2340/16501977-0474] [Medline: 20111849]
46. Koski J, Richards LG. Reliability and sensitivity to change of goal attainment scaling in occupational therapy nonclassroom educational experiences. Am J Occup Ther 2015;69 Suppl 2:6912350030p1-6912350030p5. [doi: 10.5014/ajot.2015.016535] [Medline: 26539684]
47. Khan F, Pallant JF, Turner-Stokes L. Use of goal attainment scaling in inpatient rehabilitation for persons with multiple sclerosis. Arch Phys Med Rehabil 2008 Apr;89(4):652-659. [doi: 10.1016/j.apmr.2007.09.049] [Medline: 18373995]
48. Steenbeek D, Gorter JW, Ketelaar M, Galama K, Lindeman E. Responsiveness of Goal Attainment Scaling in comparison to two standardized measures in outcome evaluation of children with cerebral palsy. Clin Rehabil 2011 Dec;25(12):1128-1139. [doi: 10.1177/0269215511407220] [Medline: 21795404]
49. Tennant A. Goal attainment scaling: current methodological challenges. Disabil Rehabil 2007;29(20-21):1583-1588. [doi: 10.1080/09638280701618828] [Medline: 17882728]
50. Palisano RJ, Haley SM, Brown D. Goal attainment scaling as a measure of change in infants with motor delays. Phys Ther 1992 Jun;72(6):432-437. [Medline: 1589463]
51. Lynch J, Lorig K, Stewart A, Gonzalez V, Ritter P. Outcome Measures for Health Education and Other Health Care Interventions. Thousand Oaks, CA: Sage Publications, Inc; 1996.
52. Lorig KR, Sobel DS, Ritter PL, Laurent D, Hobbs M. Effect of a self-management program on patients with chronic disease. Eff Clin Pract 2001;4(6):256-262 [FREE Full text] [Medline: 11769298]
53. Pang MY, Eng JJ, Lin KH, Tang PF, Hung C, Wang YH. Association of depression and pain interference with disease-management self-efficacy in community-dwelling individuals with spinal cord injury. J Rehabil Med 2009 Nov;41(13):1068-1073 [FREE Full text] [doi: 10.2340/16501977-0455] [Medline: 19894003]
54. Lester K, Stepleman L, Hughes M. The association of illness severity, self-reported cognitive impairment, and perceived illness management with depression and anxiety in a multiple sclerosis clinic population. J Behav Med 2007 Apr;30(2):177-186. [doi: 10.1007/s10865-007-9095-6] [Medline: 17318458]
55. Dal Bello-Haas V, Klassen L, Sheppard MS, Metcalfe A. Psychometric properties of activity, self-efficacy and quality-of-life measures in individuals with parkinson disease. Physiother Can 2011;63(1):47-57 [FREE Full text] [doi: 10.3138/ptc.2009-08] [Medline: 22210979]
56. Kalpakjian CZ, Scelza WM, Forchheimer MB, Toussaint LL. Preliminary reliability and validity of a Spinal Cord Injury Secondary Conditions Scale. J Spinal Cord Med 2007;30(2):131-139 [FREE Full text] [doi: 10.1080/10790268.2007.11753924] [Medline: 17591225]
57. Brooks R. EuroQol: the current state of play. Health Policy 1996 Jul;37(1):53-72. [doi: 10.1016/0168-8510(96)00822-6] [Medline: 10158943]
58. Conner-Spady BL, Marshall DA, Bohm E, Dunbar MJ, Loucks L, Al Khudairy A, et al. Reliability and validity of the EQ-5D-5L compared to the EQ-5D-3L in patients with osteoarthritis referred for hip and knee replacement. Qual Life Res 2015 Jul;24(7):1775-1784. [doi: 10.1007/s11136-014-0910-6] [Medline: 25555837]
59. Miller W, Chan C. Scireproject. Spinal Cord Independence Measure (SCIM) URL: https://scireproject.com/outcome-measures/outcome-measure-tool/spinal-cord-independence-measure-scim/ [accessed 2018-02-15] [WebCite Cache ID 73CIQWQKh]
60. Payne TJ, Andrew M, Butler KR, Wyatt SB, Dubbert PM, Mosley TH. Psychometric evaluation of the Interpersonal Support Evaluation List–Short Form in the ARIC study cohort. SAGE Open 2012 Sep 26;2(3):215824401246192-215824401246198. [doi: 10.1177/2158244012461923]
61. Williams GC, Grow VM, Freedman ZR, Ryan RM, Deci EL. Motivational predictors of weight loss and weight-loss maintenance. J Pers Soc Psychol 1996 Jan;70(1):115-126. [doi: 10.1037/0022-3514.70.1.115] [Medline: 8558405]
62. Stoyanov SR, Hides L, Kavanagh DJ, Zelenko O, Tjondronegoro D, Mani M. Mobile app rating scale: a new tool for assessing the quality of health mobile apps. JMIR Mhealth Uhealth 2015 Mar 11;3(1):e27 [FREE Full text] [doi: 10.2196/mhealth.3422] [Medline: 25760773]
63. Martin Ginis KA, Phang SH, Latimer AE, Arbour-Nicitopoulos KP. Reliability and validity tests of the leisure time physical activity questionnaire for people with spinal cord injury. Arch Phys Med Rehabil 2012 Apr;93(4):677-682. [doi: 10.1016/j.apmr.2011.11.005] [Medline: 22336103]
64. Parasuraman A. Technology Readiness Index (Tri): a multiple-item scale to measure readiness to embrace new technologies. J Serv Res 2016 Jun 29;2(4):307-320. [doi: 10.1177/109467050024001]
65. Lenker JA, Fuhrer MJ, Jutai JW, Demers L, Scherer MJ, DeRuyter F. Treatment theory, intervention specification, and treatment fidelity in assistive technology outcomes research. Assist Technol 2010;22(3):129-138. [doi: 10.1080/10400430903519910] [Medline: 20939422]
66. Borrelli B, Sepinwall D, Ernst D, Bellg AJ, Czajkowski S, Breger R, et al. A new tool to assess treatment fidelity and evaluation of treatment fidelity across 10 years of health behavior research. J Consult Clin Psychol 2005 Oct;73(5):852-860. [doi: 10.1037/0022-006X.73.5.852] [Medline: 16287385]

67. Katzman R, Brown T, Fuld P, Peck A, Schechter R, Schimmel H. Validation of a short Orientation-Memory-Concentration Test of cognitive impairment. Am J Psychiatry 1983 Jun;140(6):734-739. [doi: 10.1176/ajp.140.6.734] [Medline: 6846631]
68. Mortenson WB, Oliffe JL. Mixed methods research in occupational therapy: a survey and critique. OTJR (Thorofare N J) 2009 Jan;29(1):14-23. [doi: 10.1177/153944920902900103]
69. Tashakkori AM, Teddlie CB. Mixed Methodology: Combining Qualitative and Quantitative Approaches (Applied Social Research Methods Series #46). Thousand Oaks, CA: Sage Publications; 1998.
70. Hammell KW, Carpenter C, Dyck I. Using Qualitative Research: A Practical Introduction for Occupational and Physical Therapists. London: Elsevier Health Sciences; 2000.
71. Diggle P, Zeger SL, Liang KY, Heagerty P. Analysis of Longitudinal Data (Oxford Statistical Science Series). Oxford: Oxford University Press; 2018.
72. Morse JM, Feild PA. Qualitative Research Methods for Health Professionals. Thousand Oaks, CA: Sage Publications; 2006.
73. Sandelowski M. Sample size in qualitative research. Res Nurs Health 1995 Apr;18(2):179-183. [doi: 10.1002/nur.4770180211]
74. Pinheiro JC, Glynn IM. Mixed Effects Models in S and S-Plus. New York: Springer-Verlag; 2000.
75. Breslow NE, Clayton DG. Approximate inference in generalized linear mixed models. J Am Stat Assoc 1993 Mar;88(421):9-25. [doi: 10.2307/2290687]
76. IBM SSPS Statistics. Armonk, New York: IBM Corp; 2012.
77. Braun V, Clarke V. Using thematic analysis in psychology. Qual Res Psychol 2006 Jan;3(2):77-101 [FREE Full text] [doi: 10.1191/1478088706qp063oa]
78. Sibbald B, Roland M. Understanding controlled trials. Why are randomised controlled trials important? Br Med J 1998 Jan 17;316(7126):201 [FREE Full text] [Medline: 9468688]
79. Krefting L. Rigor in qualitative research: the assessment of trustworthiness. Am J Occup Ther 1991 Mar;45(3):214-222. [doi: 10.5014/ajot.45.3.214] [Medline: 2031523]
80. Mortenson B, MacGillivray M, Sadeghi M, Singh G, Adams J, Mills P, et al. Effect of a mobile application on the self-management skills of people with spinal cord injury. 2018 Presented at: Canadian Association of Occupational Therapists National Conference; June 19, 2018; Charlottetown, PEI.

Abbreviations

6-CIT: 6-item cognitive impairment test
EQ-5D-5L: EuroQol 5 Dimension 5 Level
GLMM: generalized linear mixed-effect model
SF-12: 12-item Short-Form Health Survey

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Protocol

Self-Monitoring by Traffic Light Color Coding Versus Usual Care on Outcomes of Patients With Heart Failure Reduced Ejection Fraction: Protocol for a Randomized Controlled Trial

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Abstract

Background: Patients with heart failure (HF) reduced ejection fraction (HFrEF) have symptoms that are more severe and experience a higher rate of hospitalization compared with HF preserved ejection fraction (HFpEF) patients. However, symptom recognition cannot be made by patients based on current approaches. This problem is a barrier to effective self-care that needs to be improved by new self-monitoring instruments and strategies.

Objective: This study describes a protocol for the self-monitoring daily diaries of weight and shortness of breath (SOB) based on the traffic light system (TLS). The primary objective is to compare the self-care between the intervention and control group. Comparison of HF knowledge, HF quality of life (HFQOL), and all-cause hospitalization between the 2 groups are the secondary objectives.

Methods: A single-blind randomized controlled trial is being conducted at the HF clinic at Tehran Heart Center (Tehran, Iran). Sixty-eight adult patients of both genders will be enrolled during admission to HF clinic. Eligible subjects will be assigned to either the intervention or control group by a block balanced randomization method. Baseline surveys will be conducted before random allocation. Participants in the intervention group will receive an integrated package consisting of (1) HF self-care education by an Australian Heart Foundation booklet on HF, (2) regular home self-monitoring of weight and SOB, and (3) scheduled call follow-ups for 3 months. Patients in the control group will receive no intervention and they only complete monthly surveys.

Results: This study is ongoing and is expected to be completed by the end of 2018.

Conclusions: This is the first trial with new self-monitoring instruments in Iran as a low and middle-income country. If the findings show a positive effect, the package will be applied in different regions with the same health care status.

Trial Registration: Iranian Registry of Clinical Trials IRCT2017021032476N1; https://en.irct.ir/trial/25296?revision=25296 (Archived by WebCite at http://www.webcitation.org/73DLICQL8)

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KEYWORDS

heart failure; outcome; self-monitoring; clinical trial

Introduction

Heart failure (HF) is a complex clinical syndrome that results from any structural and functional impairment of ventricular filling or ejection of blood. Based on left ventricle dysfunction and the left ventricle ejection fraction (LVEF), HF can be categorized as preserved ejection fraction (with LVEF≥50%, known as HFpEF or diastolic HF) and reduced ejection fraction (with LVEF ≤40%, known as HFrEF or systolic HF) [1].

As a global burden, HF affects more than 37.7 million individuals worldwide [2] and is a common condition with 1%-2% total health resources allocated in high-income countries. In low- and middle-income countries (LMICs) like Iran, HF may displace infectious diseases as the major public health issue [3]. In Iran and other Asian LMICs, HF is described as a pandemic [4], the prevalence greatly increased with age and range between 0.5% to 9.0% among different cities, regardless of time distribution [5], thus supporting the need for better HF surveillance and management strategies [3]. Patients with HF can experience various clinical outcomes including mortality, morbidity, and other patient-reported outcomes [6]. Although mortality and morbidity rates are similar for HFpEF and HFrEF, the hospital admission rates in patients with HFrEF are much higher than HFpEF [7].

HF is a leading cause of hospitalizations [8], mortality [8,9], rising health care costs (over US $39 billion annually in the United States and US $53.1 billion by 2030) [2,8-10], suboptimal self-care behavior [11], and reduced quality of life (QOL) [12]. According to a recent European Society of Cardiology Heart Failure Long-Term Registry prospective observational study, the rate of all-cause mortality and hospitalization at one-year follow-up was 8.1% and 28.2%, respectively [13]. Compared to Western countries, patients with HF in Asia and Iran are younger, have more severe signs and symptoms, and receive lower levels of treatment compared to the European Society of Cardiology and American College of Cardiology Foundation/American Heart Association Guidelines [14]. Moreover, Callender et al [3] reported that Iranian patients with HF experience significantly lower rates of admission (0.3%).

Poor self-care and low QOL among patients with HF are major global health issues [11] that are also affecting Iran [15-17]. Adequate self-care is associated with an improved health status [18], fewer symptoms, higher QOL [19], and reduced hospitalizations [18]. A lack of knowledge of symptom recognition and psychological problems have been identified as 2 key barriers [20]. Therefore, effective educational methods are essential for improved self-care [11,20]. Previous studies have shown that self-care programs for patients with HF are most effective when specialized education is combined with symptom monitoring and response management [21,22]. Practical and user-friendly self-monitoring tools can help patients recognize, monitor, report, and manage the symptoms appropriately. Without these tools, HF decompensation may not be detected in the early stages and could lead to preventable hospitalizations [23].

Patients with HF experience weight gain and other serious decompensation symptoms including shortness of breath (SOB) due to pulmonary edema, fatigue, and leg swelling [24-26]. Weight gain resulting from fluid retention is a marker of HF decompensation, and therefore, frequent weight monitoring can identify high-risk periods in the early stages to prevent hospitalization [24]. However, low compliance with weighing has been reported among patients with HF [27].

Diaries in a textual/tabular format are acceptable and creative self-monitoring tools because they reinforce patient education and facilitate their disease management [28]. Improved HF clinical and hospital outcomes have been reported by weight and symptom self-monitoring diary users [29]. However, despite the lower rate of HF-related hospitalizations [21,30], reduced mortality rate [21], and improved self-care [22], the previously reported studies used tabular format diaries and were conducted in developed countries with a higher quality of health care. The results may not apply to developing countries with significantly different health care systems and levels of health care quality.

Graph format diaries have been reported to attract and hold a person's attention for more extended periods and are the preferred format due to improved patient comprehension and information extraction [31]. Recently, a traffic light system (TLS) of diaries in graphical format have been developed [32]. The system consists of 3 different color codes: (1) red for medical alert, (2) yellow for a situation that is worsening and requires the patient to take quick-relief medications, and (3) green to show that the patient is doing well and adequately adhering to the treatment plan [33]. The TLS has been shown to be more effective in transforming information on risk assessment and disease management [32].

Wakefield et al [23] employed a pretest-posttest longitudinal design study to assess weight, and SOB self-monitoring by graphical instrumentation (other than TLS) in patients with HF. The paper revealed that self-monitoring HF patients could not complete the appropriate actions for each zone. Consequently, new strategies and instruments to actively engage patients in symptom recognition and monitoring require further research [23].

This study will combine graphical and tabular formats with TLS color coding to design weight and SOB self-monitoring diaries. Each color zone has been designed for patients to perform specified actions following symptom monitoring. The efficacy of this intervention will be compared with the usual care for

patients with HF. This is the first practical study with new user-friendly self-monitoring tools that will be conducted in Iran as an LMIC to compare the primary outcome of self-care behavior and the secondary outcomes of HF-knowledge, QOL, and all-cause hospitalization between intervention and control groups.

Methods

Study Design

This study is a parallel, single-blind, randomized controlled trial. The study protocol has been reviewed and approved (No. 9411449005) by the Institutional Review Board (IRB) at Tehran University of Medical Sciences (TUMS, Tehran, Iran). The study protocol is based on the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) 2013 guideline [34].

Study Setting

This study will be conducted at the Tehran Heart Center (THC) HF clinic affiliated with TUMS. THC is one of the best equipped diagnostic and therapeutic cardiology centers with full-time specialists and well-trained nursing staff in the region and is a referral center for cardiology in Iran with more than 1,300,000 outpatient visits, and 280,000 patient hospitalizations from 2001 to the end of 2017 [35].

Eligibility Criteria

The research nurse (author MN) will screen the medical records of adult patients (≥18 years of age) of both genders for the following inclusion criteria in the HF clinic. The eligibility of each participant will be confirmed by the HF specialist (see Textbox 1).

Intervention

In this study, the intervention is an integrated package consisting of 3 components: (1) HF self-care education, (2) regular home self-monitoring of weight and SOB, and (3) scheduled call follow-ups.

The first component of the package includes HF self-care education that will be delivered in the HF clinic of the THC according to the Australian Heart Foundation educational booklet entitled “living well with chronic HF” [38]. Individual education will be provided by the research nurse (MN) according to the participants understanding and literacy for a 40-minute face-to-face session between 8 am to 1 pm. A Farsi version of the booklet will be given to each participant. Also, during the educational session, the instructor and the participant will review the booklet content together, and the instructor will answer any questions. The booklet contains information on disease definition, diagnosis, symptoms, and ways to manage them, lifestyle issues, medicines, and other treatments. In order to obtain permission to translate the booklet to Farsi language for local use in Iran, one of the authors (MN) contacted the Australian Heart Foundation on April 5, 2016. After obtaining permission, it was translated to the Farsi language by an individual who was also proficient in the English language and knowledge of cardiovascular terminologies. Two nursing faculty members and 2 cardiology faculty members affiliated with TUMS approved the Farsi version of the booklet.

Textbox 1. Participant eligibility criteria.

Inclusion criteria

- Definitive diagnosis of heart failure by an heart failure specialist documented on the clinical record
- Heart failure reduced ejection fraction where ejection fraction ≤40% [36,1] by any method (transthoracic, or transesophageal echocardiography, and angiography)
- New York Heart Association function class II-IV
- Access to a telephone, telegram mobile application, and ability to answer phone calls
- Ability to read and write in the Farsi language
- Having a functional weighing scale (digital or analog) at home to weigh daily [23]
- The absence of diagnosed hearing loss and sight defects
- A stable hemodynamic status
- Non-smoking, no drinking alcohol, and no addiction to drugs
- Living at home and not in a homeless shelter [37]

Exclusion criteria

- Diagnosed psychiatric and cognitive conditions during the study
- Sudden death, migration, or unavailability of patients during the follow-up phase
- Recording weight and shortness of breath in the daily diary for less than 60% (<54 days) during the study
- Undergoing cardiac or other kinds of surgery with a lengthy hospital stay during the study
- Awaiting or receiving a transplanted heart or a left ventricular assistive device

The second component of the package includes regular home self-monitoring of weight and SOB and recording them in the appropriate 3-color daily diaries for 3 months. Since the graphical display of values help patients to recognize their symptoms and contact their health care provider [23], we created a paper-based weight and SOB self-monitoring daily diary color-coded system that was analogous to TLS.

Based on previous studies, a graphical representation of health-related information is the preferred method for patients compared to numerical/tabular displays [39,40] for communicating medical risk information [41]. This approach results in better participant comprehension. The patient pays attention and extracts more information with less effort [31]. Thus, both research diaries have been designed in 3 colors and categorize the participants' condition into 3 color-coded zones: green (excellent), yellow (use caution), and red (warning). The green, yellow, and red color-coded zones have been defined based on a combination of American Heart Association self-check plan for HF management [42] and the HF self-monitoring toolkit [43]. The colored diary will display recorded data in both graphical and tabular format. It is expected that this will result in a better participant understanding of their condition.

In the HF clinic, participants will be instructed by the research nurse on the daily measurement of weight and SOB and recording them in the daily diary during a 20-minute individual session between 8 am and 1 pm. The weight diary is a 7-page colored diary with instruction on the first page followed by 6 blank pages to record daily weight for 15 continuous days on each page.

At the time of referral to the THC, the HF specialist will measure the weight of eligible participants by analog weight scale (RASA scale, model 230, Iran). Then, 2 upper control limits will be determined for participants by the research nurse to identify 1 and 2.5 kg greater than the baseline weight that is considered as yellow and red zones in the weight diary, respectively [23] (see Figure 1). During instruction, the participants will be asked to weigh themselves daily after going to the toilet, before breakfast, with the same type of clothing, at the same time [38] and record it regularly in the weight diary for 3 months. If participants miss a weight measurement for any reason, they will be asked to record the reason for the missed date. They also will be instructed to contact the research nurse in case of sudden weight gain of 1 kg in one day (yellow zone) and 2.5 kg in one week (red zone) [44].

The SOB diary is a 4-page colored diary that includes instructions on the first page and 3 blank pages to record the difficulty of breathing for 30 continuous days on each page. The participants will be instructed on how to use the SOB colored diary, and how to rate the difficulty of breathing for the entire day after taking evening medications and at the end of each day for 3 months [23]. They will also be instructed to record the reason for any missed measuring dates.

The SOB rating scale was designed based on 0 to 10 pain assessment visual analog scale. In this scale, scores are categorized as follows: none (0), mild (1-3), moderate (4-6), and severe (7-10) [45] that have been marked by green, yellow, and red colors, respectively. Green, yellow, and red color zones will be explained to participants as no new or worsening (none-mild SOB), worsening with activity or at night when lying down (moderate SOB), and struggling to breath or at rest or while sitting (severe SOB), respectively [42] (see Figure 2). Participants will be instructed to contact the research nurse if they reach the yellow color zone to increase the diuretic dosage and contact with the emergency medical services in the red color zone [38].

The third component of the package includes scheduled follow-up phone calls (days 1, 3, and 7 after referral to the HF clinic and every week after that) for 3 months [21]. The research nurse will give participants a list of call dates and will call each subject in the evenings between 6 pm and 9 pm. Each follow-up phone call will last 5-15 minutes [21] and is designed to review the content of the instructional session, encourage participants to continue weight and SOB self-monitoring, and record them in the daily diaries. Also, the research nurse will ask the participants about the color zone during the previous week and will recommend the appropriate action (see Figure 3). Also, we predict that during the call follow-ups, participants in the intervention group will report another symptom that may be due to a side effect of the medications or the disease. The research nurse will be able to provide the appropriate recommendation for each symptom reported in the intervention group during these (see Figure 4).

At the end of the one-hour instructional session in the HF clinic, a plastic folder containing the instructional booklet, weight, and SOB colored diaries, pen, pencil, eraser, and a pencil sharpener will be delivered to each subject in the intervention group. They will be asked to keep diaries clean and deliver them to the research nurse at the end of the study.

Control

After randomization and allocating participants to 2 groups, those in the control group will receive the usual care. In HF clinic at THC, usual care for patients with HF is limited to a brief instruction by HF specialists on limiting water and salt intake, taking medications as prescribed, physical activity, weight monitoring and increasing the diuretic dosage in the condition of peripheral edema, weight gain, and SOB. They will receive 1 monthly phone call for 3 months. Out of respect for the ethical principles of human research, HF self-care instruction will be provided to the participants in the control group, and they will receive an educational booklet at the end of the study.

Figure 1. Colored weight daily diary. EMS: emergency medical services.

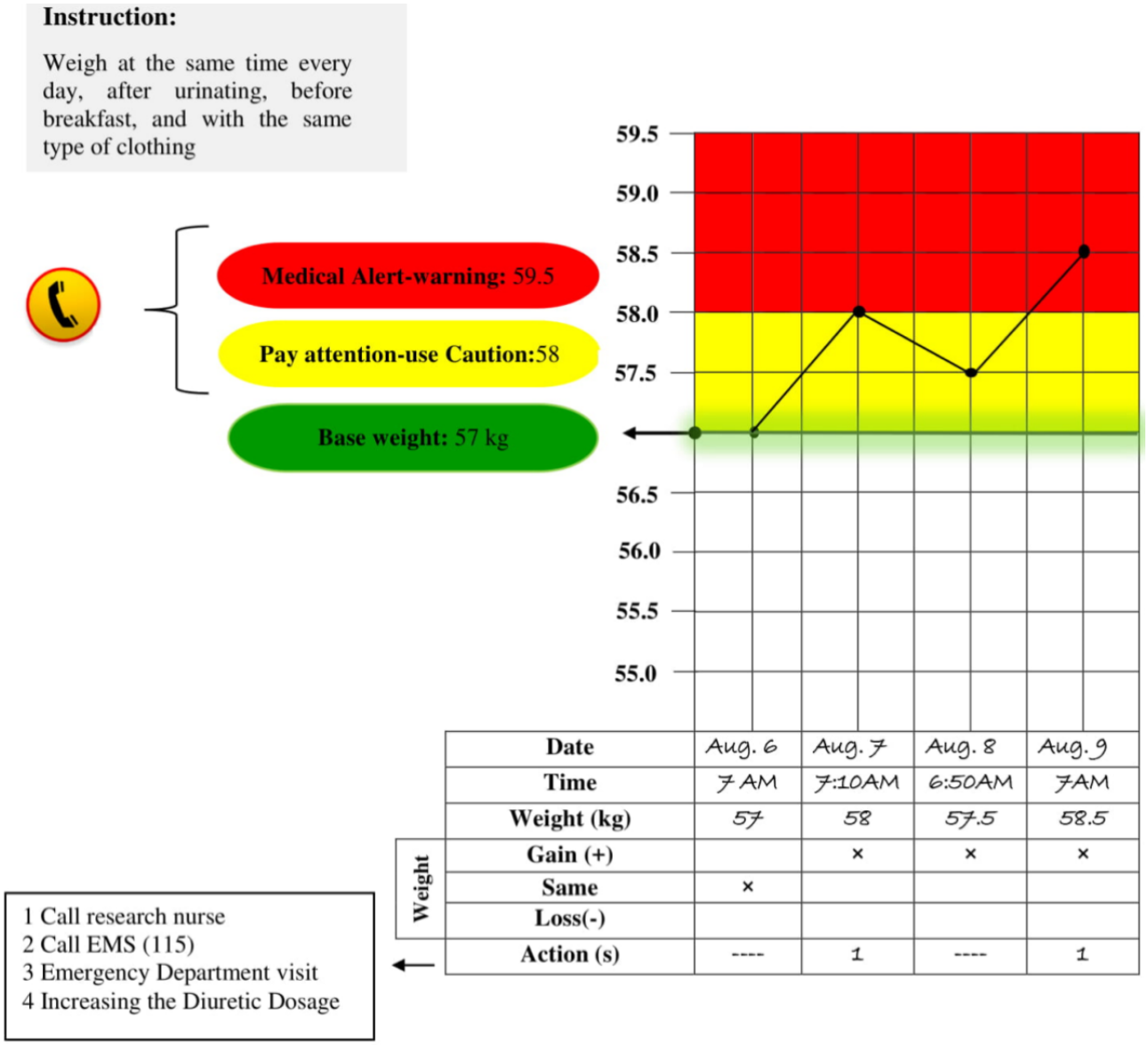


Figure 2. Colored shortness of breath daily diary. EMS: emergency medical services.

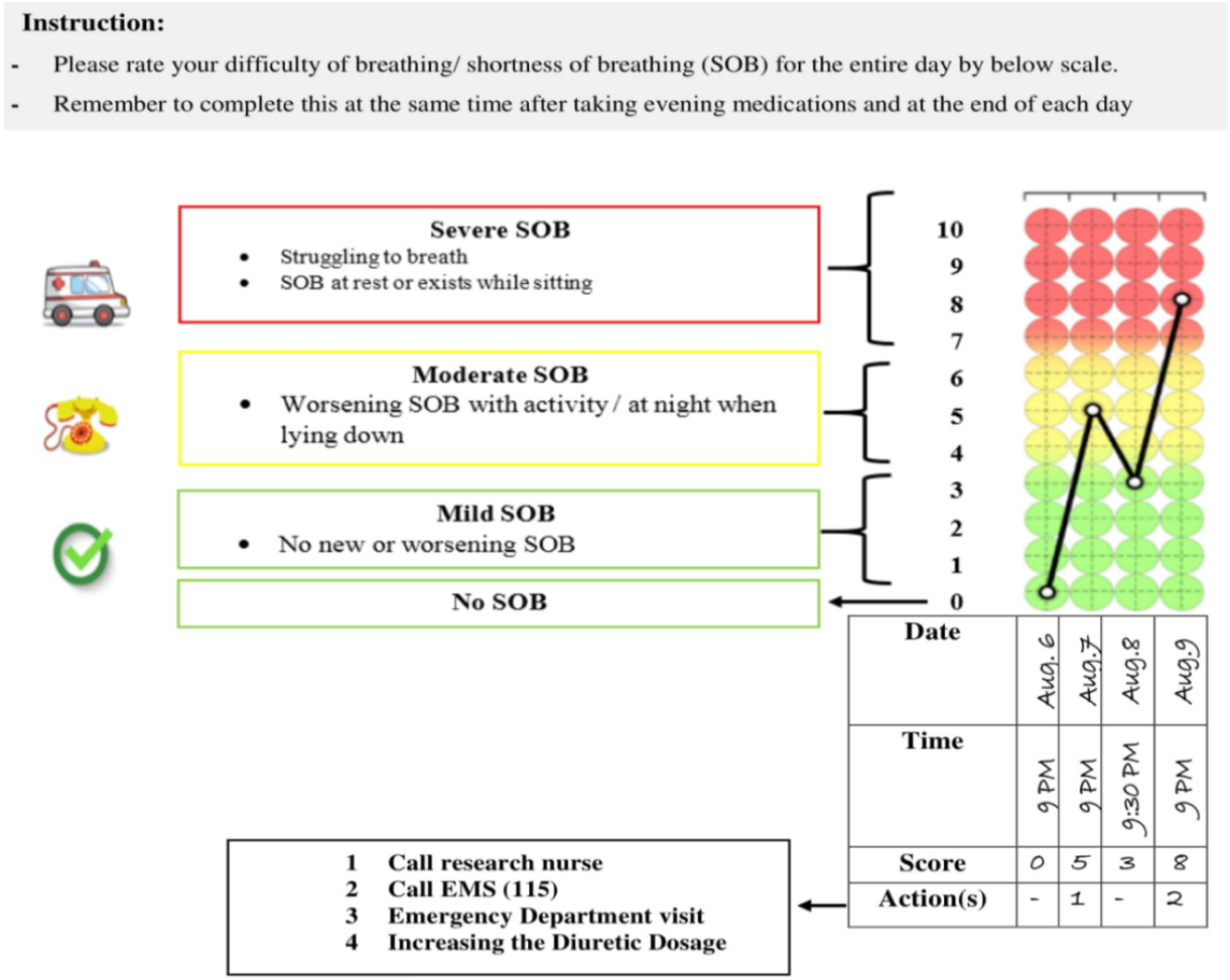


Figure 3. Flowchart of actions recommended by research nurse based on color zones of each subject's self-monitoring daily diary during call follow-ups. ED: emergency department; EMS: emergency medical services; SOB: shortness of breath.

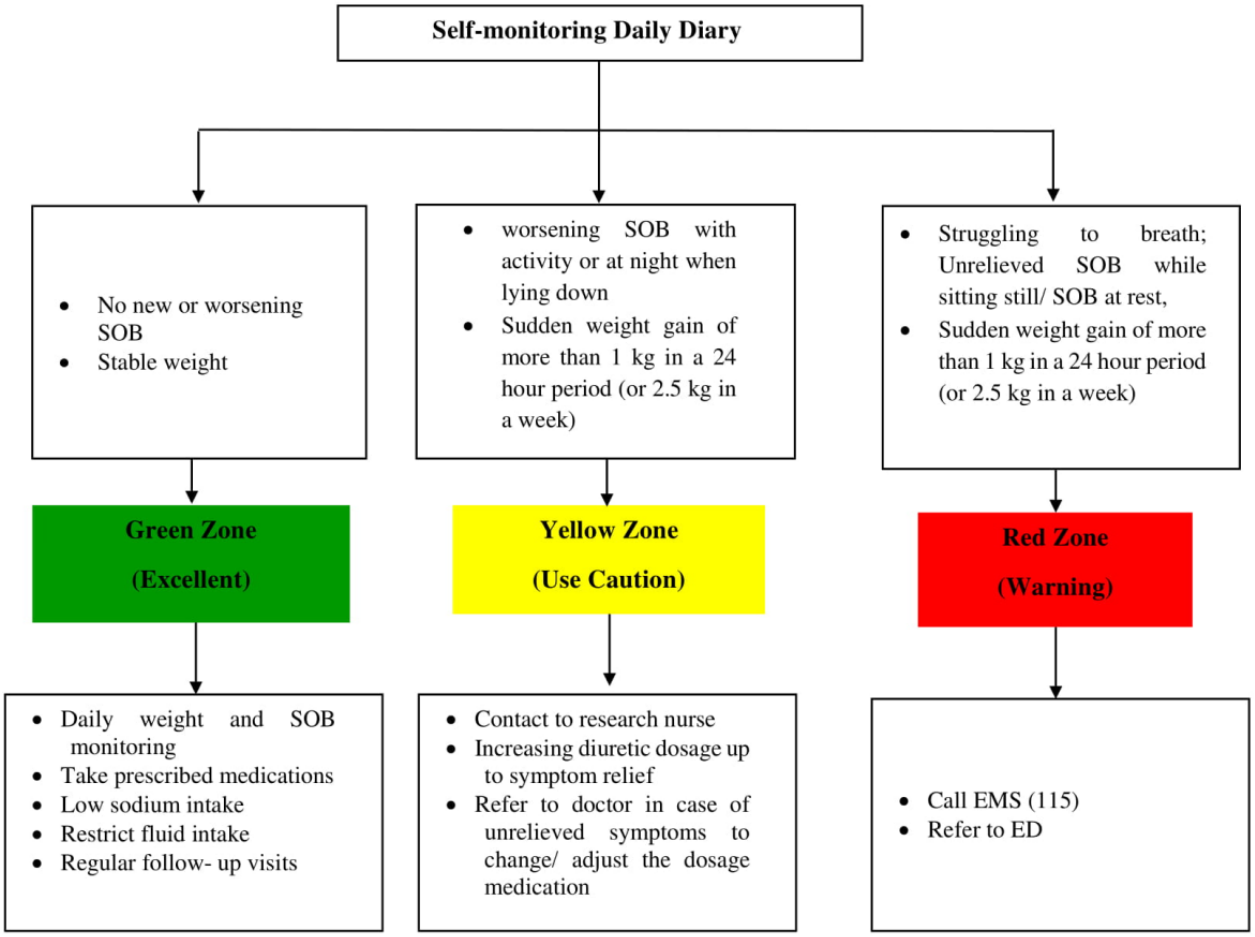
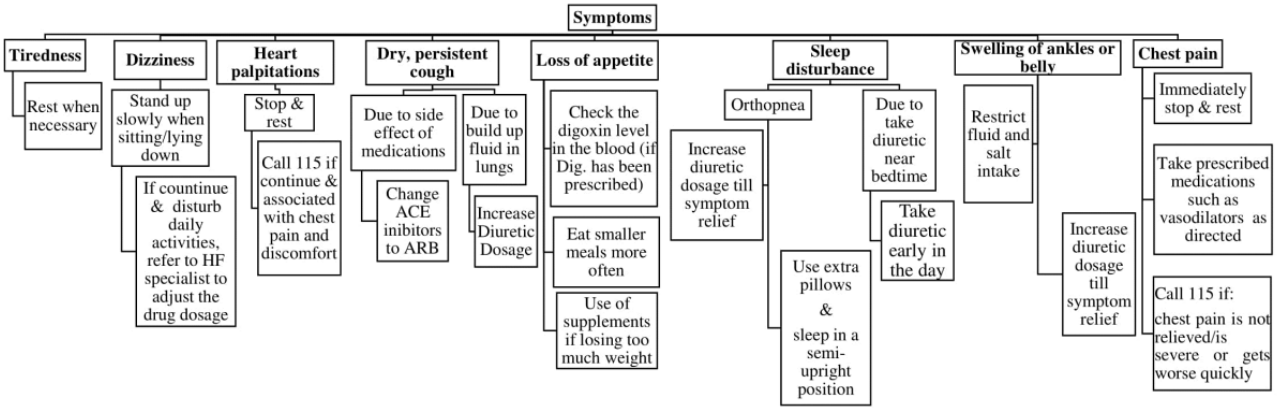


Figure 4. Flowchart of the research nurse recommendations for each symptom reported by subjects in the intervention group during the call follow-ups.



Study Measures

Primary Outcome

Self-Care Behavior

Effective self-care improvement is a priority of all clinicians caring for patients with HF [46]. In a developing country like Iran, there is a growing need to improve patient's self-care [15]. However, there is a low rate of reported admissions for HF in Iran [3]. Thus, in contrast to previous studies where hospitalization was considered the primary outcome [21,22,30] and self-care as the secondary outcome [21,22], self-care has been identified as the primary outcome in this trial.

Self-care behavior will be measured by the Self-Care of Heart Failure Index (SCHFI) version 6.2 [47] by self-reporting at baseline and monthly intervals for 3 months. SCHFI was translated into Persian and validated for Persian speaking people by Siabani et al in 2014 [48]. It consists of 3 separate scales and 22 questions: 10 for self-care maintenance, 6 for self-care management, and 6 for self-care confidence [49]. Cronbach alpha was determined for self-care maintenance (.56),

management (.64), and confidence scales (.79) [48]. Scale scores can range between 0 to 100, and a score ≥70 will be considered as adequate self-care [49]. We will ask participants to complete SCHFI by themselves at baseline and then monthly for 3 months.

Secondary Outcomes

Heart Failure Knowledge

In order to assess the effect of education and counseling on knowledge of participants with HF, the Dutch Heart Failure Knowledge Scale (DHFKS), with Cronbach alpha=.62, will be used. This scale consists of a 15 multiple-choice self-administered questionnaire concerning: general knowledge on HF (4 questions), knowledge on HF treatment (6 questions on diet, fluid restriction, and activity), and symptoms and their recognition (5 questions). The participants will be asked to choose the correct option from the three choices. The minimum score for this scale can range from 0 (no knowledge) to a maximum score of 15 (excellent knowledge) [50].

While there is no Iranian version of this scale, it was translated into the Persian language by forward-backward translation methods after obtaining permission from the scale developer [50]. The face and content validity were evaluated by an expert's opinion and discussion with patients with HF. The reliability was assessed through a pilot study among 30 patients with HF (Cronbach alpha=.62). This coefficient alpha was identical to the original one, and the internal consistency could not be improved by deleting any of the 15 items [50]. Thus, all items have been retained. Participants will be asked to provide answers to the DHFKS by themselves at baseline and the end of the study.

Quality of Life

Heart failure quality of Life (HFQOL) will be assessed by the Iranian version of the Minnesota Living with Heart Failure Questionnaire (MLHFQ) with Cronbach alpha=.95 [51]. The psychometric properties of the questionnaire were evaluated by Middel et al in 2001 (Cronbach alpha≥.80 for the scales) [52]. The MLHFQ consists of 21 questions with a 6-point Likert scale ranging from 0 (without limitation) to 5 (maximum limitation). It consists of physical and emotional dimensions. The physical dimension is the sum of the question scores (questions 1 to 7, 12, 13) while the emotional dimension is based on questions 17 to 21. Questions 8 to 11 and 14 to 16 are related to lifestyle, financial situations, and side effects of medications. The total is the sum of the 21-question score, and a lower score reflects better quality of life [53]. Since this instrument assesses HFQOL in the previous month [54], we will ask participants to complete MLHFQ by themselves at baseline and then monthly for 3 months.

All-Cause Hospitalization

Data related to all-cause hospitalization during the previous month (ie, cause, date of admission, discharge, and length of stay) will be obtained from participants in both groups by an outcome assessor blinded to study group assignment during monthly call follow-ups. In the case of admission to other health care settings except for THC, data will be collected according to the participants' self-reporting. If the participant is admitted to THC, data will be confirmed by the hospital information system following participant self-reporting.

Causes of hospital admissions will be classified according to 3 categories of cardiac admission for HF: SOB and edema relieved by diuretics, other cardiac causes (ie, chest pain, arrhythmias, or syncope), and non-cardiac causes [21]. All-cause hospital admissions will be obtained by trained research assistants who are blinded to the allocation.

Data Collection

Eligible patients will be asked to read and sign a written informed consent form. The research nurse will then collect demographic and clinical characteristics by participant self-reporting and from a medical chart and then record these in data collection forms (see Table 1). Also, participants will be asked to complete baseline surveys (SCHFI, HF knowledge, HFQOL, and health literacy) by themselves in the HF clinic before randomization.

In order to assess participant health literacy, we will use the Heart Failure-Specific Health Literacy Scale with Cronbach alpha=.71. It consists of 12 items each with 4 possible scores (1 to 4): inapplicable (1) to strongly applicable (4) where a higher score indicates a higher level of health literacy except items 1 to 4 [55]. The Iranian version of this scale was prepared after getting the developer's permission. Thus, it was first translated into Persian by a forward-backward translation method. Then, face and content validity were approved by an expert's opinion (nursing faculty, nurse practitioners, and cardiologists) and discussion with patients with HF. A pilot study was conducted to assess the reliability with 30 HF patients and where a Cronbach alpha value of .77 was determined. Deletion of items could not improve the value similar to the original scale. Therefore, we decided to retain all items [55]. We will ask the participants to complete the health literacy scale as a baseline survey.

In order to measure the HF knowledge at the end of the study, monthly self-care behavior, and the HFQOL, the outcome assessor will be blinded to study group assignments. The assessor will send the DHFKS, SCHFI, and MLHFQ to the participants in both groups by telegram mobile application in the morning of each monthly call follow-up and ask them to send answers before 6 pm of the same day.

Participant Timeline

The SPIRIT 2013 template was used to schedule enrolment, interventions, and assessments (Table 1) [34]. A schematic representation of the study design is shown in Figure 5.

Table 1. Time schedule for enrolment, interventions, and assessments in this study.

Time point	Staff member	Study period						
		Enrollment: $-t_1$[a]	Allocation: 0	Post-allocation				Close-out: t_x[b]
				t_1[c]	f_1	f_2	f_3[d]	
Enrollment								
Eligibility screen	Research nurse and HF[e] specialist	✓	—[f]	—	—	—	—	—
Informed consent	Research nurse and HF specialist	✓	—	—	—	—	—	—
Baseline characteristics and surveys	Research nurse	✓	—	—	—	—	—	—
Allocation	Research nurse	—	✓	—	—	—	—	—
Intervention								
Integrated package plus usual care	Research nurse	—	—	✓	✓	✓	✓	—
Control								
Usual care	—	—	—	✓	✓	✓	✓	—
Assessments (demographic/clinical)								
Age (years)	Research nurse	✓	—	—	—	—	—	—
Gender (male/female)	Research nurse	✓	—	—	—	—	—	—
Ethnicity	Research nurse	✓	—	—	—	—	—	—
Marital status (married/single)	Research nurse	✓	—	—	—	—	—	—
Income	Research nurse	✓	—	—	—	—	—	—
Level of education								
Elementary	Research nurse	✓	—	—	—	—	—	—
High school	Research nurse	✓	—	—	—	—	—	—
Academic	Research nurse	✓	—	—	—	—	—	—
HF-Specific Health Literacy Scale	Research nurse	✓	—	—	—	—	—	—
Body mass index (kg/m^2)	Research nurse	✓	—	—	—	—	—	—
Job (yes/no)	Research nurse	✓	—	—	—	—	—	—
Insurance (yes/no)	Research nurse	✓	—	—	—	—	—	—
Time with HF	Research nurse	✓	—	—	—	—	—	—
HF etiology (yes/no)								
Ischemic heart disease	Research nurse	✓	—	—	—	—	—	—
Cardiomyopathy	Research nurse	✓	—	—	—	—	—	—
Hypertension	Research nurse	✓	—	—	—	—	—	—
Heart valve disease	Research nurse	✓	—	—	—	—	—	—
NYHA[g] functional class (II–IV)	Research nurse	✓	—	—	—	—	—	—
Previous hospitalization (yes/no)	Research nurse	✓	—	—	—	—	—	—
Hospitalization last 3 months? (yes/no)	Research nurse	✓	—	—	—	—	—	—
Charlson comorbidity index	Research nurse	✓	—	—	—	—	—	—
Ejection fraction (%)	Research nurse	✓	—	—	—	—	—	—
Systolic blood pressure (mm Hg)	Research nurse	✓	—	—	—	—	—	—
Diastolic blood pressure (mm Hg)	Research nurse	✓	—	—	—	—	—	—
Heart rate (bpm)	Research nurse	✓	—	—	—	—	—	—

Time point	Staff member	Study period						
		Enrollment: -t_1[a]	Allocation: 0	Post-allocation				Close-out: t_x[b]
				t_1[c]	f_1	f_2	f_3[d]	
Daily weight measure (yes/no)	Research nurse	✓	—	—	—	—	—	—
Medications (yes/no)								
Angiotensin-converting enzyme inhibitor	Research nurse	✓	—	—	—	—	—	—
Angiotensin receptor blocker	Research nurse	✓	—	—	—	—	—	—
Diuretics	Research nurse	✓	—	—	—	—	—	—
Aspirin	Research nurse	✓	—	—	—	—	—	—
Statins	Research nurse	✓	—	—	—	—	—	—
Vitamin k antagonists	Research nurse	✓	—	—	—	—	—	—
Allopurinol	Research nurse	✓	—	—	—	—	—	—
Beta blocker	Research nurse	✓	—	—	—	—	—	—
Digitals	Research nurse	✓	—	—	—	—	—	—
Implantable cardiac devices (yes/no)	Research nurse	✓	—	—	—	—	—	—
Prior cardiac surgery? (yes/no)	Research nurse	✓	—	—	—	—	—	—
Arrhythmia in electrocardiography? (yes/no)	Research nurse	✓	—	—	—	—	—	—
Laboratory parameters (serum)								
Sodium	Research nurse	✓	—	—	—	—	—	—
Potassium	Research nurse	✓	—	—	—	—	—	—
Urea	Research nurse	✓	—	—	—	—	—	—
Creatinine	Research nurse	✓	—	—	—	—	—	—
Uric acid	Research nurse	✓	—	—	—	—	—	—
Hemoglobin	Research nurse	✓	—	—	—	—	—	—
Hematocrit	Research nurse	✓	—	—	—	—	—	—
Fasting blood glucose levels	Research nurse	✓	—	—	—	—	—	—
Baseline surveys								
Self-Care of HF Index	Research nurse	✓	—	—	—	—	—	—
Minnesota Living with HF Questionnaire	Research nurse	✓	—	—	—	—	—	—
Dutch HF Knowledge Scale	Research nurse	✓	—	—	—	—	—	—
Primary outcome: Self-Care of HF Index	Research assistant	—	—	—	—	✓	✓	✓
Secondary outcomes								
HF knowledge	Research assistant	—	—	—	—	—	—	✓
HF quality of life	Research assistant	—	—	—	—	✓	✓	✓
All-cause hospitalization (yes/no)	Research assistant	—	—	—	—	✓	✓	✓

[a]-t_1: Time at enrollment.

[b]t_x: Time at the end of study.

[c]t_1: Time at allocation.

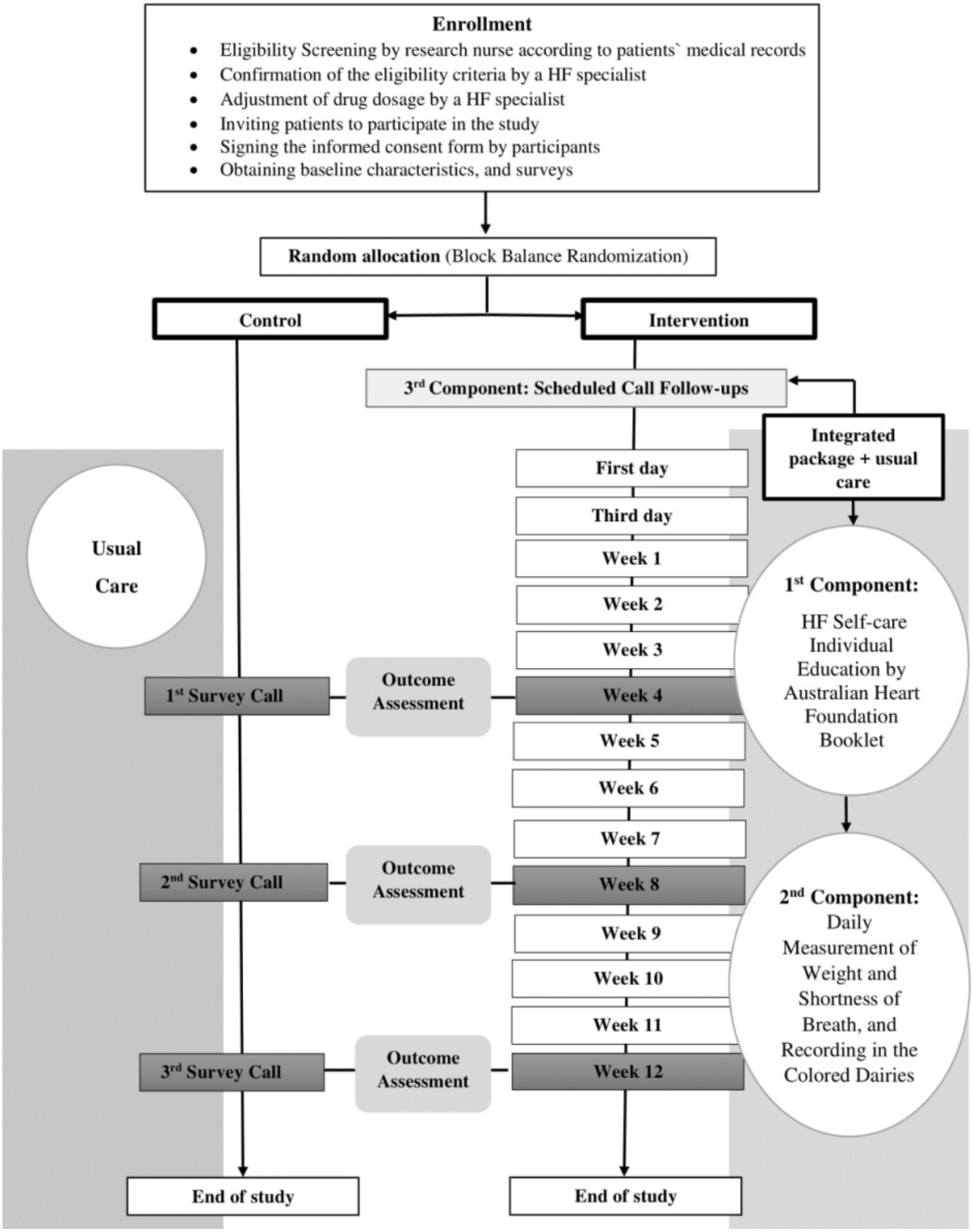
[d]f_1: Time at first month follow-up; f_2: Time at second month follow-up; f_3: Time at third month follow-up.

[e]HF: heart failure.

[f]Not applicable.

[g]NYHA: New York Heart Association.

Figure 5. Schematic representation of the study design. HF: heart failure.



Sample Size

In this study, the sample size was calculated based on the minimal clinically important difference (MCID) approach for self-care as measured by SCHFI for the primary outcome. No specific MCID for SCHFI was available to the best of our knowledge and based on our search of the PubMed database.

The suggested MCID for assessing dyspnea with the visual analog scale (0-100 score index) was the range 10-20 [56]. Thus, improving self-care for ≥10 scores from the baseline at the end of the study has been considered as MCID for the present study in order to reach a large sample size. According to the Jurgens et al [22] study in 2013, a mean of 70.8 for self-care in the control group at the end of study (90-days) and a fixed standard

deviation of 27.2 (the largest SD) have been considered. In order to calculate sample size by G*Power free software (version 3.1.9.2), the input parameters are as following: effect size (Cohen *f*) of 0.168, the alpha error probability of .05, a statistical power of 80% to detect MCID≥10 scores between the 2 groups at the end of the study, 3 times measurement of outcome with monthly intervals, and a correlation coefficient of .5 among repeated measurements. Thus, by considering the overall attrition rates of 10%, the sample size was set at 68 participants (34 participants in each group).

Participant Recruitment

During the run-in phase of the study, the research nurse at the HF clinic will be present Sunday through Wednesday of each week from 8 am to 1 pm. The nurse will screen the patients for the eligibility criteria at the time of admission. Participant screening will continue until the target population is achieved. Simultaneously, an HF specialist will confirm the subject`s eligibility and adjust the drug dosages of the eligible participants. Also, the specialist will provide each patient with additional details about the study. This is our main strategy for achieving adequate participant enrollment.

Allocation: Method and Concealment Mechanism

The block balanced randomization method will be used for allocation. Before initiation of the run- in phase of the study, the statistician (AAK) will generate the randomization plan by website Randomization.com [57]. Therefore, twenty blocks of 4 for both the intervention group (group A) and the control group (group B) will be prepared. The statistician will fold the paper containing 4-size blocks 2 times, put them in the standard envelopes and write the serial numbers on them. All envelopes will be kept at the recruitment center. Thus, for every eligible patient, the research nurse randomly selects one of the envelopes after shuffling and assign participants into intervention and control groups.

Blinding

Due to the nature of the intervention, it is impossible to blind the participants assigned to the study groups to the data collector. However, the outcome assessor will be blinded and instructed not to ask the participants whether or not they received the intervention.

Data Management

Data will be collected in paper format. A file for each subject will be stored in numerical order in a secure place and manner. Files will be maintained at the recruitment center for 3 years after completion of the study. The statistical expert will prepare the data generated by the IBM/SPSS statistical software (version 16). This expert will train the data clerk to enter the data by specific codes and labels. Also, after finishing the data entry, all data will be double checked. All forms related to the study will be kept in a locked cabinet with restricted access in the recruitment center. All reports will be prepared in a manner in which no individual participants can be identified.

Data Monitoring

Three researchers from TUMS not involved in the study and chosen by the university will monitor data and supervise the conduct of the study.

Statistical Methods

Statisticians will prepare the data sheets to collected data. Data will be entered into the SPSS software (version 16). The Kolmogorov-Smirnov test will be used to normality. A transformation approach will be used to handle non-normal distribution. For the between-group comparison of continuous and categorical baseline characteristics, independent *t* test and chi-square test will be used. For categorical variables between the 2 groups, the two-tailed Fisher exact test will be used instead of the chi-square test in the case of too small expected cell frequencies. A *P* value <.05 will be considered statistically significant.

Primary Analysis

Baseline scores for each scale of SCHFI including self-care maintenance, management, and confidence will be compared in both groups by an independent *t* test. Due to the measurement of self-care behavior at baseline and at monthly time intervals, we will calculate the mean of monthly self-care scores in order to compare the mean of self-care behavior after the intervention in both groups. Also, because of the frequent measurement of self-care behavior, we will also use *P* value correction based on the Bonferroni method [58]. A linear logistic regression procedure will be applied to determine the factors affecting self-care behavior. The odds ratio will be reported with 95% CI.

Secondary Analysis

Independent *t* tests between 2 groups will compare the mean of the HF knowledge score before and at the end of the study. The HFQOL at baseline and at monthly time intervals will be compared by the *P* value correction based on the multiple comparisons.

In order to describe the surveillance, the median of admissions to health care settings will be used. Also, the Kaplan-Meier survival analysis will be applied for a descriptive comparison of the surveillance and, a log-rank test will be used to detect the significance difference between the 2 groups. A hazard ratio will be reported with 95% CI.

Ethics Approval and Consent to Participate

The study protocol, data collection forms, educational booklet, and the template of informed consent form was reviewed and approved by the Research Ethics Committee (REC) at TUMS on February 5, 2017 (No. IR.TUMS.FNM.REC.1395.1653). Researchers are committed to updating the agreement with the IRB and REC at TUMS for any administrative and methodological changes of the study protocol which may affect the study.

In order to obtain the informed consent, the research nurse and HF specialist will introduce the trial to each eligible participant. Every eligible participant will receive an information sheet and a written informed consent. The research nurse will then obtain

written informed consent from all participants willing to participate in the trial.

The participant informed consent form will be prepared according to the Declaration of Helsinki. It gives the subject information on what the research is about and what happens following participation in the study. It contains information on "purpose of the trial, potential benefits and risks; subject`s right to refuse participation or to withdraw consent at any time; institutional affiliation and potential competing interests of the researcher; and sources of trial funding" [59].

One critical issue that the researchers will be experiencing is posttrial care. Due to the nature of the intervention, this trial will not have any harm for participants that need to be treated during or after the trial. However, the HF specialist is the responsible physician and will assess and manage participants in the event of worsening of the symptoms.

Availability of Data and Material

All study-related forms will be stored securely in the recruitment center by code number. Informed consent containing names and other personal identifiers will be stored separately from the forms identified by code number.

Intellectual property of the data belongs to the TUMS research and technology deputy. Thus, the final trial dataset/analysis will be available from the corresponding author upon request and by permission of the TUMS research and technology deputy.

Results

This paper is the first version of the protocol that has been submitted. At the time of manuscript submission, the trial is actively enrolling the participants, and the recruitment started on June 11, 2017. The study is expected to be completed in November 2017. Data will be analyzed and published by the end of 2018.

Discussion

The major concerns among patients with HF are the lack of information on the medications, worrying about both the quantity and combination of prescribed drugs, having trouble differentiating between the side effects of medications and symptoms of HF, and the lack of knowledge required to interpret symptoms or treat worsening symptoms [60]. The most critical participant issues are poor accessibility to a health care provider, receiving poor follow up, and having poor medication adherence [61].

Due to the nature of the intervention and the application of an integrated package including self-care educational booklet, graphical self-monitoring diaries based on TLS, and scheduled call follow-ups, we expect that this trial will address the patients' concerns and issues.

We anticipate that the self-care educational booklet will improve the patient`s knowledge of HF. Graphical colored self-monitoring weight and SOB diaries will improve the patients' ability to recognize their HF symptoms and help them determine the appropriate action whenever symptoms worsen. Also, scheduled call follow-ups will allow the patients to ask questions related to the disease, treatment options, and adverse effects. This will help them with referral to the proper health care setting in the early stages of the disease decompensation.

Iran is an LMIC and its health care system provides for only a brief verbal self-care instruction without any follow-up calls to patients with HF. Thus, at the end of this trial, patients in the intervention group and their caregivers may feel they are being deprived of standard care and a lack of support.

Thus, if the research findings provide positive effects, this practical intervention will be implemented for patients with HF in Iran and other countries similar to Iran. Also, the results of the research project plus the integrated package will be delivered to the noncommunicable diseases center at the Iran Ministry of Health, Education, and Treatment for consideration in the usual care of patients with HF.

Acknowledgments

This study protocol relates to the thesis of MN for an MSc degree in Critical Care Nursing (no. 882) at Tehran University of Medical Sciences (TUMS). We thank the Educational, Research and Technology Deputy and the Critical Care Nursing Department at the School of Nursing and Midwifery affiliated with TUMS for the thesis approval. We also thank the Noncommunicable Diseases Research Center (NDRC) of Endocrinology and Metabolism Research Institute affiliated with TUMS for critically reviewing and approving the research project. We thank Dr Neda Mehrdad for kindly supporting the research project approval process.

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NDRC and the Research and Technology Deputy of Nursing and Midwifery School affiliated with TUMS financially supported this research project.

Conflicts of Interest

None declared.

Authors' Contributions

MN is the principal investigator of this trial. MN, RM, AAK, GR, SG, and MZ initiated the study design. RM is the responsible physician at the Tehran Heart Center. MZ is the executive manager of the project. MN, RM, and KA helped with implementation and data collection. MN, RM, MZ, and KA prepared the informed consent and data collection forms and the educational booklet. MN and KA prepared the data for statistical analysis. AAK and GR provided statistical expertise in clinical trial design and performed the statistical analysis. All authors contributed to the refinement of the study protocol and are accountable for all aspects of the work.

References

1. Yancy C, Jessup M, Bozkurt B, Butler J, Casey DJ, Drazner M, et al. 2013 ACCF/AHA guideline for the management of heart failure: executive summary: a report of the American College of Cardiology Foundation/American Heart Association Task Force on practice guidelines. Circulation 2013 Oct 15;128(16):1810-1852. [doi: 10.1161/CIR.0b013e31829e8807] [Medline: 23741057]
2. Ziaeian B, Fonarow GC. Epidemiology and aetiology of heart failure. Nat Rev Cardiol 2016 Dec;13(6):368-378 [FREE Full text] [doi: 10.1038/nrcardio.2016.25] [Medline: 26935038]
3. Callender T, Woodward M, Roth G, Farzadfar F, Lemarie J, Gicquel S, et al. Heart failure care in low- and middle-income countries: a systematic review and meta-analysis. PLoS Med 2014 Aug;11(8):e1001699 [FREE Full text] [doi: 10.1371/journal.pmed.1001699] [Medline: 25117081]
4. Shimokawa H, Miura M, Nochioka K, Sakata Y. Heart failure as a general pandemic in Asia. Eur J Heart Fail 2015 Sep;17(9):884-892 [FREE Full text] [doi: 10.1002/ejhf.319] [Medline: 26222508]
5. Ahmadi A, Etemad K, Khaledifar A. Risk factors for heart failure in a cohort of patients with newly diagnosed myocardial infarction: a matched, case-control study in Iran. Epidemiol Health 2016;38:e2016019 [FREE Full text] [doi: 10.4178/epih.e2016019] [Medline: 27188309]
6. Zannad F, Garcia A, Anker S, Armstrong P, Calvo G, Cleland J, et al. Clinical outcome endpoints in heart failure trials: a European Society of Cardiology Heart Failure Association consensus document. Eur J Heart Fail 2013 Oct;15(10):1082-1094 [FREE Full text] [doi: 10.1093/eurjhf/hft095] [Medline: 23787718]
7. Bhatia RS, Tu JV, Lee DS, Austin PC, Fang J, Haouzi A, et al. Outcome of heart failure with preserved ejection fraction in a population-based study. N Engl J Med 2006 Jul 20;355(3):260-269. [doi: 10.1056/NEJMoa051530] [Medline: 16855266]
8. Pazos-López P, Peteiro-Vázquez J, Carcía-Campos A, García-Bueno L, de Torres J, Castro-Beiras A. The causes, consequences, and treatment of left or right heart failure. Vasc Health Risk Manag 2011;7:237-254 [FREE Full text] [doi: 10.2147/VHRM.S10669] [Medline: 21603593]
9. Roger VL. Epidemiology of heart failure. Circ Res 2013 Aug 30;113(6):646-659 [FREE Full text] [doi: 10.1161/CIRCRESAHA.113.300268] [Medline: 23989710]
10. Bui A, Horwich T, Fonarow GC. Epidemiology and risk profile of heart failure. Nat Rev Cardiol 2011 Jan;8(1):30-41 [FREE Full text] [doi: 10.1038/nrcardio.2010.165] [Medline: 21060326]
11. Jaarsma T, Strömberg A, Ben GT, Cameron J, Driscoll A, Duengen H, et al. Comparison of self-care behaviors of heart failure patients in 15 countries worldwide. Patient Educ Couns 2013 Jul;92(1):114-120. [doi: 10.1016/j.pec.2013.02.017] [Medline: 23579040]
12. Iqbal J, Francis L, Reid J, Murray S, Denvir M. Quality of life in patients with chronic heart failure and their carers: a 3-year follow-up study assessing hospitalization and mortality. Eur J Heart Fail 2010 Sep;12(9):1002-1008 [FREE Full text] [doi: 10.1093/eurjhf/hfq114] [Medline: 20615920]
13. Chioncel O, Lainscak M, Seferovic P, Anker S, Crespo-Leiro MG, Harjola V, et al. Epidemiology and one-year outcomes in patients with chronic heart failure and preserved, mid-range and reduced ejection fraction: an analysis of the ESC Heart Failure Long-Term Registry. Eur J Heart Fail 2017 Dec;19(12):1574-1585. [doi: 10.1002/ejhf.813] [Medline: 28386917]
14. Rajadurai J, Tse HF, Wang CH, Yang NI, Zhou J, Sim D. Understanding the Epidemiology of Heart Failure to Improve Management Practices: An Asia-Pacific Perspective. J Card Fail 2017 Apr;23(4):327-339 [FREE Full text] [doi: 10.1016/j.cardfail.2017.01.004] [Medline: 28111226]
15. Siabani S, Driscoll T, Davidson PM, Najafi F, Jenkins MC, Leeder SR. Self-care and Its Predictors in Patients With Chronic Heart Failure in Western Iran. J Cardiovasc Nurs 2016;31(1):22-30. [doi: 10.1097/JCN.0000000000000211] [Medline: 25419944]
16. Zamanzadeh V, Valizadeh L, Jamshidi F, Namdar H, Maleki A. Self-Care Behaviors among Patients with Heart Failure in Iran. J Caring Sci 2012 Dec;1(4):209-214 [FREE Full text] [doi: 10.5681/jcs.2012.029] [Medline: 25276697]

17. Rahnavard Z, Nodeh ZH, Hatamipour K. Congestive heart failure: Predictors of health-related quality of life in Iranian women. Contemp Nurse 2014;47(1-2):159-167. [doi: 10.5172/conu.2014.47.1-2.159] [Medline: 25267138]
18. Riegel B, Lee CS, Dickson VV, Medscape. Self care in patients with chronic heart failure. Nat Rev Cardiol 2011 Jul 19;8(11):644-654. [doi: 10.1038/nrcardio.2011.95] [Medline: 21769111]
19. Moser DK, Mann DL. Improving outcomes in heart failure: It's not unusual beyond usual care. Circulation 2002 Jun 18;105(24):2810-2812. [Medline: 12070104]
20. Siabani S, Leeder S, Davidson PM. Barriers and facilitators to self-care in chronic heart failure: a meta-synthesis of qualitative studies. Springerplus 2013;2(1):320 [FREE Full text] [doi: 10.1186/2193-1801-2-320] [Medline: 23961394]
21. DeWalt D, Malone R, Bryant M, Kosnar M, Corr K, Rothman R, et al. A heart failure self-management program for patients of all literacy levels: a randomized, controlled trial [ISRCTN11535170]. BMC Health Serv Res 2006 Mar 13;6(1):30 [FREE Full text] [doi: 10.1186/1472-6963-6-30] [Medline: 16533388]
22. Jurgens CY, Lee CS, Reitano JM, Riegel B. Heart failure symptom monitoring and response training. Heart Lung 2013;42(4):273-280. [doi: 10.1016/j.hrtlng.2013.03.005] [Medline: 23623564]
23. Wakefield B, Groves P, Drwal K, Scherubel M, Kaboli P. Evaluation of Feasibility of 2 Novel Heart Failure Monitoring Instruments to Facilitate Patient Recognition of Symptoms. J Cardiovasc Nurs 2016;31(1):42-52. [doi: 10.1097/JCN.0000000000000213] [Medline: 25419937]
24. Chaudhry SI, Wang Y, Concato J, Gill TM, Krumholz HM. Patterns of weight change preceding hospitalization for heart failure. Circulation 2007 Oct 02;116(14):1549-1554 [FREE Full text] [doi: 10.1161/CIRCULATIONAHA.107.690768] [Medline: 17846286]
25. Gwaltney C. Hearing the voice of the heart failure patient: key experiences identified in qualitative interviews. Br J Cardiol 2012;19(1):25. [doi: 10.5837/bjc.2012.004]
26. McMurray J, Adamopoulos S, Anker S, Auricchio A, Böhm M, Dickstein K, Task Force for the DiagnosisTreatment of AcuteChronic Heart Failure 2012 of the European Society of Cardiology, ESC Committee for Practice Guidelines. ESC guidelines for the diagnosis and treatment of acute and chronic heart failure 2012: The Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association (HFA) of the ESC. Eur J Heart Fail 2012 Aug;14(8):803-869 [FREE Full text] [doi: 10.1093/eurjhf/hfs105] [Medline: 22828712]
27. van der Wal HL, Jaarsma T, Moser DK, Veeger NJGM, van Gilst WH, van Veldhuisen DJ. Compliance in heart failure patients: the importance of knowledge and beliefs. Eur Heart J 2006 Feb;27(4):434-440. [doi: 10.1093/eurheartj/ehi603] [Medline: 16230302]
28. White M, Howie-Esquivel J, Caldwell MA. Improving heart failure symptom recognition: a diary analysis. J Cardiovasc Nurs 2010;25(1):7-12. [doi: 10.1097/JCN.0b013e3181b7af9e] [Medline: 20134279]
29. Eastwood CA, Travis L, Morgenstern TT, Donaho EK. Weight and symptom diary for self-monitoring in heart failure clinic patients. J Cardiovasc Nurs 2007;22(5):382-389. [doi: 10.1097/01.JCN.0000287027.49628.a7] [Medline: 17724420]
30. Jones C, Holmes G, DeWalt D, Erman B, Wu J, Cene C, et al. Self-reported recall and daily diary-recorded measures of weight monitoring adherence: associations with heart failure-related hospitalization. BMC Cardiovasc Disord 2014 Jan 31;14(1):12 [FREE Full text] [doi: 10.1186/1471-2261-14-12] [Medline: 24483776]
31. Smerecnik CMR, Mesters I, Kessels LTE, Ruiter RAC, De Vries NK, De Vries H. Understanding the positive effects of graphical risk information on comprehension: measuring attention directed to written, tabular, and graphical risk information. Risk Anal 2010 Sep;30(9):1387-1398. [doi: 10.1111/j.1539-6924.2010.01435.x] [Medline: 20561265]
32. Croucher S, Williamson GR. Risk assessment in mental health: introducing a traffic light system in a community mental health team. Open Nurs J 2013;7:82-88 [FREE Full text] [doi: 10.2174/1874434620130529004] [Medline: 23878620]
33. Ashir M, Marlowe K. Traffic Lights. Clinical Governance: An Intl J 2009 Aug 07;14(3):226-235. [doi: 10.1108/14777270910976166]
34. Chan AW, Tetzlaff JM, Gøtzsche PC, Altman DG, Mann H, Berlin JA, et al. SPIRIT 2013 explanation and elaboration: guidance for protocols of clinical trials. BMJ 2013 Jan 08;346:e7586 [FREE Full text] [Medline: 23303884]
35. Poorhosseini H, Hesameddin Abbasi S. The Tehran Heart Center. European Heart Journal 2018 Aug 03;39(29):2695-2696. [doi: 10.1093/eurheartj/ehy369]
36. Mann D, Zipes D, Libby P. Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine. Washington, DC: Elsevier; 2014:a.
37. Black J, Romano P, Sadeghi B, Auerbach A, Ganiats T, Greenfield S, BEAT-HF Research Group. A remote monitoring and telephone nurse coaching intervention to reduce readmissions among patients with heart failure: study protocol for the Better Effectiveness After Transition - Heart Failure (BEAT-HF) randomized controlled trial. Trials 2014 Apr 13;15(1):124 [FREE Full text] [doi: 10.1186/1745-6215-15-124] [Medline: 24725308]
38. Heart Foundation. 2015. Living well with chronic heart failure URL: https://www.heartfoundation.org.au/images/uploads/publications/CON-035.v5_LWWCHF-2015-web_v2.pdf.pdf [accessed 2016-09-30] [WebCite Cache ID 72oYeW9ac]
39. Goodyear-Smith F, Arroll B, Chan L, Jackson R, Wells S, Kenealy T. Patients prefer pictures to numbers to express cardiovascular benefit from treatment. Ann Fam Med 2008;6(3):213-217 [FREE Full text] [doi: 10.1370/afm.795] [Medline: 18474883]

40. Gaissmaier W, Wegwarth O, Skopec D, Müller A, Broschinski S, Politi MC. Numbers can be worth a thousand pictures: individual differences in understanding graphical and numerical representations of health-related information. Health Psychol 2012 May;31(3):286-296. [doi: 10.1037/a0024850] [Medline: 21842998]
41. Garcia-Retamero R, Dhami MK. Pictures speak louder than numbers: on communicating medical risks to immigrants with limited non-native language proficiency. Health Expect 2011 Mar;14 Suppl 1:46-57 [FREE Full text] [doi: 10.1111/j.1369-7625.2011.00670.x] [Medline: 21323820]
42. American Heart Association. 2015. Self-check Plan for Heart Failure Management URL: https://www.heart.org/-/media/files/health-topics/heart-failure/self-check-plan-for-hf-management-477328.pdf?la=en&hash=875F6CDFB9A16372FA8CABC3552D14EABFEFABCA [accessed 2016-03-21]
43. Green T. Heart failure self-monitoring toolkit. 2015. URL: https://scholarworks.umass.edu/nursing_dnp_capstone/56/ [accessed 2018-09-30] [WebCite Cache ID 72och2tBy]
44. White MF, Kirschner J, Hamilton MA. Self-care guide for the heart failure patient. Circulation 2014 Jan 21;129(3):e293-e294. [doi: 10.1161/CIRCULATIONAHA.113.003991] [Medline: 24446413]
45. Haefeli M, Elfering A. Pain assessment. Eur Spine J 2006 Jan;15 Suppl 1(Suppl 1):S17-S24 [FREE Full text] [doi: 10.1007/s00586-005-1044-x] [Medline: 16320034]
46. Moser DK, Dickson V, Jaarsma T, Lee C, Stromberg A, Riegel B. Role of self-care in the patient with heart failure. Curr Cardiol Rep 2012 Jun;14(3):265-275. [doi: 10.1007/s11886-012-0267-9] [Medline: 22437374]
47. Vellone E, Riegel B, Cocchieri A, Barbaranelli C, D'Agostino F, Antonetti G, et al. Psychometric testing of the Self-Care of Heart Failure Index Version 6.2. Res Nurs Health 2013 Oct;36(5):500-511. [doi: 10.1002/nur.21554] [Medline: 23832431]
48. Siabani S, Leeder SR, Davidson PM, Najafi F, Hamzeh B, Solimani A, et al. Translation and validation of the Self-care of Heart Failure Index into Persian. J Cardiovasc Nurs 2014;29(6):E1-E5. [doi: 10.1097/JCN.0000000000000121] [Medline: 24434822]
49. Riegel B, Lee C, Dickson V, Carlson B. An update on the self-care of heart failure index. J Cardiovasc Nurs 2009;24(6):485-497 [FREE Full text] [doi: 10.1097/JCN.0b013e3181b4baa0] [Medline: 19786884]
50. van der Wal MH, Jaarsma T, Moser DK, van Veldhuisen DJ. Development and testing of the Dutch Heart Failure Knowledge Scale. Eur J Cardiovasc Nurs 2005 Dec;4(4):273-277. [doi: 10.1016/j.ejcnurse.2005.07.003] [Medline: 16126459]
51. Eskandari S, Heravi KM, Rejeh N, Ebadi A, Montazeri A. Translation and Validation Study of the Iranian Version of Minnesota Living with Heart Failure Questionnaire. Payesh J 2015;14(4):475-484.
52. Middel B, Bouma J, de Jongste M, van Sonderen E, Niemeijer MG, Crijns H, et al. Psychometric properties of the Minnesota Living with Heart Failure Questionnaire (MLHF-Q). Clin Rehabil 2001 Oct;15(5):489-500. [doi: 10.1191/026921501680425216] [Medline: 11594639]
53. Carvalho V, Guimarães G, Carrara D, Bacal F, Bocchi EA. Validação da versão em português do Minnesota Living with Heart Failure Questionnaire. Arq. Bras. Cardiol 2009 Jul;93(1):39-44. [doi: 10.1590/S0066-782X2009000700008]
54. Garin O, Soriano N, Ribera A, Ferrer M, Pont A, Alonso J, Grupo IC-QoL. [Validation of the Spanish version of the Minnesota Living with Heart Failure Questionnaire]. Rev Esp Cardiol 2008 Mar;61(3):251-259 [FREE Full text] [Medline: 18361898]
55. Matsuoka S, Kato N, Kayane T, Yamada M, Koizumi M, Ikegame T, et al. Development and Validation of a Heart Failure-Specific Health Literacy Scale. J Cardiovasc Nurs 2016;31(2):131-139. [doi: 10.1097/JCN.0000000000000226] [Medline: 26049813]
56. Make B. How can we assess outcomes of clinical trials: the MCID approach. COPD 2007 Sep;4(3):191-194. [doi: 10.1080/15412550701471231] [Medline: 17729062]
57. Randomization.com. 2017. URL: http://randomization.com/
58. Chen SY, Feng Z, Yi X. A general introduction to adjustment for multiple comparisons. J Thorac Dis 2017 Jun;9(6):1725-1729 [FREE Full text] [doi: 10.21037/jtd.2017.05.34] [Medline: 28740688]
59. World Medical Association. 2008. Ethical principles for medical research involving human subjects URL: https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/ [accessed 2018-09-30] [WebCite Cache ID 72oiWmzYg]
60. Rogers A, Addington-Hall J, McCoy A, Edmonds P, Abery A, Coats A, et al. A qualitative study of chronic heart failure patients' understanding of their symptoms and drug therapy. Eur J Heart Fail 2002 Jun;4(3):283-287 [FREE Full text] [Medline: 12034153]
61. Grange J. The role of nurses in the management of heart failure. Heart 2005 May;91 Suppl 2(suppl 2):ii39-42; discussion ii43 [FREE Full text] [doi: 10.1136/hrt.2005.062117] [Medline: 15831611]

Abbreviations

DHFKS: Dutch Heart Failure Knowledge Scale
HF: heart failure
HFpEF: heart failure preserved ejection fraction
HFQOL: heart failure quality of life

HFrEF: heart failure reduced ejection fraction
IRB: institutional review board
LMIC: low- and middle-income country
LVEF: left ventricle ejection fraction
MCID: minimal clinically important difference
MLHFQ: Minnesota Living with Heart Failure Questionnaire
NYHA: New York Heart Association
QOL: quality of life
REC: research ethical committee
SCHFI: Self-Care Heart Failure Index
SOB: shortness of breath
SPIRIT: Standard Protocol Items: Recommendations for Interventional Trials
THC: Tehran Heart Center
TLS: traffic light system
TUMS: Tehran University of Medical Sciences

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Protocol

Comparing the Effectiveness of Clinicians and Paraprofessionals to Reduce Disparities in Perinatal Depression via the Mothers and Babies Course: Protocol for a Cluster-Randomized Controlled Trial

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Abstract

Background: Postpartum depression is highly prevalent in low-income women and has significant health and mental health effects on mother and child. Home visiting (HV) programs provide services to large numbers of perinatal women in the United States and are a logical setting for delivering mental health services. Although there are interventions that reduce the risk of developing postpartum depression among low-income women, none have used nonhealth or nonmental health professionals as interventionists.

Objective: This study aimed to outline the protocol of a cluster randomized trial funded by the Patient-Centered Outcomes Research Institute that evaluates whether the Mothers and Babies (MB) group intervention, when led by paraprofessional home visitors, is more efficacious than usual care. It will also examine if MB, when led by home visitors, is not inferior to MB delivered by mental health professionals (MHPs). MB has previously demonstrated efficacy when delivered by MHPs, and pilot work indicated promising results using home visitors to deliver the intervention.

Methods: A cluster randomized trial is being conducted with 38 HV programs. Sixteen HV programs will deliver MB using MHPs, 16 will deliver MB using paraprofessional home visitors, and 6 will deliver usual HV services. The study employs a modified covariate-constrained randomization design at the site level. We anticipate recruiting 933 women aged ≥16 years enrolled in HV programs, who are 33 or more weeks' gestation and speak either English or Spanish. Women in the 2 intervention arms will receive the 6-session MB group intervention. Baseline, postintervention, 12-week postpartum, and 24-week postpartum assessments will be conducted to assess client outcomes. The primary outcome will be the change in Quick Inventory of Depressive Symptomatology Self-Report 16 scores from baseline to 24-week follow-up. Secondary outcomes associated with core MB content will also be examined. Semistructured interviews will be conducted with home visitors and MHPs who are group facilitators and 90 study participants to gain data on intervention successes and challenges. Analyses will proceed at the participant level. Primary analyses for depressive symptoms score at 24 weeks postpartum will involve a linear mixed model, controlling for baseline symptoms and other covariates, and random effects to account for clustering.

Results: We have recruited 838 women through the end of August 2018. Recruitment will be completed at the end of September 2018.

Conclusions: There is considerable potential to disseminate MB to HV programs throughout the United States. Should our results demonstrate home visitor efficacy when compared with usual care and/ noninferiority between home visitors and MHPs

in improving mental health outcomes, no additional financial resources would be required for the existing HV staff to implement MB. Should this study determine that home visitors are less effective than MHPs, we will generate more wide-scale evidence on MB effectiveness when led by MHPs.

Trial Registration: ClinicalTrials.gov NCT02979444; https://clinicaltrials.gov/ct2/show/NCT02979444 (Archived by Webcite at http://www.webcitation.org/archive.php)

International Registered Report Identifier (IRRID): PRR1-10.2196/11624

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KEYWORDS

depression; postpartum; pregnancy; randomized controlled trial; community health

Introduction

Background

Postpartum depression is a serious mental health disorder that poses significant health and mental health risks for mothers and their infants [1]. Research suggests that prevalence rates of postpartum depression are higher among low-income women than among middle- or high-income women [2,3]. There is also consistent evidence that low-income women are less likely to receive mental health services in the perinatal (ie, pregnancy until child's first birthday) period than their more affluent counterparts due to a variety of factors, including stigma related to mental health service use and lack of access to community-based mental health providers [4,5]. Postpartum depression is a particularly serious problem for low-income women. It is estimated that more than 10% of infants from low-income households have a mother who has major depression and more than 50% have a mother with some depressive symptoms [6]. Postpartum depression also has negative consequences for maternal parenting practices. Compared with women not suffering from postpartum depression, depressed women tend to be less positive, less spontaneous, and less responsive with their infants [7]. Postpartum depression has been linked to developmental delays among infants of depressed mothers, including social interaction difficulties, attachment insecurity, and cognitive impairments [8,9].

Systematic reviews have highlighted an array of efficacious postpartum depression preventive interventions [10]. Among those interventions that have demonstrated efficacy, the majority use health (eg, nurses, midwives) or mental health (eg, psychologists) professionals to deliver individualized or group-based interventions [10]. One exception is the use of peers to deliver peer support via phone [11], although this study was conducted in Canada with predominately white, upper- and middle-class women. As such, there are no interventions led by nonhealth or nonmental health professionals that have demonstrated efficacy in preventing the onset of postpartum depression and reduction of depressive symptoms among low-income women.

Home visiting (HV) programs that provide services to perinatal women are one of the largest avenues through which perinatal women come to the attention of service providers, making HV a unique and viable setting for delivering mental health services. Although professional HV models exist (eg, nurse-family partnership), most HV programs in the United States use paraprofessional home visitors, who lack formal training in the helping professions [12]. Maternal depression is an enormous challenge facing HV programs, with an estimated 10 to 15% of HV clients exhibiting major depressive disorder (MDD) and another 45 to 50% exhibiting subthreshold depressive symptoms [13]. Furthermore, there is consistent evidence that low-income women exhibiting depressive symptoms—including women enrolled in HV programs—do not access mental health treatment in the community [4]. Lack of available mental health professionals (MHPs), stigma in seeking mental health services, and logistical challenges (eg, childcare, transportation) are a few of the barriers low-income women face when seeking mental health services. For those clients who do access services, most perinatal women are likely to receive pharmacological treatments [14], despite the fact that the vast majority of perinatal women prefer nonpharmacologic interventions [5]. HV programs are ideal settings for delivering mental health care to perinatal women because their mission is not stigmatizing and HV programs tend to be trusted entities in the communities they serve [13,15]. Several interventions aimed at treating postpartum depression among women in HV programs have been developed and empirically tested to show efficacy, including an in-home cognitive behavioral therapy (CBT) intervention delivered by licensed masters-level social workers [16,17], a culturally adapted version of interpersonal psychotherapy delivered by masters-level psychiatric nurses [18], and listening visits delivered by home visitors or obstetrician clinic staff focused on empathic listening, collaborative problem solving, and assessment of need for additional mental health treatment [19]. This study was born out of HV programs' need and desire for a low-cost intervention focused on the prevention of postpartum depression, given the large number of women with subthreshold symptoms at risk for developing MDD.

Prior Work

Previously, study investigators established the efficacy of a group-based intervention—Mothers and Babies (MB)—in preventing the onset of postpartum depression and reducing depressive symptoms *when led by mental health professionals* in a group setting [20-22]. On the basis of these randomized controlled trials (RCTs), MB is listed as an evidence-based practice in the Health Research and Services Administration registry and is also listed on the Substance Abuse and Mental Health Services Administration Evidence-Based Program Registry [23]. Subsequently, the principal investigator (PI) and colleagues worked closely with HV clients, staff, and other key

stakeholders to develop training and implementation protocols to facilitate implementation of the MB group model *by paraprofessional home visitors*. In particular, training protocols and instructor manuals were modified to provide greater clarity on key aspects of MB's cognitive-behavioral underpinnings. Results from a pilot study with 2 HV programs in Baltimore indicated that women receiving the MB group intervention delivered by paraprofessional home visitors showed improvements in depressive symptoms, suggesting that the MB intervention could be delivered by home visitors instead of MHPs (unpublished data [24]). This project builds on this preliminary work by evaluating the effectiveness of the MB group model when delivered by paraprofessional home visitors.

MB is a 6-session group intervention with content based on 2 key theoretical frameworks—CBT and attachment theory. MB contains 3 modules that align with key CBT elements: pleasant activities, thoughts, and social support and contact with others. Within each module, intervention recipients first are taught to connect each CBT concept with their mood, with subsequent content providing specific skills and techniques to help them cope with stress and depressive symptoms. Attachment theory is woven throughout the curriculum to help intervention participants promote connection with their infants. For example, one way attachment theory is integrated into the pleasant activities module is to highlight that parents can engage in pleasant activities with their child or children which simultaneously can improve a parent's mood and attachment with their child or children.

Study Aims

This study is a cluster-randomized controlled trial (C-RCT) in which HV clients receive either (1) MB group delivered by MHPs, (2) MB group delivered by paraprofessional home visitors, or (3) usual HV services. There are 4 specific aims for this study; the first 2 reflect our primary study aims, with the remaining 2 reflecting secondary aims:

> Aim 1 (primary aim): Evaluate efficacy of MB delivered by paraprofessional home visitors in comparison with usual care (ie, HV without MB) on patient-reported outcomes, including depressive symptoms, quality of life, parenting practices, engagement in pleasant activities, and relationship with one's partner.
>
> Aim 2 (primary aim): Assuming efficacy in #1, assess noninferiority (NI) of MB delivered by paraprofessionals versus MHPs.
>
> Aim 3 (secondary aim): Explore patient characteristics as potential covariates and effect modifiers.
>
> Aim 4 (secondary aim): Examine the feasibility and acceptability of MB delivered by paraprofessional home visitors and MHPs.

Methods

Study Design and Intervention Delivery

As noted above, this study is a C-RCT with 3 study arms: (1) MB group delivered by MHPs, (2) MB group delivered by paraprofessional home visitors, or (3) usual HV services. This study was approved by the Northwestern University's institutional review board (IRB). The MB group curriculum has 6 sessions, with each session designed to last 90 to 120 min. The curriculum consists of 3 modules that map onto key components of CBT: pleasant activities, thoughts, and contact with others. The first part of each module teaches participants to understand how a given component influences their mood. Subsequently, participants receive concrete skills related to each module. These skills provide participants with a *toolkit* of skills they can use to improve their mood. We refer to each 6-session MB group as a cohort. Each cohort meets weekly for 6 consecutive weeks at the HV program site, with occasional groups skipping a week due to inclement weather or holidays. Light refreshments are provided at each session. Transportation to the sessions and child care supports are also provided for participants, if necessary. All MB sessions are audio-recorded using a portable device for purposes of examining intervention fidelity. The study design called for random selection of 20% of these audio sessions to be assessed and coded for fidelity. The group facilitator transfers the recordings to Northwestern University's research team within 24 hours of each individual session using a secure Northwestern University box account. At the end of August 2018, 115 cohorts were completed. Implementation of all prenatal MB cohorts will be completed by October 2018.

Interventionist Training and Supervision

We have trained 105 paraprofessional (bachelor's degree or less) home visitors and supervisors from 16 program sites that are using home visitors to deliver the MB intervention. Of the 105 home visitors trained, to date, 33 have delivered the intervention. We have also trained 32 MHPs from the 16 intervention sites using MHPs to deliver MB; 21 of these MHPs have delivered the intervention. MHPs, for the purposes of this study, are masters-level professionals in the areas of child and family studies, psychology, psychiatry, social work, or a related field with a minimum of 5 years' experience working with families and young children. These MHPs live and work in the states in which they deliver the intervention, and either the participating HV programs or a state professional association (eg, The Illinois Association for Infant Mental Health) recruited them.

The study PI led MB trainings, consisting of 8 to 12 contact hours, for home visitors and MHPs. The PI conducted a total of 19 trainings in the 7 participating states. All the trainings maintained the same contact hours with trainees but were delivered in 3 formats: in-person, webinar, and telephone. HV supervisors from each of the HV programs (irrespective of study arm) also attended the training. The MB training covers the conceptual underpinnings of MB (eg, its cognitive-behavioral framework), a brief history of previous implementation of the MB program with diverse perinatal populations, instruction on the format of the MB instructor manual, and instruction on how to maximize the use of the group format when delivering MB. Training includes discussion of each MB session from start to finish. Training is interactive with opportunities for discussion and modeling communication of material by the PI. Training also involves group activities, where training attendees practice delivering curriculum material and receive extensive feedback

on strengths and areas needing improvement from the trainer and other training participants.

Home visitors and MHPs receive phone supervision from the PI the first time they deliver MB. During these supervision sessions, the PI first debriefs the completed MB session and then helps the facilitator plan for the subsequent group session. For home visitors who continue to facilitate groups, the HV program manager assumes the supervisory role—with support from the research team. Along with support from the PI during supervision, MHPs and paraprofessional home visitors can share and receive feedback via the study ListServ, which includes other HV staff, MHPs, HV supervisors, and the research team.

Recruitment and Informed Consent

Women meeting eligibility criteria for the C-RCT are approached by HV staff who explain the MB intervention and research study. Interested women complete a referral form with the HV staff and are informed that a Northwestern University research assistant (RA) will contact them with more information about the research study. HV staff send the referral forms to the Northwestern research team via email or fax. RAs share responsibility for calling referred women to explain the study in more detail and complete the informed consent process with eligible participants who indicate interest in study participation.

The Northwestern University's IRB granted a waiver of written documentation of consent, allowing Web-based informed consent via Research Electronic Data Capture (REDCap) [25] or consent via telephone for potential participants without easy access to Web-based resources. If the referred participant meets eligibility criteria and is interested in participating in the study, the RA indicates that a Web link with instruction on completing the baseline assessment via REDCap will be emailed or texted to them.

Participants are informed via informed consent and during all assessments that they may choose to not answer any question at any time for any reason and that not answering questions will not affect their relationship with their HV programs or ability to keep receiving the MB intervention (for those enrolled in the 2 intervention arms). Both the Web-based consent form and the study surveys are available in English and Spanish. Each time a study participant fills out a survey, the survey includes a prompt to the participant asking if they wish to continue participation by completing the next survey.

A waiver of parental permission was granted to waive the signature of parents of children who are participants (pregnant women ≥16 years and <18 years). This study involves minimal risk to the participants by only requiring the administration of Web-based surveys or telephone interviews to collect data. Guidance from the US Department of Health and Human Services Office of Research Protections indicates that individuals aged less than 18 years can consent to study participation without parental consent if the study procedures for which they are consenting are such that they could provide consent outside the research context.

Before beginning group facilitation, all facilitators receive a Web-based informed consent form via REDCap that they must complete before their first group session. In addition to the consent, facilitators are asked to complete a brief demographics questionnaire before facilitating groups and a survey inquiring about supervision support they receive after facilitating each cohort. All consented MHP and home visitors who facilitated an MB cohort are eligible to participate in a semistructured interview. The intervention coordinator approaches them after they have completed facilitation of their last MB cohort. Northwestern University's IRB approved all recruitment and consent procedures.

Study Participants

Our recruitment goal for the C-RCT is 933 pregnant women. The 38 HV programs participating in this project enroll clients via referrals from prenatal care clinics; Women, Infants, and Children programs; and other settings working with pregnant women. HV programs implementing MB groups will implement an average of 5 MB cohorts, over the course of the project. Women aged 16 years and older enrolled in HV programs who are 33 or more weeks' gestation and speak either English or Spanish are eligible for enrollment. Exclusion criteria have been minimized; however, women who have significant cognitive limitations will be excluded as it is not likely they will be able to fully engage in the group-based intervention activities and discussion. Women with high-risk medical and pregnancy conditions will also be excluded as this may preclude women from regularly attending intervention sessions. Women are not excluded based on race and ethnicity or based on demographic characteristics other than the ability to speak English or Spanish.

Study Sites

HV programs in Illinois, Ohio, Minnesota, Missouri, Michigan, Iowa, and West Virginia that indicated the ability to recruit approximately 40 pregnant women over a 16- to 18-month timeframe were recruited to participate in the study. All HV programs recruit women at high risk for poor pregnancy and parenting outcomes via referrals from prenatal care clinics, community outreach, and current program participation. Moreover, 45 HV programs agreed to participate in the study. We staggered the start of implementation among the programs so that only a subset of the program sites was beginning to implement at one time.

Randomization

The study employed a modified covariate-constrained randomization [26] design at the HV program level, using unequal (1:3:3; control: MHP delivery of MB: paraprofessional delivery of MB) allocation, with intention to achieve relative balance in a set of prespecified program-level potential covariates. There are 3 variables for which we chose to control imbalance at the study site level at baseline through this approach:

1. Percent non-white clients as reported by the site (treated as a continuous variable).
2. Site yearly client volume (also reported by site and treated as a continuous variable).
3. Population density of the site area (continuous variable).

The covariate-constrained method of randomization allows for efficient balance of multiple covariates at once and is

recommended over other methods (ie, simple randomization or matching) for cluster-randomized trials [26]. The general procedure involves:

1. Enumerating a large subset of possible allocation schemes.
2. Evaluating (im)balance for each variable of interest (in this case we have 3) for each possible allocation.
3. If the (im)balance is acceptable according to some prespecified criterion, then we save this scheme in a smaller subset of potential allocations for implementation.
4. Of those that meet acceptable levels of imbalance, we randomly select 1 allocation for use in this study.

We chose the *P* value corresponding to the Kruskal-Wallis test as our criterion for "balance" in step #3 above. If the *P* value for each of the 3 variables is larger than .30 for a given simulated allocation scheme, that particular allocation is deemed "acceptable." This criterion is adapted from the "Minimal Sufficient Balance" principle from Zhao et al [27] in the individual sequential randomization literature.

Randomization occurred in 3 waves for logistical purposes. The first wave included 14 sites (2 control, 6 mental health professional, 6 HV), the second included 19 sites (4 control, 7 mental health professional, 8 HV), allocation ratio was slightly off in this wave to account for dropout sites), and the third included 12 sites (1 control, 6 mental health professional, 5 HV). Thus, we randomized a total of 45 sites in 3 waves.

After randomization, 7 programs dropped out, thereby yielding a total of 38 active study sites; 6 of these sites removed themselves before implementing the intervention and 1 after beginning implementation and enrolling participants. Data collected from all study participants will be used in the analysis. Among the 38 active study sites, 16 HV programs are receiving the MB intervention delivered by MHPs, 16 are receiving MB intervention delivered by HV paraprofessionals, and 6 programs serve as control sites and are not implementing the MB intervention.

As the study aimed to assess both (1) efficacy of MB delivered by HV in comparison with control and (2) NI of MB when delivered by HV compared with MHPs, sample size considerations and allocation ratio accounted for each. We chose unequal allocation with fewer women in the control arm so that we could first assess efficacy of the HV model versus control. To show efficacy—a significant and meaningful difference between the 2 arms—sample size requirements were not as large as in the NI setting. The NI aim requires larger numbers of women in the 2 active intervention arms; thus, we chose to enroll threefold the number of women in the 2 active intervention arms to ensure maximal efficiency for NI analyses.

Data Collection Procedures and Study Assessments

The study includes 4 data collection time points—baseline, immediately post-intervention (or 8 weeks after the baseline for control participants), 12 weeks postpartum, and 24 weeks postpartum. Participants will receive US $20 remuneration after completing the baseline, 12-week, and 24-week assessments for a total of US $60. Baseline and follow-up data will be collected and managed using REDCap. Baseline data will be collected within 2 to 3 weeks of establishing client eligibility and participation agreement. Women who do not complete the Web-based baseline assessment in this timeframe will be contacted by phone by the RA to complete the assessment by phone, ensuring that baseline data are collected before the first MB group.

Table 1 describes the study's outcome indicators, measures, and data collection time points. This study's primary outcome is reduction in depressive symptoms with several secondary outcomes (eg, behavioral activation, mood regulation) that are closely linked with MB content. For our primary outcome of depressive symptoms, continuous higher scores on the Quick Inventory of Depressive Symptomatology Self-Report 16 (QIDS-SR16) [28] indicate greater depressive symptomatology. For our secondary outcome of major depressive episodes, endorsing 5 or more items on the Maternal Mood Scale and interference with current life activities indicates a possible major depressive episode. For our secondary outcomes of behavioral activation, pleasant activities, mood regulation, social support, decentering, relationships with one's partner, and subjective well-being, increased scores over time indicate improvement. For our secondary outcome of perceived stress, decreased scores over time indicate improvement. For the secondary outcome of responsive and reactive parenting, higher scores on the Parental Cognitions and Conduct toward the Infant Scale [29] subscales indicate greater self-efficacy, hostile-reactive parenting, perceived parental impact, and parental overprotection over time.

We are collecting data on MB acceptability via 3 data modalities. First, we are conducting brief semistructured interviews with 90 intervention participants—45 who received MB led by MHPs and 45 who received MB led by paraprofessional home visitors. Second, we are conducting brief semistructured interviews with all home visitors and MHPs who deliver MB. Third, all participants will complete brief paper-and-pencil checklists immediately after receiving an MB session. Group facilitators will collect these checklists. We ask each intervention participant to rate each session using 3 questions used in previous MB studies: "how much did you enjoy today's group session?", "how well did you understand what we talked about during today's group session?", and "how often do you think you will use the skills and information that you were given during today's group session?"

To assess feasibility of MB delivered by MHPs and home visitors, we are collecting data on (1) number of completed intervention sessions (dosage) and (2) fidelity of intervention implementation. Completed intervention sessions and participant attendance are documented by MHPs and home visitors delivering MB on a form created for use in this study. Fidelity of intervention implementation is being assessed by reviews of audiotaped sessions. All MB sessions will be audiotaped, and a random sample of 20% will be reviewed for protocol adherence by 2 trained coders performing independent ratings of fidelity.

Table 1. Study outcome indicators, measures, scoring, and data collection time points.

Outcome indicator	Measure	Scoring range	Scoring interpretation	Baseline	Postintervention	12 weeks postpartum	24 weeks postpartum
Primary outcome							
Depressive symptoms	Quick Inventory of Depressive Symptomatology Self-Report 16 (QIDS-SR16) [28]	0-27	Higher score: greater depressive symptomatology	✓	✓	✓	✓
Secondary outcomes							
Depressive symptoms	Edinburgh Postpartum Depression Scale [30]	0-30	>10: possible depression	✓			
Major depressive episodes	Maternal Mood Screener [31]	0-9	≥5 symptoms and interference with current life activities: possible major depressive episode	✓		✓	✓
Behavioral activation	Behavioral Activation Depression Scale [32]	0-54	Higher score: greater behavioral activation	✓		✓	✓
Pleasant activities	Pleasant Activities Schedule [33]	0-44	Higher score: greater frequency and enjoyment of activities	✓		✓	✓
Mood regulation	Negative Mood Regulation Scale [34]	30-150	Higher score: greater expectancies for negative mood regulation	✓		✓	✓
Social support	Medical Outcomes Study (MOS) Social Support Survey [35]	1-5	Higher mean score: greater perceptions of social support	✓		✓	✓
Decentering	Experiences Questionnaire [36]	11-55	Higher score: greater decentering and rumination	✓		✓	✓
Relationship with partner	Dyadic Adjustment Scale[37]	7-43	Higher score: greater relationship satisfaction	✓		✓	✓
Responsive and reactive parenting	Parental Cognitions and Conduct toward the Infant Scale [29]	0-10	Higher mean scores: greater self-efficacy, hostile-reactive parenting, perceived parental impact, parental overprotection			✓	✓
Subjective well-being	Flourishing Scale [38]	8-56	Higher score: greater psychological resources and strengths	✓		✓	✓
Perceived stress	4-item Perceived Stress Scale [39]	0-16	Higher score: greater perceived stress	✓		✓	✓

Retention Strategies

Recruitment procedures emphasize the importance of participating in all MB sessions and remaining in the study through the 24-week postpartum assessment. The research team obtains ample tracking information at baseline, which includes the participants' name, email address, home and cell phone numbers, mailing address, HV site, and secondary contacts indicated by the participant. The research team updates contact information and each participant's preferred mode of communication (eg, phone, text, Facebook) at each follow-up assessment. We allow participants without easy access to the internet and those less comfortable completing surveys electronically to complete follow-up surveys by phone. We conduct intensive follow-up with participants throughout the study via monthly communication from the RAs using the participant's preferred modes of contact. We follow all study participants through the 24-week postpartum assessment regardless of their attendance at intervention sessions or completion of previous assessments.

Data Monitoring Plan

The intervention coordinator refers any study participant who endorses thoughts of self-harm on the QIDS-SR16, Edinburgh Postnatal Depression Scale, or Maternal Mood Screener to the HV program supervisor. The supervisor uses his or her agency's protocol to make a determination of the necessary action needed to ensure the safety of the study participant. The research team

notifies the PI and research project manager immediately of any such referrals. In addition, should a participant indicate experience of severe depressive symptoms upon completion of a depression scale assessment, study staff notify the supervisor at the HV program to provide appropriate referrals for their client's mental health treatment linkage. In addition to following up with the HV supervisor, RAs also follow-up with study participants to ensure they are not in immediate danger of harming themselves and provide a list of resources to the participant. The statistical team, in collaboration with the rest of the study team, developed a series of data status and quality reports via an automated task, which study staff review multiple times per week. They include participant status, missing survey and overall data, mood assessment summaries, and intervention adherence reports.

Statistical Analysis

Data Management

Study data are collected and managed using REDCap, a secure Web-based application designed to support data capture for research studies, hosted and supported by Northwestern University's Clinical and Translational Science Institute. Web-based survey data completed by participants are directly linked to the REDCap project. Data are periodically exported to an SAS database that is only accessible to study personnel on a password-protected shared project drive. The research study coordinator, the biostatistician, and the statistical analyst conduct periodic audits of the data to ensure accuracy over the course of the project.

All data records are identified using an identification number only and do not contain other personally identifying information. All forms containing personal identifying information, including a master list linking names with identification numbers, consent forms, and receipts for subject remuneration payments, are maintained in a file cabinet that is locked at all times and on a password-protected computer, with access only by the study team. Identifying information (eg, personal and

contact information) is kept separate from the other data. All subject information collected is kept in secure, password-protected files on Northwestern University's servers with access restricted to authorized personnel only. Audio-recordings of MB group sessions will be stored as password-protected electronic files on a secure computer. Once the study is completed, including data coding and qualitative analysis, all audio-recordings will be erased. We will inform participants that coded data will be deidentified.

Outcomes

Primary outcome of interest for Aims #1 to #3 will be the QIDS-SR16 score as determined by participant self-report at 24 weeks postpartum. We will control for baseline QIDS-SR16 score and treat this measure as a continuous variable. It ranges from 0 to 27 points, where higher scores signify increased depressive symptoms. QIDS-SR16 translates into depressive categories such that a score of less than 5 points indicates no depression, a score ranging from 6 to 10 indicates mild depression, 11 to 15 signifies moderate depression, 16 to 20 indicates severe depression, and anything above 20 would be labeled as very severe [28]. As a result, we deem a 5-unit change or difference in score to be meaningful (as a jump in 5 points would result in an increase in depression severity tier for any individual patient). Secondary outcomes will address key components of the MB intervention. They include incidence of major clinical depression, behavioral activation, engagement in pleasant activities, mood regulation, social support, decentering, perceived stress, responsive parenting, relationship with partner, and subjective well-being.

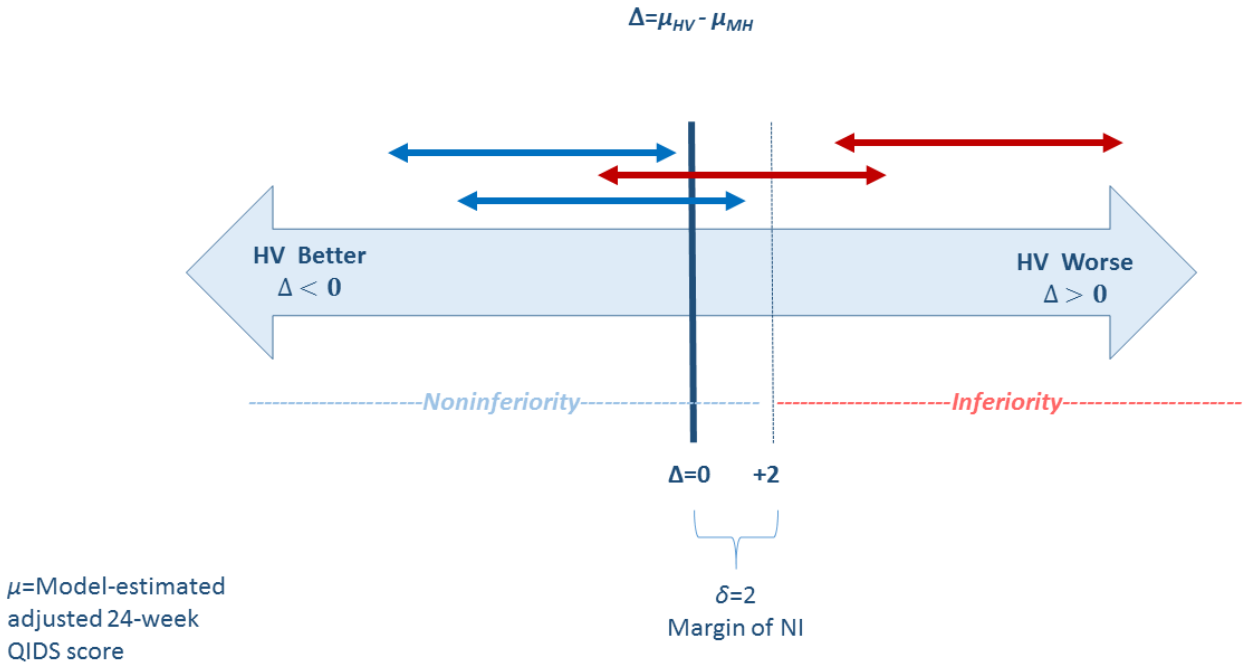
Statistical Methods

Descriptive statistics will summarize baseline characteristics (both site-level and participant-level) overall and by arm. As appropriate, mean (SD) (or median [inner quartile range] will be used in cases of skewed or nonnormal empirical distributions) and frequency (proportions) will summarize continuous and categorical data, respectively. Analyses will employ normal theory methodology as appropriate, and in cases of violations of assumptions, transformations and nonparametric analyses may be utilized. We used SAS version 9.4 (SAS Institute Inc.; Cary, NC; 2012) [40] to perform randomization, and we plan to use both SAS (version 9.4) and R (version 3.4.1 or higher) [41] for final analyses and reporting. We used the Power **a**nd Sample Size (PASS) Software (NCSS, LLC; Kaysville, Utah; 2011)[42] for all power and sample size calculations.

Analyses will proceed at the participant level. Primary analyses for QIDS-SR16 score at 24 weeks postpartum will involve a linear mixed model for continuous outcome with independent variables of baseline QIDS-SR16, study arm (3-level factor), and site-level baseline covariates used in randomization algorithm. We plan to account for clustering effects via inclusion of a random site effect, which will allow for distinction of between- and within-site variance. Intracluster correlation coefficients (ICCs) will be estimated via variance components estimates. Intervention effect will first be evaluated via the adjusted Wald type III test for significant study arm effect at the 5% level of significance. If arm is significant at the 5% level, analyses evaluating the superiority (Aim #1) of HV-led intervention versus control will proceed with Tukey correction for multiple pairwise hypothesis tests. Assuming the Tukey-adjusted *P* value for this comparison falls below the 5% level of significance in favor of the HV-led arm, we will further assess the NI (Aim #2) via pairwise comparison (using Tukey correction) of adjusted 24-month QIDS-SR16 in home visitor–led versus MHP-led arms. Figure 1 depicts the margin and zone of NI for this comparison.

The double-sided arrows represent 95% CI for the model-estimated adjusted mean 24-week difference in QIDS-SR16 score between arms. Note that higher score signifies more depressive symptoms; thus, if the estimated difference (HV minus MHP score) is larger than zero, the HV arm has on average worse depressive symptoms. As the prespecified margin of NI is 2 units on the QIDS-SR16 scale, we will claim NI if the upper limit of the adjusted 95% CI for the paraprofessional home visitor–led arm minus the MHP-led arm comparison remains below 2. The red arrows indicate scenarios in which we cannot claim NI, and the blue arrows indicate scenarios in which the criterion for NI is met.

Figure 1. Margin of noninferiority (NI). HV: home visiting; QIDS: Quick Inventory of Depressive Symptomatology.



Using the same analytic approach, we will add covariate-by-arm interaction terms in the aforementioned model to explore whether effectiveness of intervention varies by patient characteristics (Aim #3). The covariates to be explored include race and ethnicity, first-time mother, and geographic type of HV program (urban, suburban, or rural). These analyses are more exploratory in nature, and thus power and sample size considerations do not focus on interaction effects. As a result, we anticipate evaluating interaction effects at the 10% level of significance without adjustment for multiple hypothesis tests. Qualitative data analysis methods will evaluate feasibility and acceptability of MB in each setting (Aim #4), and the details of these analyses will be specified elsewhere.

Additional analyses surrounding Aims #1 to #3 will employ longitudinal methods, utilizing all study data at all time points (ie, inclusion of a fixed study time point effect). Secondary outcomes will all be analyzed in this fashion with the exception being binary response variables (eg, depression onset). In these cases, models will involve appropriate link and distributional assumptions (logit and binomial, respectively). For the participants receiving active intervention (either paraprofessional home visitor–led or MHP-led MB), we will examine a "dose" variable in relation to outcomes. This dose variable will be defined as the number of sessions (of 6 possible) attended for an individual participant.

We plan to conduct analyses on the modified intent-to-treat dataset whereby all participants randomized with data at the 24-week postpartum time point will be analyzed according to the arm to which they were allocated. We will further perform a sensitivity analysis on the "as treated" dataset. Those in either active intervention arm will be considered "treated" if they attend at least 4 of the 6 sessions required for the MB course.

Power and sample size considerations allowed for some missing data and, as specified in our approved research plan, we have allowed for entire clusters to drop out of each arm; however, in the event of large amounts of missing data (ie, more than 15%), we will explore multiple imputation analyses. We will examine rates of missing data for all variables and determine whether the rates vary by participant characteristics, HV program location, or intervention arm. These summarizations will inform potential biases resulting from missing data. The mixed effects models planned for analyses are generally robust for unbalanced data across study time points. If multiple imputation methods are merited, we will impute at least five datasets to generate an estimated average intervention effect. These analyses will again serve as sensitivity analyses to the previously outlined analyses.

Power and Sample Size Considerations

As in any C-RCT, power and sample size considerations depend heavily on ICC estimates. In general, it is recommended that these calculations account for anticipated ICC, as failure to do so in the design phase leads to an increase in type II error (ie, result in underpowered studies) [43,44]. Without previous knowledge of ICC(s) in this population with respect to our primary outcome, we explored a range of ICCs (0.001 to 0.05). Power calculations assume a SD in primary outcome of approximately 6 points (on the QIDS-SR16), with a meaningful difference corresponding to 5 points on average across arms.

Table 2. Required sample size for 90% power in noninferiority aim.

ICC[a]	Sites, n		Study participants per site for analyses, n	Study participants recruited per site (allowing for 15% attrition), n
	HV[b]	MHP[c]		
.001	16	16	17	20
.01	16	16	20	23
.02	16	16	25	29
.03	16	16	33	39
.04	16	16	49	58
.05	16	16	97	114
.001	15	15	19	22
.01	15	15	22	26
.02	15	15	28	33
.03	15	15	38	45
.04	15	15	62	73
.05	15	15	168	198

[a]ICC: intracluster correlation coefficient.

[b]HV: home visiting.

[c]MHP: mental health professional.

Thus, for the superiority aim, we calculated power based on the average ability to detect at least a 5-point mean difference between control sites and paraprofessional home visitor–led sites. Power calculations assumed a 5%/3=1.7% level of significance to account for 3 pairwise comparisons. This is an approach that we deem conservative as it mirrors the Bonferroni correction for multiple hypothesis tests.

We have 38 active sites: 6 controls, 16 paraprofessional home visitor–led sites, and 16 MHP-led sites. We plan to recruit an average of 27 participants per site, allowing for up to 15% attrition (ie, 23 participants on average for analyses). These assumptions allow for more than 95% power to detect a mean difference of 5 points in QIDS-SR16 across arms for an ICC of 0.01. Even if 1 of the 6 sites drops out, and if ICC is as large as 0.05 (which we deem unlikely), we still anticipate over 85% power for analyses addressing the efficacy aim (Aim #1).

Power for the NI aim will require ability to detect a smaller (margin of NI of 2 points) mean difference across arms. We anticipate over 90% power to detect a margin of NI of 2 points on the QIDS-SR16 scale if we assume an ICC of 0.01 and 16 sites in each of the intervention arms with 23 participants for analyses, on average, per site. This allows for up to 15% attrition overall. We anticipate some sites to be over or underperforming, and thus, unequal representation per site is inevitable. Our hope is that the precautions taken with respect to the randomization algorithm that attempts to control imbalance in yearly volume and population density will offset biases created by over/underrepresentation for participants at specific sites. Although we do not anticipate ICC to be larger than 0.01 [43], we present the required sample size per site in Table 2 to ensure 90% power under the same assumptions for all scenarios explored. We also present sample size requirements in the event that one of the active sites drops out in each of the intervention arms (ie, 15 sites per arm). Notice that if ICC is larger than 0.02 (which we are not anticipating, although it remains possible), our projected sample size does not allow for 90% power in this case. As these assumptions are all rather conservative, we argue adequate power for detection of both superiority and NI. Power calculations for assessment of heterogeneity of intervention effects depending on participant characteristics (Aim #3) require even more assumptions for which we have little information. Thus, we do not necessarily anticipate power to detect specific effects within subgroups or power to detect interaction effects, but we plan to use the analyses outlined here to explore these effects.

Results

This study is in progress. Recruitment for this C-RCT commenced in January 2017, and we anticipate enrollment will continue through September 2018. Through the end of August 2018, we have enrolled 838 women into the study. We have completed qualitative interviews with 5 home visitors and 6 MHPs who have delivered MB cohorts and who will not be facilitating future cohorts, and 55 participants who have received the intervention.

Discussion

Comparison With Prior Work and Future Possibilities

This study integrates a low-cost intervention into HV programs, some of which are being infused with new federal funding through the Affordable Care Act. These HV programs serve large numbers of perinatal women at risk for major depression who are often overlooked by the existing mental health services. Should we find that women receiving MB from paraprofessional home visitors exhibit (1) better mental health outcomes than women receiving usual care and (2) similar improvements to women receiving MB from MHPs, there is considerable

potential to expand this intervention to HV programs across the country. This is feasible as home visitors are already employed at the setting in which the intervention occurs, thus minimizing the need to procure additional, potentially costly, resources. No previous studies have demonstrated efficacy in preventing the onset of postpartum depression among low-income women using interventions led by nonhealth professionals or non-MHPs. As such, this study will also advance the field of postpartum depression prevention.

This study also allows for the delivery of mental health services outside the public mental health system. The difficulties of paying for prevention and early intervention are well documented, as most health plans require a diagnostic code for billing and do not reimburse for prevention of mental illness including depression. The novel integration of a depression prevention intervention into HV programs provides a potential avenue for delivering depression prevention to women at increased risk for developing major depression in the postpartum period.

Study Limitations

The study has some limitations that need to be recognized. We are collaborating with HV programs in 7 states in the Midwest. As these sites only represent a subset of HV programs across the country, study results may not be generalizable to all HV programs nationwide. Moreover, HV programs in this study primarily used the Healthy Families America or Parents as Teachers model, thereby potentially limiting generalizability to HV programs using other HV models. Our study is also limited in its ability to examine mediating effects on our primary outcome of depressive symptoms. Although this study represents one of the largest studies to date to examine the effects of a postpartum depression preventive intervention, we did not power the study to formally test for the mediating role of our secondary outcomes—for example, behavioral activation, social support—on depressive symptoms. As with any study, the sample size considerations were based on multiple assumptions (eg, ICC, SD), and if these assumptions are incorrect, the required sample size may be over or underestimated. Finally, multiple sites dropped out as previously indicated; however, we accounted for this potential dropout (both at the site and participant level) in our sample size considerations.

Conclusions

Despite these limitations, we feel that this study is likely to increase patient engagement in HV programs. As such, study participants will not only see improvements in their own mental health, but are likely to experience greater benefit from the services and supports provided by HV programs aimed at improving positive parenting behaviors, increasing linkages with prenatal and postpartum care, and increasing the use of child preventive health care services (eg, timely well-child visits). Thus, we believe that this study has important implications for improving maternal and child health in multiple domains during the perinatal period.

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Authors' Contributions

JKJ is the research project manager on the randomized controlled trial (RCT) and was a major contributor in writing the manuscript. JDC is the biostatistician for the RCT and was a major contributor in writing the manuscript. ADi is the research coordinator on the RCT and was a major contributor in writing the manuscript. MS is the implementation coordinator on the RCT and was a contributor in writing the manuscript. ADe is the research assistant on the RCT and was a contributor in writing the manuscript. JSM is the research assistant on the RCT and was a contributor in writing the manuscript. SDT is the principal investigator for the RCT and was a major contributor in writing the manuscript.

Conflicts of Interest

None declared.

Multimedia Appendix 1

Peer-review report.

[PDF File (Adobe PDF File), 72KB - resprot_v7i11e11624_app1.pdf]

References

1. Gaynes BN, Gavin N, Meltzer-Brody S, Lohr KN, Swinson T, Gartlehner G, et al. Perinatal depression: prevalence, screening accuracy, and screening outcomes. Evid Rep Technol Assess (Summ) 2005 Feb(119):1-8. [Medline: 15760246]

2. O'hara MW, Swain AM. Rates and risk of postpartum depression—a meta-analysis. Int Rev Psychiatry 2009 Jul 11;8(1):37-54. [doi: 10.3109/09540269609037816]
3. Rich-Edwards JW, Kleinman K, Abrams A, Harlow BL, McLaughlin TJ, Joffe H, et al. Sociodemographic predictors of antenatal and postpartum depressive symptoms among women in a medical group practice. J Epidemiol Community Health 2006 Mar;60(3):221-227 [FREE Full text] [doi: 10.1136/jech.2005.039370] [Medline: 16476752]
4. Abrams LS, Dornig K, Curran L. Barriers to service use for postpartum depression symptoms among low-income ethnic minority mothers in the United States. Qual Health Res 2009 Apr;19(4):535-551. [doi: 10.1177/1049732309332794] [Medline: 19299758]
5. Leis JA, Mendelson T, Perry DF, Tandon SD. Perceptions of mental health services among low-income, perinatal African-American women. Womens Health Issues 2011;21(4):314-319. [doi: 10.1016/j.whi.2011.03.005] [Medline: 21712144]
6. Vericker T, Macomber J, Golden O. The Urban Institute. Infants of depressed mothers living in poverty: opportunities to identify and serve URL: https://www.urban.org/sites/default/files/publication/29086/412199-Infants-of-Depressed-Mothers-Living-in-Poverty-Opportunities-to-Identify-and-Serve.PDF [WebCite Cache ID 7122GEJDm]
7. van Doesum KT, Hosman CM, Riksen-Walraven JM, Hoefnagels C. Correlates of depressed mothers' sensitivity toward their infants: the role of maternal, child, and contextual characteristics. J Am Acad Child Adolesc Psychiatry 2007 Jun;46(6):747-756. [doi: 10.1097/CHI.0b013e318040b272] [Medline: 17513987]
8. Grace SL, Evindar A, Stewart DE. The effect of postpartum depression on child cognitive development and behavior: a review and critical analysis of the literature. Arch Womens Ment Health 2003 Nov;6(4):263-274. [doi: 10.1007/s00737-003-0024-6] [Medline: 14628179]
9. Sohr-Preston SL, Scaramella LV. Implications of timing of maternal depressive symptoms for early cognitive and language development. Clin Child Fam Psychol Rev 2006 Mar;9(1):65-83. [doi: 10.1007/s10567-006-0004-2] [Medline: 16817009]
10. Dennis C, Dowswell T. Psychosocial and psychological interventions for preventing postpartum depression. Cochrane Database Syst Rev 2013 Feb 28(2):CD001134. [doi: 10.1002/14651858.CD001134.pub3] [Medline: 23450532]
11. Dennis CL, Hodnett E, Kenton L, Weston J, Zupancic J, Stewart DE, et al. Effect of peer support on prevention of postnatal depression among high risk women: multisite randomised controlled trial. BMJ 2009;338:a3064 [FREE Full text] [Medline: 19147637]
12. Olds DL, Robinson J, O'Brien R, Luckey DW, Pettitt LM, Henderson CR, et al. Home visiting by paraprofessionals and by nurses: a randomized, controlled trial. Pediatrics 2002 Sep;110(3):486-496. [Medline: 12205249]
13. Ammerman RT, Putnam FW, Bosse NR, Teeters AR, Van Ginkel JB. Maternal depression in home visitation: a systematic review. Aggress Violent Behav 2010 May;15(3):191-200 [FREE Full text] [doi: 10.1016/j.avb.2009.12.002] [Medline: 20401324]
14. Huybrechts KF, Palmsten K, Mogun H, Kowal M, Avorn J, Setoguchi-Iwata S, et al. National trends in antidepressant medication treatment among publicly insured pregnant women. Gen Hosp Psychiatry 2013;35(3):265-271 [FREE Full text] [doi: 10.1016/j.genhosppsych.2012.12.010] [Medline: 23374897]
15. Paris R, Dubus N. Staying connected while nurturing an infant: a challenge of new motherhood. Fam Relat 2005 Jan 19;54(1):72-83 [FREE Full text] [doi: 10.1111/j.0197-6664.2005.00007.x]
16. Ammerman RT, Putnam FW, Stevens J, Bosse NR, Short JA, Bodley AL, et al. An open trial of in-home CBT for depressed mothers in home visitation. Matern Child Health J 2011 Nov;15(8):1333-1341 [FREE Full text] [doi: 10.1007/s10995-010-0691-7] [Medline: 20936338]
17. Ammerman RT, Putnam FW, Altaye M, Stevens J, Teeters AR, Van Ginkel JB. A clinical trial of in-home CBT for depressed mothers in home visitation. Behav Ther 2013 Sep;44(3):359-372 [FREE Full text] [doi: 10.1016/j.beth.2013.01.002] [Medline: 23768664]
18. Beeber LS, Holditch-Davis D, Perreira K, Schwartz TA, Lewis V, Blanchard H, et al. Short-term in-home intervention reduces depressive symptoms in early head start Latina mothers of infants and toddlers. Res Nurs Health 2010 Feb;33(1):60-76 [FREE Full text] [doi: 10.1002/nur.20363] [Medline: 20043296]
19. Segre LS, Brock RL, O'Hara MW. Depression treatment for impoverished mothers by point-of-care providers: a randomized controlled trial. J Consult Clin Psychol 2015 Apr;83(2):314-324 [FREE Full text] [doi: 10.1037/a0038495] [Medline: 25486371]
20. Tandon SD, Leis JA, Mendelson T, Perry DF, Kemp K. Six-month outcomes from a randomized controlled trial to prevent perinatal depression in low-income home visiting clients. Matern Child Health J 2014 May;18(4):873-881 [FREE Full text] [doi: 10.1007/s10995-013-1313-y] [Medline: 23793487]
21. Tandon SD, Perry DF, Mendelson T, Kemp K, Leis JA. Preventing perinatal depression in low-income home visiting clients: a randomized controlled trial. J Consult Clin Psychol 2011 Oct;79(5):707-712. [doi: 10.1037/a0024895] [Medline: 21806298]
22. McFarlane E, Burrell L, Duggan A, Tandon D. Outcomes of a randomized trial of a cognitive behavioral enhancement to address maternal distress in home visited mothers. Matern Child Health J 2017 Mar;21(3):475-484 [FREE Full text] [doi: 10.1007/s10995-016-2125-7] [Medline: 27535131]

23. Substance Abuse and Mental Health Services Administration (SAMHSA). National registry of evidence-based programs and practices. 2018. URL: https://www.samhsa.gov/nrepp [WebCite Cache ID 712Df8oZ3]
24. Tandon S, Perry D, Mendelson T, Kemp K. Results from a pilot study using paraprofessional home visitors to deliver a postpartum depression preventive intervention. Unpublished data 2018.
25. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)--a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform 2009 Apr;42(2):377-381 [FREE Full text] [doi: 10.1016/j.jbi.2008.08.010] [Medline: 18929686]
26. Ivers NM, Halperin IJ, Barnsley J, Grimshaw JM, Shah BR, Tu K, et al. Allocation techniques for balance at baseline in cluster randomized trials: a methodological review. Trials 2012 Aug 01;13:120 [FREE Full text] [doi: 10.1186/1745-6215-13-120] [Medline: 22853820]
27. Zhao W, Hill MD, Palesch Y. Minimal sufficient balance-a new strategy to balance baseline covariates and preserve randomness of treatment allocation. Stat Methods Med Res 2015 Dec;24(6):989-1002 [FREE Full text] [doi: 10.1177/0962280212436447] [Medline: 22287602]
28. Rush AJ, Trivedi MH, Ibrahim HM, Carmody TJ, Arnow B, Klein DN, et al. The 16-Item Quick Inventory of Depressive Symptomatology (QIDS), clinician rating (QIDS-C), and self-report (QIDS-SR): a psychometric evaluation in patients with chronic major depression. Biol Psychiatry 2003 Sep 01;54(5):573-583. [Medline: 12946886]
29. Boivin M, Pérusse D, Dionne G, Saysset V, Zoccolillo M, Tarabulsy GM, et al. The genetic-environmental etiology of parents' perceptions and self-assessed behaviours toward their 5-month-old infants in a large twin and singleton sample. J Child Psychol Psychiatry 2005 Jun;46(6):612-630. [doi: 10.1111/j.1469-7610.2004.00375.x] [Medline: 15877767]
30. Cox JL, Holden JM, Sagovsky R. Detection of postnatal depression. Development of the 10-item Edinburgh Postnatal Depression Scale. Br J Psychiatry 1987 Jun;150:782-786. [Medline: 3651732]
31. Vázquez FL, Muñoz RF, Blanco V, López M. Validation of Muñoz's Mood Screener in a nonclinical Spanish population. Eur J Psychol Assess 2008 Jan;24(1):57-64. [doi: 10.1027/1015-5759.24.1.57]
32. Kanter JW, Mulick PS, Busch AM, Berlin KS, Martell CR. The Behavioral Activation for Depression Scale (BADS): psychometric properties and factor structure. J Psychopathol Behav Assess 2006 Oct 25;29(3):191-202. [doi: 10.1007/s10862-006-9038-5]
33. MacPhillamy DJ, Lewinsohn PM. The pleasant events schedule: studies on reliability, validity, and scale intercorrelation. J Consult Clin Psychol 1982;50(3):363-380. [doi: 10.1037/0022-006X.50.3.363]
34. Catanzaro SJ, Mearns J. Measuring generalized expectancies for negative mood regulation: initial scale development and implications. J Pers Assess 1990;54(3-4):546-563. [doi: 10.1080/00223891.1990.9674019] [Medline: 2348341]
35. Sherbourne CD, Stewart AL. The MOS social support survey. Soc Sci Med 1991;32(6):705-714. [Medline: 2035047]
36. Teasdale JD, Moore RG, Hayhurst H, Pope M, Williams S, Segal ZV. Metacognitive awareness and prevention of relapse in depression: empirical evidence. J Consult Clin Psychol 2002 Apr;70(2):275-287. [Medline: 11952186]
37. Crane DR, Middleton KC, Bean RA. Establishing criterion scores for the Kansas Marital Satisfaction Scale and the Revised Dyadic Adjustment Scale. Am J Fam Ther 2000 Jan;28(1):53-60. [doi: 10.1080/019261800261815]
38. Diener E, Wirtz D, Tov W, Kim-Prieto C, Choi D, Oishi S, et al. New well-being measures: short scales to assess flourishing and positive and negative feelings. Soc Indic Res 2009 May 28;97(2):143-156. [doi: 10.1007/s11205-009-9493-y]
39. Cohen S, Hoberman HM. Positive events and social supports as buffers of life change stress. J Appl Social Pyschol 1983 Apr;13(2):99-125. [doi: 10.1111/j.1559-1816.1983.tb02325.x]
40. SAS Institute Inc. 2012. SAS 9.4 URL: https://support.sas.com/documentation/94/ [accessed 2018-10-30] [WebCite Cache ID 73ZJU8J4x]
41. R Core Team. 2011. R: A language and environment for statistical computing URL: http://www.r-project.org/ [accessed 2018-10-30] [WebCite Cache ID 73ZJXR1LH]
42. Hintze J. NCSS, LLC. 2011. PASS 11 URL: https://www.ncss.com/software/pass/ [accessed 2018-10-30] [WebCite Cache ID 73ZJYiG6V]
43. Raab GM, Butcher I. Balance in cluster randomized trials. Stat Med 2001 Feb 15;20(3):351-365. [Medline: 11180306]
44. Turner EL, Li F, Gallis JA, Prague M, Murray DM. Review of recent methodological developments in group-randomized trials: part 1-design. Am J Public Health 2017 Dec;107(6):907-915. [doi: 10.2105/AJPH.2017.303706] [Medline: 28426295]

Abbreviations

CBT: cognitive behavioral therapy
C-RCT: cluster-randomized controlled trial
HV: home visiting
ICC: intracluster correlation coefficient
IRB: institutional review board
MB: Mothers and Babies
MDD: major depressive disorder
MHP: mental health professional

NI: noninferiority
PI: principal investigator
QIDS-SR16: Quick Inventory of Depressive Symptomatology Self-Report 16
RA: research assistant
RCT: randomized controlled trial
REDCap: Research Electronic Data Capture

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Protocol

Effect of Increasing Levels of Web-Based Behavioral Support on Changes in Physical Activity, Diet, and Symptoms in Men With Prostate Cancer: Protocol for a Randomized Controlled Trial

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Abstract

Background: More than 3.1 million men in the United States are prostate cancer survivors. These men may improve their physical function, quality of life, and potentially their prognosis by adopting healthier lifestyle habits. The internet provides a scalable mechanism to deliver advice and support about improving physical activity and dietary habits, but the feasibility and acceptability of a Web-based lifestyle intervention and the dose of support necessary to improve health behaviors are not yet known.

Objectives: The Community of Wellness is a Web-based intervention focused on supporting exercise and healthy dietary practices for men with prostate cancer. The objectives of this study were to determine the feasibility, acceptability, and preliminary efficacy of the Community of Wellness Web portal among prostate cancer survivors by conducting a randomized controlled trial (RCT) comparing 4 levels of additive Web-based content and interaction with participants: Level 1 (Teaching; Control), Level 2 (Teaching + Tailoring), Level 3 (Teaching + Tailoring + Technology), and Level 4 (Teaching + Tailoring + Technology + Touch).

Methods: This is a single-blinded RCT comparing 3 levels of behavioral support within the Community of Wellness Web portal intervention (Levels 2 to 4) with each other and with the control condition (Level 1). The control condition receives general static Web-based educational information only on physical activity and dietary habits, self-efficacy for behavior change, motivation for physical activity, and changes in anxiety and treatment-related side effects. We will enroll and randomize 200 men with prostate cancer equally to 4 levels of the Community of Wellness Web-based intervention for 3 months (50 men per level).

Surveys will be completed by self-report at baseline, 3 months (immediately postintervention), and 6 months (3 months postintervention). Feasibility and acceptability will be assessed by enrollment statistics, Web-based usage metrics, and surveys at the 3-month time point. We will also conduct focus groups after the postintervention follow-up assessment in a sample of enrolled participants to evaluate elements of usability and acceptability that cannot be obtained via surveys.

Results: Enrollment is ongoing, with 124 enrolled. Study completion (6-month follow-up) is expected by July 2019.

Conclusions: The goal of the study is to identify the level of support that is feasible, acceptable, promotes behavior change, and improves health in men with prostate cancer to inform future efforts to scale the program for broader reach.

Trial Registration: ClinicalTrials.gov NCT03406013; https://clinicaltrials.gov/ct2/show/NCT03406013 (Archived by WebCite at http://www.webcitation.org/73YpDIoTX).

International Registered Report Identifier (IRRID): PRR1-10.2196/11257

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KEYWORDS

prostatic neoplasm; survivorship; diet; exercise; internet; behavior; text messaging; accelerometry

Introduction

Nearly 3 million men in the United States are living with prostate cancer [1], and median survival time following diagnosis for these older men is 16 years [1-3]. During this time, men with prostate cancer might experience adverse effects of aging and persistent side effects of cancer treatment that reduce their physical function, quality of life (QoL), and potentially their prognosis [4-8]. A cancer diagnosis is a *teachable moment* when individuals are often motivated to change behavior to reduce risk of adverse health outcomes and optimize QoL [9-16]. However, advice provided is often inconsistent, and the current standard of care does not support resources for lifestyle behavior change for men with prostate cancer in the United States [17].

For men with prostate cancer, regular physical activity is an excellent strategy to offset age- and treatment-related declines in physical functioning, mental health, and QoL [18]. We and others have shown that when prescribed appropriate physical activity in the form of either aerobic and/or resistance exercise training, it might manage acute and chronic treatment-related symptoms and side effects [10,19-22]. Furthermore, recent observational evidence from our team and others suggests that engaging in sufficient amounts of aerobic activities may reduce prostate cancer progression [11] and prostate cancer–specific death [23-27]. Despite the evidence for physical activity benefits in men with prostate cancer, more than 75% of prostate cancer survivors fail to achieve recommended amounts of aerobic exercise and only 4% engage in any resistance exercise [28]. Prostate cancer survivors may fail to meet the physical activity recommendations because they are not receiving information about the effects of specific types of exercise on the health outcomes that are most important for them. A recent study reported that prostate cancer survivors on androgen deprivation therapy regard a physician's general recommendation to be physically active as important; however, they are frustrated when providers lack specific knowledge about the type of exercise they should do and lack knowledge on how exercise specifically affects their cancer and related health issues [29-33].

In addition, accumulating evidence from our team suggests that several dietary factors may reduce the risk of prostate cancer progression and death, including greater intakes of cruciferous vegetables, vegetable fat, fish, and cooked tomatoes and lower intake of whole milk and poultry with skin [11,34-43]. Many of these dietary factors (eg, cruciferous vegetables, cooked tomatoes, and whole milk) appear to have specific associations with prostate cancer progression and are not included in general nutrition guidelines for cancer survivors [10]. Furthermore, excess supplementation of vitamins or minerals may increase risk of prostate cancer progression, yet cancer survivors, including men with prostate cancer, report high use of dietary supplements [44,45].

Successful interventions that promote healthy lifestyles can be challenging to scale to the broader population and may not readily reach those persons who are most in need [46]. Center-based lifestyle programs specific to cancer survivors are rare and, if available, tend to be offered only in major academic medical centers in urban areas, whereas home-based interventions have been tested in other cancers [47] including prostate cancer [48]. They are rarely comprehensive enough to address both physical activity and dietary change and raise challenges for tailoring programs to individual needs, maintaining safety and efficacy, and sustaining motivation, especially when counseling is an integral part and would be difficult to maintain indefinitely [49,50]. For optimal engagement, there is a need to provide appropriate content, accommodations, and reinforcement in a way that can successfully promote behavior change [51]. The internet provides a potentially scalable and economical way of delivering lifestyle interventions to cancer survivors [52]. There is 1 Web-based trial (Prostate 8) focused on diet, exercise, and not smoking that has been fully enrolled and will be published soon (NCT02470936). No studies published to date are specific to men with prostate cancer and none simultaneously address physical activity and dietary change while elucidating the types and levels of behavioral support that are effective [53]. For example, men with prostate cancer cite lack of specific guidance for exercise and lack of motivation as barriers to physical activity [33]; thus, interventions that attempt to systematically remove these barriers might be particularly effective but have not yet been evaluated. Another important consideration for future implementation and scalability is identifying the level of *intensity* of an intervention that produces a meaningful benefit. In their translational model of survivorship care, for example,

Alfano et al call for trials that evaluate whether or not developing and delivering a survivorship care plan alone for survivors is enough to improve their outcomes or if a more interactive process is necessary [54].

On the basis of the evidence indicating that diet and physical activity habits might offer benefits for men living with prostate cancer, we developed a multisite, national, pilot feasibility study to build and test a Web-based interactive lifestyle management program, the "Community of Wellness," to provide tools and support for men with prostate cancer to optimize their health through physical activity and diet. It is unclear what types and how much support men may need to make meaningful changes using a Web-based tool; therefore, the objective of this project is to identify optimal combinations of different types and levels of support for diet and physical activity behavior change. To address this objective, we will conduct a randomized controlled trial (RCT) to establish the feasibility and acceptability of the Web-based intervention and explore the preliminary efficacy of levels of support to improve diet and physical activity behaviors, motivational behaviors, and symptoms and side effects associated with prostate cancer and its treatment.

Methods

Study Design and Setting

The "Community of Wellness" study is supported by the Movember Foundation and is part of their broader initiative—*TrueNTH USA*. The study is a single blinded, parallel 4-arm RCT comparing 3 levels of increasing behavioral support with a usual care group that receives Web-based general educational information only. Although participants will know which study arm they are randomized to, outcomes are based on self-reported surveys completed by men online; thus, analysts can remain blinded to group assignment. We aim to enroll and randomize 200 men with prostate cancer equally to 1 of the 4 study arms for 3 months. Men complete surveys online at baseline, 3 months (postintervention), and 6 months (3 months postintervention). We will also conduct focus groups after the postintervention follow-up assessment in a subsample of enrolled participants to evaluate elements of usability and acceptability that cannot be obtained via standardized surveys.

Study Population

The study population is men with a history of prostate cancer. Men are eligible to participate if they self-report receiving a prostate cancer diagnosis, are aged 18 years or older, able to read English on a computer screen, and have a personal device that has internet access and text messaging and a personal email address. Men are not eligible to participate if they report any contraindications to exercise based on the American College of Sports Medicine exercise preparticipation screening criteria [47] and do not receive a physician clearance to participate in moderate intensity physical activity. In addition, men who are currently receiving chemotherapy or radiation therapy will be required to receive a physician clearance before enrollment. Eligibility is assessed via phone screening, and eligible men provide consent online.

Consented participants are randomly assigned to 1 of the 4 Levels of intervention (n=50 per group). Recruitment is based out of 4 academic medical centers (Oregon Health & Science University [OHSU, primary study coordinating center], University of California San Francisco [UCSF], University of Colorado Denver [UC Denver], and Emory University). The primary recruitment approach will use patient databases to identify potential participants who will be mailed a letter and study brochure that directs them to contact research staff at the coordinating center to learn more about the study. In addition to this approach, clinics will have study brochures in waiting and exam rooms. Once deemed eligible, men are emailed a link to provide consent and complete surveys online, and once these are completed, they receive a separate link to access the Web portal where they will access their randomized level of the intervention. The study is approved by 3 institutional review boards at OHSU, UCSF, and UC Denver and is under review at Emory University.

Study Arms

Our overarching goal is to support healthy diet and physical activity among men with prostate cancer; thus, we aim for a program that has strong acceptability and feasibility and which is also effective and can be broadly disseminated. The intervention was informed by the social cognitive theory that focuses on individual behavior change by including intervention components that addressed key constructs of self-control, expectations, and behavioral capability by including information about exercise for cancer survivors and tailored recommendations for diet and exercise, observational learning by including exercise videos and diet recipes, reinforcement by including technological components that provided feedback on goals, and promotion of self-efficacy through the use of health coaches [55]. We also incorporated techniques to promote user engagement with digital interventions by including credible information that was tailored to address the health needs of prostate cancer survivors and their desire to have information about health behaviors that are specific to their disease [33] as well as the use of prompts to facilitate motivation [56]. The intervention is structured around supporting 3 specific physical activity recommendations (aerobic, strength, and flexibility/balance exercise) that align with recommendations from the American College of Sports Medicine and 8 dietary recommendations (intake of cruciferous vegetables, cooked tomatoes, fish, processed meat, poultry with skin, whole milk, vegetable fat, and vitamin supplements) that are consistent with the scientific literature on diet and prostate cancer at the time of the study's development (approximately 2016).

Table 1. Intervention components available from the Community of Wellness Web portal by level.

Level[a]	Type of support	Component[b]
1	Teaching; educational information about exercise and diet, presented in a static website format	Exercise guidelines for prostate cancer survivors[b]; diet guidelines for prostate cancer survivors[b]; exercising safely with various health issues[b]; and resources (exercises and recipes for recommended foods)[b]
2	Tailoring; Level 1 plus personalized exercise and diet advice	Personalized exercise prescription and diet recommendation[b] and videos of recommended exercises[b]
3	Technology; Levels 1 to 2 plus technology support	Text messaging to support and reinforce diet and physical activity behaviors; Fitbit Alta plus physical activity progress reports based on physical activity tracker data[b]; and self-report log of progress toward diet and exercise goals[b]
4	Touch; Levels 1 to 3 plus *live* personal support from a health coach	Phone consult with diet and exercise coaches (30 min each) and ongoing Web-based (via email) support from diet and exercise coaches

[a]Each progressive level receives the intervention components of the level before it; for example, a participant randomized to Level 3 technology receives all the components of Levels 1 to 3 but not 4.

[b]Items available on the Web portal.

Each study arm provides additive levels of behavioral support accessed via a Web portal that can be viewed on multiple computing devices including a personal computer, tablet, or smartphone. The 4 study arms are as follows: Teaching (Level 1; usual care control), Tailoring (Level 2), Technology (Level 3), and Touch (Level 4). Each level receives the tools and resources of the prior level such that Level 4 participants receive the most intervention components and is the only level to include additional personal contact via phone and email between a participant and a health coach. Table 1 summarizes the intervention components that are accessible to men who are randomized to each of the 4 arms.

The intervention components are described in more detail below.

Level 1: Teaching

This level contains Web-based static information about physical activity and diet advice for men with prostate cancer.

Level 2: Teaching + Tailoring

This level contains the content in Level 1 plus personalized exercise and diet advice. Men in this group answer a series of questions about their exercise and diet habits and preferences at baseline to generate a personalized exercise and diet program. In addition, men in this group receive access to instructional exercise videos. The exercise programs generated for men are based on the evidence for exercise as a strategy to manage side effects and symptoms for prostate cancer, slow prostate cancer progression, reduce overall mortality risk, and/or improve physical functioning [9,10,19-21,27,57-62]. Tailoring of each program is based on a man's response to a series of questions that ask about his health status, current and past prostate cancer treatments, health goals for exercise, current participation in aerobic and strengthening types of physical activity based on responses to the Rapid Assessment of Physical Activity questionnaire [63], resources for exercise (ie, access to an exercise facility, home exercise equipment, etc), and time available for exercise. A man's stated health goals dictate the mode (aerobic and/or resistance training) of exercise training in his prescription; his exercise resources further dictate the type of training selected for his program (ie, machine weights in a gym vs resistance bands at home); his health status, prostate cancer treatments, and current exercise levels dictate the exercise intensity of his prescribed program; and his available time dictates the frequency and length of prescribed training sessions (Figure 1).

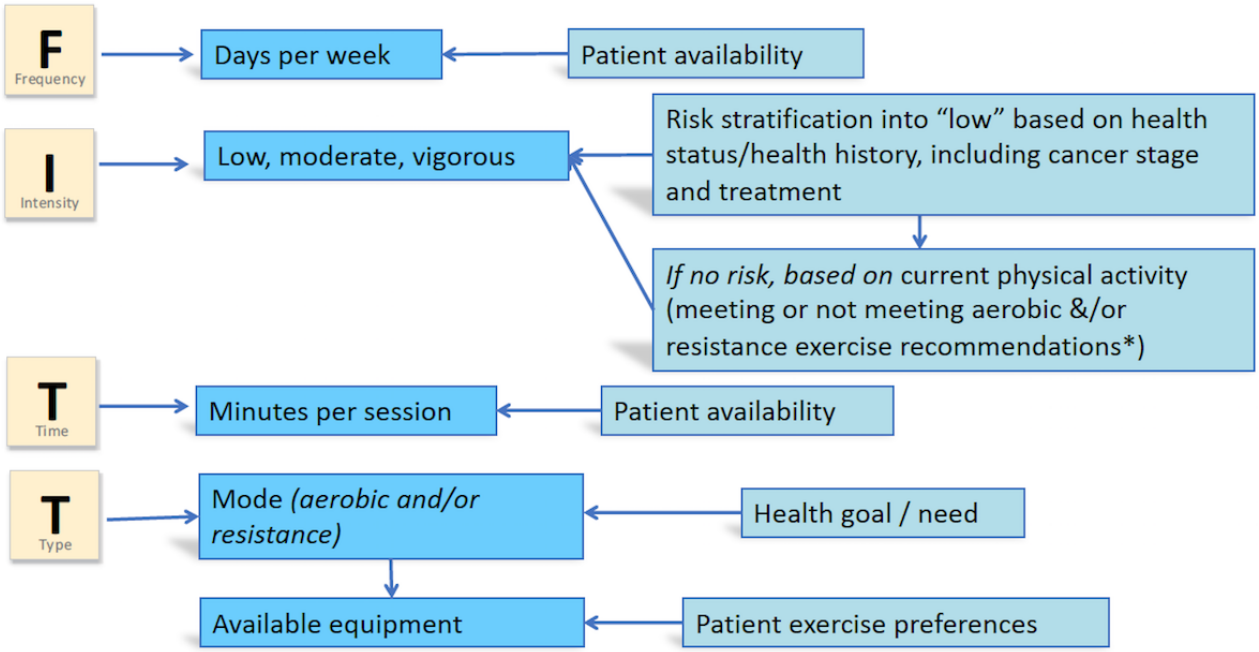
Similarly, we assess men's usual dietary habits using a validated food frequency questionnaire (FFQ) [64], benchmark his usual diet against 8 dietary recommendations we have developed based on the literature, and provide tailored advice on how he can improve his diet. Our recommendations are based on a review of the literature on diet and prostate cancer progression as of August 2016 [16] and also take into consideration recommendations from the American Cancer Society and dietary guidance provided for prevention of major chronic illnesses (eg, American Heart Association and American Diabetes Association recommendations). See Figure 2 for an example of how information would be provided back to participants about whether or not they are meeting dietary recommendations.

After receiving their personalized advice and access to instructional videos, men do not receive any further feedback to support behavior change.

Level 3: Teaching + Tailoring + Technology

This level contains the content provided in Levels 1 and 2 plus technology support for changing physical activity and diet habits. Men in this group are asked to log their diet and exercise behavior through the website and can view their progress over time. These men also receive a physical activity tracking device (Fitbit Alta; mailed to the participant) that interfaces with the Web portal and educational and motivational text messages about healthy diet and physical activity habits. Men are encouraged to use the Fitbit as a motivational tool and they can be synched to the portal where men can see displays of their time spent in physical activity, distance covered, and steps. Men do not receive separate physical activity goals related to use of their Fitbit. A total of 90 automated text messages are sent over the entire intervention period, averaging 4 texts per week. About 25% (23/90) of text messages ask the participant to reply to the message to promote an interactive experience.

Figure 1. Algorithm to generate a tailored exercise prescription based on participant input. *Current physical activity determined by answers to the Rapid Assessment of Physical Activity (PA) questionnaire that determines how regularly men participate in moderate or vigorous aerobic exercise and resistance exercise. Men who are meeting current PA guidelines may be prescribed a vigorous intensity program, men who engage in aerobic or resistance exercise, but not enough to meet guidelines may be prescribed a moderate intensity program, while men who are inactive or sedentary will be prescribed a low intensity program.



Level 4: Teaching + Tailoring + Technology + Touch

This level contains the content provided in Levels 1 to 3 plus interactive support via phone and online with research staff to support diet and exercise behavior change. Men in this group have the option to receive 2 30-min phone consultations, 1 with an exercise coach (certified athletic trainer) and 1 with a diet coach (registered cancer dietician). Participants also have the ability to receive ongoing advice from coaches via email sent through the Web portal. Men can email either coach as little or as often as they would like for the 12-week intervention period. Figure 3 provides a screenshot of a Level 4 dashboard.

Randomization Assignment

The randomization scheme was for 4 arms, stratified by site (up to 5 sites were accommodated), with a block size of 4. The randomization sequence generation and randomization assignments were handled by study staff who were blinded to participants' identifiers or any screening information. The randomization allocation sequence was generated by a staff statistician at the UCSF and shared with coinvestigators and team members at UCSF. Screening and enrollments were handled centrally by study team members at Oregon Health & Sciences University (OHSU). As patients enrolled, OHSU staff would request randomization allocations by site from UCSF staff by email; allocations were obtained by UCSF staff (who were blinded to patient identifying information) from the sequence following a consecutive order and communicated back by email to OHSU, typically within 24 hours. OHSU study staff then provided the appropriate Web intervention to each participant, based on the assignment received from UCSF. The randomization was done using *proc plan* in SAS v9.4.

Safety

An important consideration for any program that delivers an exercise prescription or recommendation via the internet is ensuring participant safety. Information about how to perform the prescribed exercises and general tips for safe exercising are available on the Web portal. In addition, we have attempted to minimize the risk of adverse events during exercise by excluding men who may be at risk because of their current health status and/or prostate cancer treatment, unless they receive clearance from their physician to participate in moderate intensity exercise. In addition, the generated exercise prescription takes into account a man's current health status, including whether or not he is currently receiving treatment for his prostate cancer with surgery, radiation or chemotherapy, ADT, or immunotherapy. For example, any man currently in active treatment is prescribed a low-intensity exercise program, regardless of other health indicators. If a man has no health indicators that dictate that he receives a low-intensity exercise program, the intensity of exercise is prescribed based on his self-reported baseline exercise levels so that the program is safe and effectively provides a sufficient stimulus for adaptation.

Figure 2. Example of the assessment and feedback that will be provided to a participant about how well he meets the dietary recommendations in the Community of Wellness.

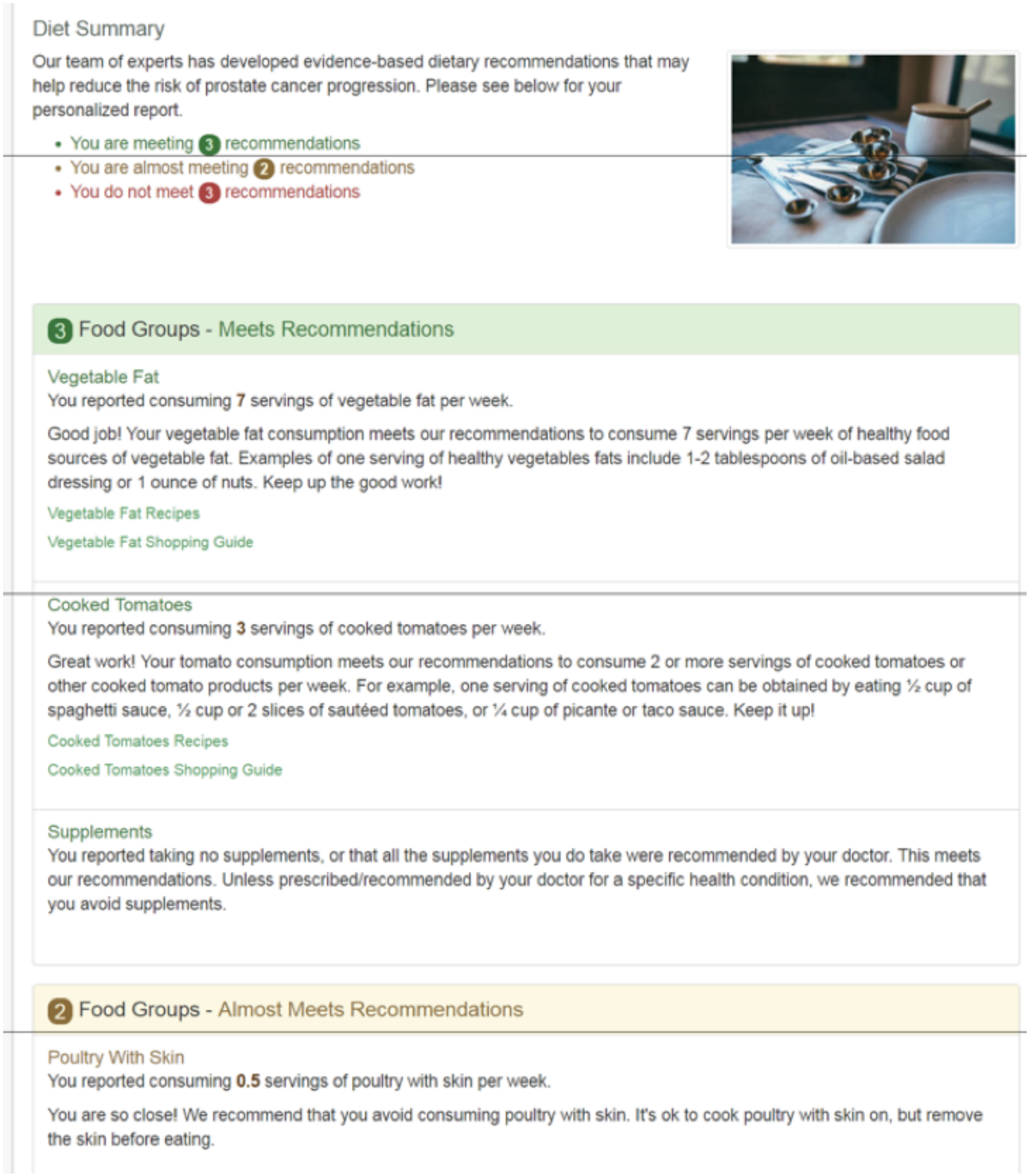


Figure 3. Example of a Level 4 "Dashboard" to help men navigate to different elements of the portal.

Outcome Measures

We will evaluate acceptability and feasibility of the Community of Wellness intervention after 3 months via surveys, usage analytics from the Web portal, and focus groups. We will also assess study retention percentage of participants completing surveys) at 3 and 6 months as a reflection of acceptability and feasibility. Secondarily, we will explore the effectiveness of the different levels of the intervention on self-reported changes in diet or physical activity habits, QoL, and self-efficacy after 3 months and 6 months. To describe characteristics of our sample, we also ask men to self-report sociodemographic information (ie, age, race/ethnicity, marital, and employment status) and their cancer and health histories using an in-house questionnaire designed for this study.

Acceptability and Feasibility

To assess acceptability and feasibility of the Web-based intervention levels, we will evaluate accrual, participant retention, and adherence. We will measure accrual as the percentage of the target sample enrolled within a 1-year recruitment period. We expect to enroll the full sample (n=200) within this time frame. We will also collect information to allow us to determine the feasibility of recruitment, for example, percentage of men eligible and percentage of men enrolled out of the total contacted about the study. We will measure retention as the percentage of participants who complete postintervention and postfollow-up surveys out of the total sample. We expect to retain 80% of the full sample postintervention (n=160) and 80% of the postintervention sample (n=128) at follow-up. We will measure adherence as the number of times a man accesses the Web portal during the intervention period (quantified as the number of log-ins). We expect 100% of men to adhere to a single log-in and that the number of log-ins will significantly differ across levels, with Level 1 having the lowest and Level 4 having the highest adherence. We will measure the technical usage statistics for the Web portal, including frequency of log-ins, individual page views, and access of exercise videos. Post intervention, participants in each level are also asked to assess their use and the helpfulness of the Web portal, its components, and other study tools through an online survey.

Adherence to Diet and Exercise Recommendations

To estimate the effect of the intervention on behavior change, we will compare item-level data (eg, minutes per week of moderate activity, minutes per week of vigorous activity, and servings per week of cruciferous vegetables) at baseline and 3 months from the Community Healthy Activities Model Program for Seniors (CHAMPS) physical activity survey [65,66] and a validated FFQ [67]. We will examine behaviors overall as part of a "behavior score" (see below) and with a focus on activities and dietary components that correspond to our recommendations.

The CHAMPS survey is administered at baseline, 3 months, and 6 months. This validated survey estimates total weekly energy expenditure (in kilocalories per week) from physical activities for older adults. The 41-item questionnaire asks about recent engagement in specific types of vigorous-, moderate-, and light-intensity activities per week and the frequency and duration of participation. Specific items can be categorized as aerobic or resistance exercise, and responses to these items will be evaluated to determine how closely a man complied with his prescribed training program. In addition, we can calculate weekly energy expenditure in moderate- and/or vigorous-intensity activities separately for comparison with other studies.

The validated Harvard TH Chan School of Public Health FFQ for adults from 2007 is administered at baseline, 3 months, and 6 months [68]. This 132-item survey assesses dietary intake in categories from "never or less than once per month" to "6 or more times per day." The original survey asks about intake over

the past year; we modified the survey for this study to ask about intake over the last month.

In addition to the responses to standard surveys, participants who receive technology support (Levels 3 and 4) complete weekly online surveys to report their progress toward meeting their exercise and diet recommendations. Participants report the number and type (eg, aerobic or resistance) of exercise sessions, average session duration, and exercise intensity. Men also report which of the recommended dietary habits they worked on, if they met any of diet goals, and which goals were the most challenging. This type of charting is used to provide another form of behavioral support; we can also use the data to further evaluate adherence to recommendations.

We will calculate a "behavior score" based on how well each participants' self-reported diet and exercise habits match the 8 dietary and 3 exercise recommendations. For each of the 11 targeted behaviors, participants will be assigned 0 points if they do not meet that recommendation, 1 point if they almost meet the recommendation, and 2 points if they meet the recommendation. The overall score ranges from 0 to 22, with higher values indicating closer adherence to the exercise and diet recommendations. To calculate the score, a priori numeric criteria were defined for not meeting, almost meeting, or meeting each of the 11 recommendations. These criteria were used in the design of the intervention to provide tailored feedback to participants randomly assigned to Levels 2 or above. For example, the recommendation for fish was to consume 2 or more servings per week. Men consuming less than 1 serving per week are considered "not meeting" the recommendation and receive 0 points toward the composite score; men eating more than 1 serving per week but less than 2 servings per week are considered "almost meeting" and given 1 point; and those eating more than 2 servings per week are "meeting the recommendation" and given 2 points. We will examine mean scores for each group at baseline and 3 months and changes in scores from baseline to 3 months. The development and application of a behavior score like this comes from literature examining healthy lifestyles and risk of chronic disease. For example, members of our team previously reported the development and validation of a lifestyle score for the prevention of lethal prostate cancer, which incorporated several of the diet and exercise components recommended in this study [69].

Other "healthy lifestyle" scores, computed similarly, have been developed and shown to be useful for summarizing lifestyle-disease relationships in other disease areas, such as hypertension or cardiac death [70,71].

To assess adherence to use of technology support via physical activity tracking devices for men in Levels 3 or 4, we will assess the number of days they wore their wearable device during the study period. We will also consider data from the wearable device to describe the average number of steps taken per day, active minutes per week, and miles covered per week.

Fatigue and Sleep Quality

Fatigue and sleep quality are assessed using validated instruments at baseline, 3 months, and 6 months. The Patient Reported Outcome Measurement Information System 7-item Short Form-Fatigue questionnaire [72] is used to assess changes in cancer-related fatigue. The Pittsburgh Sleep Quality Index is used to assess changes in sleep quality [73,74].

Self-Efficacy for Physical Activity and Diet

Self-efficacy for physical activity will be measured with a standard 6-item questionnaire at baseline, 3 months, and 6 months [75]. Self-efficacy for diet will also be collected at 3 and 6 months using a similar approach by having participants rate their confidence in performing each recommended task (eg, consume 2 or more servings of cooked tomatoes per week) using a Likert scale. We will evaluate whether baseline self-efficacy predicts response to the intervention arms and whether the interventions improve self-efficacy for physical activity and diet compared with control.

Stage of Change for Physical Activity

The Physical Activity Stage Assessment is a 5-item measure of a person's readiness to engage in recommended levels of physical activity and has been used in prior studies of cancer survivors [47]. We will evaluate the influence of the behavioral support on readiness to engage in physical activity.

Focus Groups

Focus groups will be conducted post intervention to evaluate elements of usability and acceptability that will provide greater depth of information beyond what can be obtained via surveys. Focus group participants will be recruited from each of the different levels of intervention, to gain insight into participant experience at each of the levels. Focus groups will be conducted by phone so that we do not exclude participants who cannot travel to each study site. There is not an a priori selection of the focus group subsample; rather, we will examine the demographic data once each site is fully enrolled and contact a representative sample from the study population based on age, race/ethnicity, disease stage, time since diagnosis, and intervention arm.

Statistical Considerations

Statistical Power

The primary outcomes for this pilot are acceptability and feasibility, as assessed by percent accrued in 1 year, percent recruited out of total contacted, and retention at 3 months. We anticipate enrolling 100% of the target 200 in 1 year, enrolling 3% of the total sample contacted via mass mailings, and retaining 80% of participants at 3 months. With 200 participants, we will be able to identify a retention proportion of 80% at 3 months (95% CI limits 74.5%-85.5%) and should be able to identify the other more extreme proportions with higher precision and tighter confidence limits. We will also assess the proportion completing surveys at 6 months, secondarily. If we assume 160 individuals complete the 3-month surveys, then we will have 80% power to detect a retention proportion at 6 months of 80% with a 95% confidence limit of 73.8% to 86.2%.

For the secondary outcome of behavior change, we will compute a composite *behavior score* at baseline and 3 months based on the self-reported survey data and as described above. With 50 participants per group, there is 80% of power to detect an effect size of 0.57 at a 2-sided alpha of .05 when comparing the change in score from baseline to 3 months for an intervention group

(either Levels 2, 3, or 4) compared with the reference group (Level 1). For example, assuming on average men in the reference group (Level 1) experience a 2-point increase in scores from baseline to 3 months, 50 participants in Level 1 and 50 participants in Level 2 would provide power of 80% or higher if there is an average increase of 4.85 points or greater in Level 2, with an SD of 5. As a pilot study, multiple testing adjustments were not accounted for.

Proposed Statistical Analyses

We will examine the distribution of baseline covariates selected a priori (eg, age, race, clinical stage, body mass index, time since diagnosis, treatments received, current stage, and education level), overall and by group assignment. We will compute the time to enroll and proportions retained in the study (defined as completing at least one follow-up survey), overall and by arm, at 3 and 6 months. We will compare the dropout rates overall and across arms using chi-square or Fisher exact tests, as appropriate. Secondarily, we will examine the exercise and diet behavior data at baseline and 3 months for each study arm using descriptive statistics, such as means, medians, and interquartile range, and compare across arms using *t* tests and Wilcoxon rank sum tests. We will undertake an intent-to-treat analysis. We will also examine responses to the 6-month survey to explore retention and possible maintenance of behavior changes in longer term.

Our primary outcomes of this pilot RCT are accrual and participant retention. We will summarize eligibility, accrual, and retention using descriptive statistics and explore whether these factors differ by sociodemographic (ie, age, race/ethnicity, marital status, and employment) variables. In addition, we will examine adherence using the metrics described above (outcomes), overall and by randomization group.

We will explore changes in the secondary outcome metrics (eg, physical activity, diet, fatigue, and sleep quality) by describing data from baseline, 3 months, and 6 months for each study arm using descriptive statistics such as means, medians, and interquartile range. We will also examine whether change in physical activity and diet behavior, self-efficacy, fatigue, or sleep quality differs between the 4 levels of the intervention at baseline versus 3 months using *t* test, chi-square, analysis of variance, linear, and logistic regression methods, as appropriate. We will examine each group versus the reference (Level 1) as well as explore the hypothesis regarding whether increasing level of intervention corresponded to increase in uptake of the recommended behavior changes. We will consider primarily continuous variables when describing behavior change in each arm. For example, our first focus will be on whether individuals met, almost met, or did not meet the recommendations, and we will examine differences in the *behavior score* as described above. Next, we will consider the actual intakes of specific food groups of interest (eg, total servings of fish per week) and total minutes spent in each category of exercise (aerobic, strength, and flexibility) as continuous variables. We will also consider categorical variables to capture more broad indicators of positive behavior change using *i* cut points such as “increased in at least one dietary component, yes/no” or “increased in at least one exercise component, yes/no.” We will consider adjustment for important baseline covariates that may be associated with our outcomes, selected a priori [76]. We will also explore if exercise and diet self-efficacy and physical activity stage of change at baseline influence adherence to the intervention or the effect of the intervention on the secondary behavior change outcomes.

Results

Development of the Community of Wellness website is complete, has been beta-tested, and is currently being evaluated in the RCT. This RCT is open for enrollment (ClinicalTrials.gov NCT03406013) and anticipates completing enrollment by the end of 2018. Recruitment is open at 3 of the 4 academic medical centers (OHSU, UCSF, UC Denver, and Emory University [pending]) with the target population of 50 men enrolled at each site for a total of 200 subjects. OHSU achieved their recruitment goal and enrolled 50 men. UCSF is actively recruiting, with 27 men currently enrolled, and UC Denver is just open. We expect to fully accrue to the trial by January 2019, with final data collection complete by July 2019.

Discussion

We have developed a tailored, self-directed, and scalable Web-based intervention accessible via computer, tablet, or phone to promote lifestyle behaviors associated with better QoL and reduced risk of cancer recurrence/progression for men with prostate cancer. Although there are many general informational websites for cancer patients [77], the study Web portal provides a variety of tools and resources to empower prostate cancer survivors to improve their physical, emotional, and mental health, including tailored exercise and diet recommendations, contemporary technology-based support tools, and health coaching. A recent meta-analysis identified 15 internet-based programs that delivered a lifestyle-based (ie, physical activity and/or diet) intervention in cancer survivors [53]. An overall positive effect was found for increasing physical activity and reducing body mass index, but findings were mixed or inconclusive for cancer treatment–related symptoms, QoL, self-efficacy, and dietary change. Only 3 programs included, but were not specific to, men with prostate cancer. Thus, it is not known whether a Web-based program that delivers both exercise and diet advice and provides multiple levels of behavior change support is feasible, acceptable, and shows preliminary efficacy to improve diet and physical activity behaviors in prostate cancer survivors.

Although the internet is an increasingly common approach to building scalable programs for behavioral interventions, it remains unclear how Web-based programs should be designed to achieve the intended goal of behavior change. This pilot RCT will address this gap in our knowledge. We will determine the acceptability and feasibility, and estimate the effect on behavior, of 4 additive levels of Web-based tools, from Web-based information (Level 1) + personalized exercise and diet recommendations and training plans (Level 2) + text messages, a physical activity tracker (Level 3) + 1 phone counseling session with an exercise trainer and 1 session with a dietician (Level 4). A trade-off to adding tools is the resources required to implement and sustain them in an ever-changing technology

environment. A purely technology-based program may also lack the interpersonal contact, which might be an important component for behavior change in men with prostate cancer [53]. Thus, in comparison with a control level of static educational content on physical activity and diet, this study will systematically evaluate layers of additional support for changing physical activity and diet behavior. Depending on the outcomes from our pilot, future research may include further optimizing of the Web portal using the Multiphase Optimization Strategy framework to identify which components of the intervention are driving behavior change and SMART (Sequential, Multiple Assignment, Randomized Trial) trial designs to determine how to optimally tailor these to the varying needs of men with prostate cancer [78].

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Conflicts of Interest

None declared.

References

1. Cancer. Atlanta: American Cancer Society; 2018. Cancer Facts and Figures 2018 URL: https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2018/cancer-facts-and-figures-2018.pdf [accessed 2018-10-23] [WebCite Cache ID 73OLyZf4u]
2. Abern MA, Aronson WJ, Terris MK, Kane CJ, Presti JC, Amling CL, et al. Delayed radical prostatectomy for intermediate-risk prostate cancer is associated with biochemical recurrence: possible implications for active surveillance from the SEARCH database. Prostate 2013 Mar;73(4):409-417. [doi: 10.1002/pros.22582] [Medline: 22996686]
3. Freedland SH, Humphreys EB, Mangold LA, Eisenberger M, Dorey FJ, Walsh PC, et al. Risk of prostate cancer-specific mortality following biochemical recurrence after radical prostatectomy. J Am Med Assoc 2005 Jul 27;294(4):433-439. [doi: 10.1001/jama.294.4.433] [Medline: 16046649]
4. Chang D, Joseph D, Ebert M, Galvão DA, Taaffe D, Denham J, et al. Effect of androgen deprivation therapy on muscle attenuation in men with prostate cancer. J Med Imaging Radiat Oncol 2014 Apr;58(2):223-228. [doi: 10.1111/1754-9485.12124] [Medline: 24118850]
5. Galvão DA, Taaffe D, Spry N, Joseph D, Turner D, Newton RU. Reduced muscle strength and functional performance in men with prostate cancer undergoing androgen suppression: a comprehensive cross-sectional investigation. Prostate Cancer Prostatic Dis 2009;12(2):198-203. [doi: 10.1038/pcan.2008.51] [Medline: 18852703]
6. Iadeluca L, Mardekian J, Chander P, Hopps M, Makinson GT. The burden of selected cancers in the US: health behaviors and health care resource utilization. Cancer Manag Res 2017;9:721-730 [FREE Full text] [doi: 10.2147/CMAR.S143148] [Medline: 29238222]
7. Leach C, Bellizzi K, Hurria A, Reeve BB. Is it my cancer or am i just getting older?: Impact of cancer on age-related health conditions of older cancer survivors. Cancer 2016 Jun 15;122(12):1946-1953 [FREE Full text] [doi: 10.1002/cncr.29914] [Medline: 27159822]
8. Winters-Stone KM, Moe E, Graff JN, Dieckmann NF, Stoyles S, Borsch C, et al. Falls and frailty in prostate cancer survivors: current, past, and never users of androgen deprivation therapy. J Am Geriatr Soc 2017 Jul;65(7):1414-1419 [FREE Full text] [doi: 10.1111/jgs.14795] [Medline: 28263373]
9. Kenfield SA, Stampfer MJ, Giovannucci E, Chan JM. Physical activity and survival after prostate cancer diagnosis in the health professionals follow-up study. J Clin Oncol 2011 Feb 20;29(6):726-732 [FREE Full text] [doi: 10.1200/JCO.2010.31.5226] [Medline: 21205749]
10. Winters-Stone KM, Dobek JC, Bennett JA, Maddalozzo GF, Ryan CW, Beer TM. Skeletal response to resistance and impact training in prostate cancer survivors. Med Sci Sports Exerc 2014 Aug;46(8):1482-1488 [FREE Full text] [doi: 10.1249/MSS.0000000000000265] [Medline: 24500540]
11. Richman EL, Kenfield SA, Stampfer MJ, Paciorek A, Carroll PR, Chan JM. Physical activity after diagnosis and risk of prostate cancer progression: data from the cancer of the prostate strategic urologic research endeavor. Cancer Res 2011 Jun 01;71(11):3889-3895 [FREE Full text] [doi: 10.1158/0008-5472.CAN-10-3932] [Medline: 21610110]
12. Bluethmann S, Basen-Engquist K, Vernon S, Cox M, Gabriel K, Stansberry S, et al. Grasping the 'teachable moment': time since diagnosis, symptom burden and health behaviors in breast, colorectal and prostate cancer survivors. Psychooncology 2015 Oct;24(10):1250-1257 [FREE Full text] [doi: 10.1002/pon.3857] [Medline: 26060053]
13. Demark-Wahnefried W, Rock CL, Patrick K, Byers T. Lifestyle interventions to reduce cancer risk and improve outcomes. Am Fam Physician 2008 Jun 01;77(11):1573-1578 [FREE Full text] [Medline: 18581838]

14. Demark-Wahnefried W, Aziz NM, Rowland JH, Pinto BM. Riding the crest of the teachable moment: promoting long-term health after the diagnosis of cancer. J Clin Oncol 2005 Aug 20;23(24):5814-5830 [FREE Full text] [doi: 10.1200/JCO.2005.01.230] [Medline: 16043830]
15. McBride CM, Clipp E, Peterson BL, Lipkus IM, Demark-Wahnefried W. Psychological impact of diagnosis and risk reduction among cancer survivors. Psychooncology 2000;9(5):418-427. [Medline: 11038480]
16. Peisch S, Van Blarigan EL, Chan J, Stampfer M, Kenfield SA. Prostate cancer progression and mortality: a review of diet and lifestyle factors. World J Urol 2017 Jun;35(6):867-874 [FREE Full text] [doi: 10.1007/s00345-016-1914-3] [Medline: 27518576]
17. Rock CL, Doyle C, Demark-Wahnefried W, Meyerhardt J, Courneya KS, Schwartz AL, et al. Nutrition and physical activity guidelines for cancer survivors. CA Cancer J Clin 2012;62(4):243-274 [FREE Full text] [doi: 10.3322/caac.21142] [Medline: 22539238]
18. Chadd J, McDonagh M, Valtonen M, Horner-Johnson W, Eden K, Guise J, et al. Exercise interventions for prostate cancer survivors receiving hormone therapy systematic review. Transl J Am Coll Sports Med 2017 Jan;2(1):1-9 [FREE Full text] [doi: 10.1249/TJX.0000000000000025]
19. Winters-Stone KM, Dieckmann N, Maddalozzo GF, Bennett JA, Ryan CW, Beer TM. Resistance exercise reduces body fat and insulin during androgen-deprivation therapy for prostate cancer. Oncol Nurs Forum 2015 Jul;42(4):348-356. [doi: 10.1188/15.ONF.348-356] [Medline: 26148314]
20. Winters-Stone K, Dobek J, Bennett J, Dieckmann N, Maddalozzo G, Ryan C, et al. Resistance training reduces disability in prostate cancer survivors on androgen deprivation therapy: evidence from a randomized controlled trial. Arch Phys Med Rehabil 2015 Jan;96(1):7-14 [FREE Full text] [doi: 10.1016/j.apmr.2014.08.010] [Medline: 25194450]
21. Winters-Stone KM, Lyons KS, Dobek J, Dieckmann NF, Bennett JA, Nail L, et al. Benefits of partnered strength training for prostate cancer survivors and spouses: results from a randomized controlled trial of the Exercising Together project. J Cancer Surviv 2016 Dec;10(4):633-644. [doi: 10.1007/s11764-015-0509-0] [Medline: 26715587]
22. Fornusek C, Kilbreath SL. Exercise for improving bone health in women treated for stages I-III breast cancer: a systematic review and meta-analyses. J Cancer Surviv 2017 Oct;11(5):525-541. [doi: 10.1007/s11764-017-0622-3] [Medline: 28639157]
23. Kenfield SA, Stampfer MJ, Giovannucci E, Chan JM. Physical activity and survival after prostate cancer diagnosis in the health professionals follow-up study. J Clin Oncol 2011 Feb 20;29(6):726-732 [FREE Full text] [doi: 10.1200/JCO.2010.31.5226] [Medline: 21205749]
24. Wang Y, Jacobs EJ, Gapstur SM, Maliniak ML, Gansler T, McCullough ML, et al. Recreational physical activity in relation to prostate cancer-specific mortality among men with nonmetastatic prostate cancer. Eur Urol 2017 Dec;72(6):931-939. [doi: 10.1016/j.eururo.2017.06.037] [Medline: 28711382]
25. Friedenreich CM, Wang Q, Neilson HK, Kopciuk KA, McGregor SE, Courneya KS. Physical activity and survival after prostate cancer. Eur Urol 2016 Dec;70(4):576-585 [FREE Full text] [doi: 10.1016/j.eururo.2015.12.032] [Medline: 26774959]
26. Bonn SE, Sjölander A, Lagerros YT, Wiklund F, Stattin P, Holmberg E, et al. Physical activity and survival among men diagnosed with prostate cancer. Cancer Epidemiol Biomarkers Prev 2015 Jan;24(1):57-64 [FREE Full text] [doi: 10.1158/1055-9965.EPI-14-0707] [Medline: 25527697]
27. Richman EL, Kenfield SA, Stampfer MJ, Paciorek A, Carroll PR, Chan JM. Physical activity after diagnosis and risk of prostate cancer progression: data from the cancer of the prostate strategic urologic research endeavor. Cancer Res 2011 Jun 01;71(11):3889-3895 [FREE Full text] [doi: 10.1158/0008-5472.CAN-10-3932] [Medline: 21610110]
28. Ottenbacher A, Yu M, Moser RP, Phillips SM, Alfano C, Perna FM. Population estimates of meeting strength training and aerobic guidelines, by gender and cancer survivorship status: findings from the Health Information National Trends Survey (HINTS). J Phys Act Health 2015 May;12(5):675-679. [doi: 10.1123/jpah.2014-0003] [Medline: 24834485]
29. Bourke L, Homer K, Thaha M, Steed L, Rosario D, Robb K, et al. Interventions for promoting habitual exercise in people living with and beyond cancer. Cochrane Database Syst Rev 2013 Sep 24(9):CD010192. [doi: 10.1002/14651858.CD010192.pub2] [Medline: 24065550]
30. Nyrop K, Deal A, Williams G, Guerard E, Pergolotti M, Muss HB. Physical activity communication between oncology providers and patients with early-stage breast, colon, or prostate cancer. Cancer 2016 Feb 01;122(3):470-476 [FREE Full text] [doi: 10.1002/cncr.29786] [Medline: 26566177]
31. Forbes CC, Blanchard CM, Mummery WK, Courneya K. Prevalence and correlates of strength exercise among breast, prostate, and colorectal cancer survivors. Oncol Nurs Forum 2015 Mar;42(2):118-127 [FREE Full text] [doi: 10.1188/15.ONF.42-02AP] [Medline: 25806879]
32. Tran S, Walker LM, Wassersug RJ, Matthew AG, McLeod DL, Robinson JW. What do Canadian uro-oncologists believe patients should know about androgen deprivation therapy? J Oncol Pharm Pract 2014 Jun;20(3):199-209. [doi: 10.1177/1078155213495285] [Medline: 24122850]
33. Keogh JW, Patel A, MacLeod RD, Masters J. Perceived barriers and facilitators to physical activity in men with prostate cancer: possible influence of androgen deprivation therapy. Eur J Cancer Care (Engl) 2014 Mar;23(2):263-273. [doi: 10.1111/ecc.12141] [Medline: 24134506]

34. Yang M, Kenfield SA, Van Blarigan EL, Batista JL, Sesso HD, Ma J, et al. Dietary patterns after prostate cancer diagnosis in relation to disease-specific and total mortality. Cancer Prev Res (Phila) 2015 Jun;8(6):545-551 [FREE Full text] [doi: 10.1158/1940-6207.CAPR-14-0442] [Medline: 26031631]
35. Wang W, Yang M, Kenfield SA, Hu FB, Stampfer MJ, Willett WC, et al. Nut consumption and prostate cancer risk and mortality. Br J Cancer 2016 Dec 26;115(3):371-374 [FREE Full text] [doi: 10.1038/bjc.2016.181] [Medline: 27280637]
36. Van Blarigan EL, Kenfield SA, Yang M, Sesso HD, Ma J, Stampfer MJ, et al. Fat intake after prostate cancer diagnosis and mortality in the Physicians' Health Study. Cancer Causes Control 2015 Aug;26(8):1117-1126 [FREE Full text] [doi: 10.1007/s10552-015-0606-4] [Medline: 26047644]
37. Richman EL, Stampfer MJ, Paciorek A, Broering JM, Carroll PR, Chan JM. Intakes of meat, fish, poultry, and eggs and risk of prostate cancer progression. Am J Clin Nutr 2010 Mar;91(3):712-721 [FREE Full text] [doi: 10.3945/ajcn.2009.28474] [Medline: 20042525]
38. Richman EL, Carroll PR, Chan JM. Vegetable and fruit intake after diagnosis and risk of prostate cancer progression. Int J Cancer 2012 Jul 01;131(1):201-210 [FREE Full text] [doi: 10.1002/ijc.26348] [Medline: 21823116]
39. Peisch S, Van Blarigan EL, Chan J, Stampfer M, Kenfield SA. Prostate cancer progression and mortality: a review of diet and lifestyle factors. World J Urol 2017 Jun;35(6):867-874 [FREE Full text] [doi: 10.1007/s00345-016-1914-3] [Medline: 27518576]
40. Chan JM, Holick CN, Leitzmann MF, Rimm EB, Willett WC, Stampfer MJ, et al. Diet after diagnosis and the risk of prostate cancer progression, recurrence, and death (United States). Cancer Causes Control 2006 Mar;17(2):199-208. [doi: 10.1007/s10552-005-0413-4] [Medline: 16425098]
41. Pettersson A, Kasperzyk JL, Kenfield SA, Richman EL, Chan JM, Willett WC, et al. Milk and dairy consumption among men with prostate cancer and risk of metastases and prostate cancer death. Cancer Epidemiol Biomarkers Prev 2012 Mar;21(3):428-436 [FREE Full text] [doi: 10.1158/1055-9965.EPI-11-1004] [Medline: 22315365]
42. Richman E, Kenfield S, Stampfer M, Giovannucci E, Chan JM. Egg, red meat, and poultry intake and risk of lethal prostate cancer in the prostate-specific antigen-era: incidence and survival. Cancer Prev Res (Phila) 2011 Dec;4(12):2110-2121 [FREE Full text] [doi: 10.1158/1940-6207.CAPR-11-0354] [Medline: 21930800]
43. Chavarro J, Stampfer M, Hall M, Sesso H, Ma J. A 22-y prospective study of fish intake in relation to prostate cancer incidence and mortality. Am J Clin Nutr 2008 Nov;88(5):1297-1303 [FREE Full text] [doi: 10.3945/ajcn.2008.26419] [Medline: 18996866]
44. Kenfield SA, Van Blarigan EL, DuPre N, Stampfer MJ, Chan JM. Selenium supplementation and prostate cancer mortality. J Natl Cancer Inst 2015 Jan;107(1):360 [FREE Full text] [doi: 10.1093/jnci/dju360] [Medline: 25505227]
45. Lawson KA, Wright ME, Subar A, Mouw T, Hollenbeck A, Schatzkin A, et al. Multivitamin use and risk of prostate cancer in the National Institutes of Health-AARP Diet and Health Study. J Natl Cancer Inst 2007 May 16;99(10):754-764. [doi: 10.1093/jnci/djk177] [Medline: 17505071]
46. van der Bij AK, Laurant M, Wensing M. Effectiveness of physical activity interventions for older adults: a review. Am J Prev Med 2002 Feb;22(2):120-133. [Medline: 11818183]
47. Hawkes A, Chambers S, Pakenham K, Patrao T, Baade P, Lynch B, et al. Effects of a telephone-delivered multiple health behavior change intervention (CanChange) on health and behavioral outcomes in survivors of colorectal cancer: a randomized controlled trial. J Clin Oncol 2013 Jun 20;31(18):2313-2321. [doi: 10.1200/JCO.2012.45.5873] [Medline: 23690410]
48. Demark-Wahnefried W, Morey MC, Sloane R, Snyder DC, Miller PE, Hartman TJ, et al. Reach out to enhance wellness home-based diet-exercise intervention promotes reproducible and sustainable long-term improvements in health behaviors, body weight, and physical functioning in older, overweight/obese cancer survivors. J Clin Oncol 2012 Jul 01;30(19):2354-2361 [FREE Full text] [doi: 10.1200/JCO.2011.40.0895] [Medline: 22614994]
49. Finlay A, Wittert G, Short CE. A systematic review of physical activity-based behaviour change interventions reaching men with prostate cancer. J Cancer Surviv 2018 May 16 Epub ahead of print. [doi: 10.1007/s11764-018-0694-8] [Medline: 29770953]
50. Alfano C, Bluethmann S, Tesauro G, Perna F, Agurs-Collins T, Elena J, et al. NCI funding trends and priorities in physical activity and energy balance research among cancer survivors. J Natl Cancer Inst 2016 Jan;108(1). [doi: 10.1093/jnci/djv285] [Medline: 26547926]
51. Garnett C, Crane D, West R, Brown J, Michie S. Identification of behavior change techniques and engagement strategies to design a smartphone app to reduce alcohol consumption using a formal consensus method. JMIR Mhealth Uhealth 2015 Jun 29;3(2):e73 [FREE Full text] [doi: 10.2196/mhealth.3895] [Medline: 26123578]
52. Kuijpers W, Groen W, Aaronson N, van Harten WH. A systematic review of web-based interventions for patient empowerment and physical activity in chronic diseases: relevance for cancer survivors. J Med Internet Res 2013 Feb 20;15(2):e37 [FREE Full text] [doi: 10.2196/jmir.2281] [Medline: 23425685]
53. Roberts A, Fisher A, Smith L, Heinrich M, Potts HW. Digital health behaviour change interventions targeting physical activity and diet in cancer survivors: a systematic review and meta-analysis. J Cancer Surviv 2017 Dec;11(6):704-719 [FREE Full text] [doi: 10.1007/s11764-017-0632-1] [Medline: 28779220]
54. Alfano C, Smith T, de Moor JS, Glasgow R, Khoury M, Hawkins N, et al. An action plan for translating cancer survivorship research into care. J Natl Cancer Inst 2014 Nov;106(11) [FREE Full text] [doi: 10.1093/jnci/dju287] [Medline: 25249551]

55. Rogers L, Matevey C, Hopkins-Price P, Shah P, Dunnington G, Courneya KS. Exploring social cognitive theory constructs for promoting exercise among breast cancer patients. Cancer Nurs 2004;27(6):462-473. [Medline: 15632787]
56. Gourlan M, Bernard P, Bortolon C, Romain A, Lareyre O, Carayol M, et al. Efficacy of theory-based interventions to promote physical activity. A meta-analysis of randomised controlled trials. Health Psychol Rev 2016;10(1):50-66. [doi: 10.1080/17437199.2014.981777] [Medline: 25402606]
57. Cormie P, Newton RU, Spry N, Joseph D, Taaffe DR, Galvão DA. Safety and efficacy of resistance exercise in prostate cancer patients with bone metastases. Prostate Cancer Prostatic Dis 2015 Jun;18(2):196. [doi: 10.1038/pcan.2015.6] [Medline: 25964200]
58. Cormie P, Galvão DA, Spry N, Joseph D, Chee R, Taaffe D, et al. Can supervised exercise prevent treatment toxicity in patients with prostate cancer initiating androgen-deprivation therapy: a randomised controlled trial. BJU Int 2015 Feb;115(2):256-266 [FREE Full text] [doi: 10.1111/bju.12646] [Medline: 24467669]
59. Galvão DA, Spry N, Denham J, Taaffe D, Cormie P, Joseph D, et al. A multicentre year-long randomised controlled trial of exercise training targeting physical functioning in men with prostate cancer previously treated with androgen suppression and radiation from TROG 03.04 RADAR. Eur Urol 2014 May;65(5):856-864. [doi: 10.1016/j.eururo.2013.09.041] [Medline: 24113319]
60. Galvão DA, Taaffe D, Spry N, Joseph D, Newton RU. Combined resistance and aerobic exercise program reverses muscle loss in men undergoing androgen suppression therapy for prostate cancer without bone metastases: a randomized controlled trial. J Clin Oncol 2010 Jan 10;28(2):340-347. [doi: 10.1200/JCO.2009.23.2488] [Medline: 19949016]
61. Galvão DA, Nosaka K, Taaffe DR, Spry N, Kristjanson LJ, McGuigan MR, et al. Resistance training and reduction of treatment side effects in prostate cancer patients. Med Sci Sports Exerc 2006 Dec;38(12):2045-2052. [doi: 10.1249/01.mss.0000233803.48691.8b] [Medline: 17146309]
62. Segal RJ, Reid RD, Courneya KS, Malone SC, Parliament MB, Scott CG, et al. Resistance exercise in men receiving androgen deprivation therapy for prostate cancer. J Clin Oncol 2003 May 01;21(9):1653-1659. [doi: 10.1200/JCO.2003.09.534] [Medline: 12721238]
63. Topolski TD, LoGerfo J, Patrick DL, Williams B, Walwick J, Patrick MB. The Rapid Assessment of Physical Activity (RAPA) among older adults. Prev Chronic Dis 2006 Oct;3(4):A118 [FREE Full text] [Medline: 16978493]
64. Chasan-Taber S, Rimm EB, Stampfer MJ, Spiegelman D, Colditz GA, Giovannucci E, et al. Reproducibility and validity of a self-administered physical activity questionnaire for male health professionals. Epidemiology 1996 Jan;7(1):81-86. [Medline: 8664406]
65. Hekler EB, Buman MP, Haskell WL, Conway TL, Cain KL, Sallis JF, et al. Reliability and validity of CHAMPS self-reported sedentary-to-vigorous intensity physical activity in older adults. J Phys Act Health 2012 Feb;9(2):225-236 [FREE Full text] [doi: 10.1123/jpah.9.2.225] [Medline: 22368222]
66. Stewart AL, Mills KM, King AC, Haskell WL, Gillis D, Ritter PL. CHAMPS physical activity questionnaire for older adults: outcomes for interventions. Med Sci Sports Exerc 2001 Jul;33(7):1126-1141. [doi: 10.1097/00005768-200107000-00010] [Medline: 11445760]
67. Rimm E, Giovannucci E, Stampfer M, Colditz G, Litin L, Willett WC. Reproducibility and validity of an expanded self-administered semiquantitative food frequency questionnaire among male health professionals. Am J Epidemiol 1992 May 15;135(10):1114-1126. [doi: 10.1016/0895-4356(95)00551-X] [Medline: 1632423]
68. Feskanich D, Rimm EB, Giovannucci EL, Colditz GA, Stampfer MJ, Litin LB, et al. Reproducibility and validity of food intake measurements from a semiquantitative food frequency questionnaire. J Am Diet Assoc 1993 Jul;93(7):790-796. [doi: 10.1016/0002-8223(93)91754-E] [Medline: 8320406]
69. Kenfield S, Batista J, Jahn J, Downer M, Van Blarigan EL, Sesso H, et al. Development and application of a lifestyle score for prevention of lethal prostate cancer. J Natl Cancer Inst 2016 Mar;108(3) [FREE Full text] [doi: 10.1093/jnci/djv329] [Medline: 26577654]
70. Chiuve S, Fung T, Rexrode K, Spiegelman D, Manson J, Stampfer M, et al. Adherence to a low-risk, healthy lifestyle and risk of sudden cardiac death among women. J Am Med Assoc 2011 Jul 06;306(1):62-69 [FREE Full text] [doi: 10.1001/jama.2011.907] [Medline: 21730242]
71. Forman JP, Stampfer MJ, Curhan GC. Diet and lifestyle risk factors associated with incident hypertension in women. J Am Med Assoc 2009 Jul 22;302(4):401-411 [FREE Full text] [doi: 10.1001/jama.2009.1060] [Medline: 19622819]
72. Cessna J, Jim H, Sutton S, Asvat Y, Small B, Salsman J, et al. Evaluation of the psychometric properties of the PROMIS Cancer Fatigue Short Form with cancer patients. J Psychosom Res 2016 Feb;81:9-13 [FREE Full text] [doi: 10.1016/j.jpsychores.2015.12.002] [Medline: 26800633]
73. Owen DC, Parker KP, McGuire DB. Comparison of subjective sleep quality in patients with cancer and healthy subjects. Oncol Nurs Forum 1999;26(10):1649-1651. [Medline: 10573681]
74. Buysse D, Reynolds C, Monk T, Berman S, Kupfer DJ. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. Psychiatry Res 1989 May;28(2):193-213. [doi: 10.1016/0165-1781(89)90047-4] [Medline: 2748771]
75. Marcus BH, Selby VC, Niaura RS, Rossi JS. Self-efficacy and the stages of exercise behavior change. Res Q Exerc Sport 1992 Mar;63(1):60-66. [doi: 10.1080/02701367.1992.10607557] [Medline: 1574662]

76. de Boer MR, Waterlander W, Kuijper L, Steenhuis I, Twisk JW. Testing for baseline differences in randomized controlled trials: an unhealthy research behavior that is hard to eradicate. Int J Behav Nutr Phys Act 2015 Jan 24;12:4 [FREE Full text] [doi: 10.1186/s12966-015-0162-z] [Medline: 25616598]
77. Short CE, Gelder C, Binnewerg L, McIntosh M, Turnbull D. Examining the accessibility of high-quality physical activity behaviour change support freely available online for men with prostate cancer. J Cancer Surviv 2018 Feb;12(1):10-17. [doi: 10.1007/s11764-017-0638-8] [Medline: 28871558]
78. Collins LM, Murphy SA, Strecher V. The multiphase optimization strategy (MOST) and the sequential multiple assignment randomized trial (SMART): new methods for more potent eHealth interventions. Am J Prev Med 2007 May;32(5 Suppl):S112-S118 [FREE Full text] [doi: 10.1016/j.amepre.2007.01.022] [Medline: 17466815]

Abbreviations

CHAMPS: Community Healthy Activities Model Program for Seniors
FFQ: food frequency questionnaire
QoL: quality of life
RCT: randomized controlled trial
UCSF: University of California, San Francisco

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Protocol

Use of Dental Practices for the Identification of Adults With Undiagnosed Type 2 Diabetes Mellitus or Nondiabetic Hyperglycemia: Protocol for a Systematic Review

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Abstract

Background: Type 2 diabetes mellitus (T2DM) is a growing global health burden and is expected to affect more than 590 million people by the year 2035. Evidence exists to demonstrate that dental settings have been used for risk assessment and identification of individuals who may be at high risk for T2DM or who may already unknowingly have the condition.

Objective: This protocol aims to outline the methodology that will be undertaken to synthesize the literature relating to the use of primary care (nonhospital-based) dental services for the identification of undiagnosed T2DM or prediabetes—often termed nondiabetic hyperglycemia—in adult patients.

Methods: This paper outlines the protocol that will be followed to conduct a systematic review and meta-analysis of the available literature. The protocol outlines the aims, objectives, search strategy, data extraction and data management methods, as well as the statistical analysis plan. The Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols guidelines were followed in developing the protocol as were elements of the Cochrane handbook.

Results: We expect the systematic review to be completed within 18 months of publication of this protocol and expect to see a high degree of heterogeneity in the existing literature.

Conclusions: This review is of importance as it will synthesize the existing evidence base and inform future studies in the field. Following the publication of the protocol, the review will be registered on Prospective Register of Systematic Reviews. Following the completion of the review, results will be published in a suitable peer-reviewed journal.

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KEYWORDS

adults; case-finding; dental; diabetes; nondiabetic hyperglycemia; risk assessment

Introduction

Type 2 diabetes mellitus (T2DM) is a growing public health concern, accounting for 10% of the UK National Health Service (NHS) budget, a proportion predicted to rise to 17% by 2035 [1]. In addition to the 3.8 million people currently diagnosed with T2DM in the United Kingdom, it is estimated that almost 1 million UK residents have undiagnosed T2DM [2] and a further 12 million are at high risk for developing the condition [3]. Globally, the incidence of T2DM is expected to exceed 592 million by the year 2035 [4]. Individuals may remain undiagnosed for many years due to the condition being symptom-free in its early stages [5]. This has implications for the secondary prevention and management of the condition.

The UK National Screening Committee states that there are benefits to early identification of individuals at risk for

developing diabetes and those with nondiabetic hyperglycemia (NDH), also known as prediabetes, as well as those with undiagnosed diabetes [3]. Advances in diabetes care mean that earlier detection may reduce the risk of complications, such as heart attacks, stroke, and blindness [6,7]. Evidence exists that diabetes is preventable in those at high risk [8]. Hence, the NHS has developed the Diabetes Prevention Programme. Novel approaches to identify cases of previously undiagnosed diabetes and high-risk individuals may result in improved health outcomes, improved quality of life for patients, and reductions in cost to the NHS.

In the United Kingdom, 60% of the adult population routinely attends high-street dentists for regular check-ups, even when they have no concerns [9]. Furthermore, patients' diabetes status influences their dental management; therefore, it is useful for dentists to be aware of this condition. Using dental visits for early diabetes detection represents a unique opportunity to access large proportions of the population for diabetes screening.

The National Institute for Care and Health Excellence pathways exist for allied health care professionals, including dentists, relating to risk assessment for diabetes [10] in community and primary care settings. Some UK community pharmacists perform risk assessment of patients for diabetes. However, using primary dental practices has not been widely explored as an option for identifying high-risk individuals and, therefore, represents a potential missed opportunity.

Studies conducted in the United States have indicated that dental practices can be effective in identifying those at high risk for diabetes [11-13]. There have also been studies in Europe that support these findings [14-16]. Dental practices in the United Kingdom may also offer the opportunity for proactive, early case detection of high-risk individuals and those who already unknowingly have T2DM.

Despite the existing literature published in the field to date, no published systematic reviews have synthesized the current evidence base for the use of primary care dental settings for the detection of T2DM and NDH. The aim of this protocol is to outline the design of a systematic review investigating the available literature for utilizing dental settings to case-find previously undiagnosed T2DM and NDH. The primary aim of the review will be to establish the identification rate of previously undiagnosed diabetes and NDH and the opinions, benefits, and barriers related to case-finding T2DM and NDH in dental settings.

Methods

Protocol Guidelines Followed

The intention to conduct a systematic review is evidenced through registration with the prospective register of systematic reviews (PROSPERO), the Web-based international prospective register of systematic reviews, at the time of protocol conception. This protocol followed the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols 2015 statement [17] alongside elements from the Cochrane handbook for systematic reviews [18].

Review Question and Objective

This review aims to identify the literature relating to the use of primary care (nonhospital-based) dental services for the identification of undiagnosed T2DM and NDH—often termed prediabetes—in adult patients. The review will have a particular focus on the pick-up rate of new cases of NDH and T2DM with the following additional questions, which this review will aim to answer:

- What methodology was utilized within the dental practice for case-finding?
- What were the recruitment rates within the studies?
- What are the opinions of patients and health care professionals relating to such services?
- What are the reported barriers to uptake of any such implemented services?
- What are the reported benefits of utilizing such services?

The Population Intervention Control Outcome format was followed; this format involves clearly identifying participants, intervention, comparator, and outcome within the research question. For this review, these were patients (P) aged >18 years attending primary care (nonspecialist practice) dental services. The specific intervention (I) for this review is focused on the risk assessment methods used for identification of T2DM or NDH (prediabetes). It is recognized that a number of methods for risk assessment of patients have been discussed in the literature. This includes using questionnaires, finger-prick point-of-care testing, gingival crevicular fluid samples, and both one- and two-stage procedures utilizing a combination of these methods; these differing methods will act as the comparators (C). This review will attempt to capture and compare the full range of assessments used.

Outcome Measure

The primary outcome measure for this systematic review is the identification of patients with NDH or T2DM using risk assessment methods in dental care settings. The secondary outcomes include identification of methodologies utilized in the dental practice for case-finding, establishing recruitment rates in the studies, and gaining insight into the opinions of patients and health care professionals relating to case-finding. In addition, the review will aim to enhance the understanding of reported barriers to uptake of any such implemented services and any reported identified benefits to utilizing dental settings to case-find NDH and T2DM.

Inclusion and Exclusion Criteria

The inclusion and exclusion criteria have been presented in Textboxes 1 and 2, respectively.

Textbox 1. Inclusion criteria.

- Adults aged >18 years
- English language literature
- Diabetes risk assessment conducted
- Risk assessment based in primary care dental settings

Textbox 2. Exclusion criteria.

- Non-English language
- Animal studies
- Nonprimary care dental settings

Table 1. Draft of search strategy to be used.

Query	Items found
Search (((((((((screening) OR “risk assessment”) OR “case detection”) OR “case finding”) OR “identification”) OR “risk detection”) OR “diagnosis”)) AND ((((((((((“diabetes mellitus”) OR “diabetes”) OR “type 2 diabetes”) OR “type two diabetes”) OR TTDM) OR T2DM) OR prediabetes) OR Pre-diabetes) OR “non diabetic hyperglycaemia”) OR NDH)) AND (((((dental) OR dentistry) OR “primary dental care”) OR “general dental practice”) OR dentist)	1466
Search ((((dental) OR dentistry) OR “primary dental care”) OR “general dental practice”) OR dentist	73,7631
Search (((((((((“diabetes mellitus”) OR “diabetes”) OR “type 2 diabetes”) OR “type two diabetes”) OR TTDM) OR T2DM) OR prediabetes) OR Pre-diabetes) OR “non diabetic hyperglycaemia”) OR NDH	600,088
Search ((((((screening) OR “risk assessment”) OR “case detection”) OR “case finding”) OR “identification”) OR “risk detection”) OR “diagnosis”	3,232,401

Search Strategy

To identify the eligible literature, the following electronic bibliographic databases will be searched: Medical Literature Analysis and Retrieval System Online, PubMed, The Cochrane Library, and Web of Science. The reference lists of all eligible full texts will be searched for additional papers for inclusion. In addition to electronic databases, trial registries such as Clinicaltrials.gov will be searched.

The search strategy will include terms relating to or describing the identification of NDH and T2DM in dental settings. The search terms will be adapted for use with other bibliographic databases in combination with database-specific filters for controlled trials, where these are available (Table 1). There will be restrictions to English language only. Searches will be limited to 1950—search date to allow for replication. Furthermore, the searches will be rerun just before the final analyses and further studies retrieved for inclusion.

Risk of Bias

This review will not be restricted to only randomized controlled trials. A published and validated risk of bias assessment tool appropriate to the study type will be utilized [19] independently by two reviewers to determine the bias associated with included papers. The tool will be specific to the study design, and all papers included in the review will be appraised by the authors. Disagreement will be resolved by discussion, and where required, a third author will be consulted.

Data Extraction and Data Management

The search will be undertaken; all returned papers will have title and abstract screened independently by two researchers to establish studies that potentially meet the inclusion criteria. Calibration exercises will be undertaken until authors are consistent in their acceptance of suitable papers. Where there is disagreement regarding a paper’s exclusion, consensus will be reached by a third reviewer. For the papers included, full text will be reviewed by the two authors, and any further exclusions will be determined by consensus and agreement among authors with reason for exclusions reported. Reason for exclusion at full-text stage will be recorded.

Electronic data extraction forms will be developed and piloted. The standardized prepiloted form will be used to extract data from included studies to assess the study quality and evidence synthesis. Extracted information will include the following: study setting, population and participant demographics and baseline characteristics; details of the intervention and control conditions; study methodology; recruitment, completion, and pick-up rates; outcomes and times of measurement; indicators of acceptability to users; suggested mechanisms of intervention action; and information about assessment of the risk of bias. This information will be collected independently by the two reviewers with discrepancies identified and resolved through discussion and, if required, with the third author. Where data are missing, attempts will be made to retrieve the data by contacting study authors. The key data to be extracted are presented in Textbox 3.

Textbox 3. Key data to be extracted.

- Study ID:
- Reviewer ID and name:
- Date of completion of this form:
- Title of report:
- Source [journal year; volume: pages]:
- Authors:
- Type of report [eg, full paper or abstract or unpublished]:
- Country where the trial was conducted:
- Funders of the study:
- Dates study was conducted:
- Type of study design [eg, observational or clinical trial (randomized, parallel, or cluster, etc)]
- Was the study multicenter? If so, how many centers were there?
- Risk of bias criteria—[dependent on study type]
- Inclusion criteria
- Exclusion criteria
- Participant information
  i. Age
  ii. Gender
  iii. Ethnicity
- Risk assessment method used
- Screening process
- Recruitment rates
- Prevalence of undiagnosed type 2 diabetes mellitus (T2DM) and nondiabetic hyperglycemia (NDH)
- Method for diagnosis of T2DM or NDH
- Stakeholder opinions [patients or dental team or health care professionals, etc]
- Barriers to risk assessment in dental settings
- Key findings
- Additional comments

Electronic data extraction form will be developed in Microsoft Excel with care to ensure that updated versions do not overwrite previous iterations of extracted data.

Strategy for Synthesis

If the included studies are sufficiently homogenous, a quantitative synthesis will be undertaken. However, it is anticipated that the included studies will demonstrate high levels of heterogeneity, resulting in a descriptive synthesis approach. The descriptive synthesis will be structured around the primary and secondary outcomes of the review. It is anticipated that there will be limited scope for meta-analysis because of the range of different outcomes measured, although we expect the percentage of cases of undiagnosed T2DM and NDH to be well reported across the assumed small number of existing studies. However, where studies have used the same risk assessment strategy with the same outcome measure, results will be pooled and meta-analysis undertaken. Any meta-analysis conducted will use a random effects model to pool data given the expected high levels of heterogeneity expected between studies.

Results

We expect the systematic review to be completed within 18 months of the publication of this protocol and expect to observe a high degree of heterogeneity in the existing literature.

Discussion

This review is of importance as it will synthesize the existing evidence base and inform future studies in the field. Following the publication of the protocol, the review will be registered on PROSPERO. Following the completion of the review, results will be published in a suitable peer-reviewed journal.

Conflicts of Interest

None declared.

References

1. Hex N, Bartlett C, Wright D, Taylor M, Varley D. Estimating the current and future costs of Type 1 and Type 2 diabetes in the UK, including direct health costs and indirect societal and productivity costs. Diabet Med 2012 Jul;29(7):855-862. [doi: 10.1111/j.1464-5491.2012.03698.x] [Medline: 22537247]
2. Health matters: preventing Type 2 Diabetes.: Public Health England; 2018. URL: https://www.gov.uk/government/publications/health-matters-preventing-type-2-diabetes/health-matters-preventing-type-2-diabetes [WebCite Cache ID 73koMxWl8]
3. Murray C, Richards M, Newton J, Fenton K, Anderson H, Atkinson C, et al. UK health performance: findings of the Global Burden of Disease Study 2010. The Lancet 2013 Mar;381(9871):997-1020. [doi: 10.1016/S0140-6736(13)60355-4]
4. Guariguata L, Whiting DR, Hambleton I, Beagley J, Linnenkamp U, Shaw JE. Global estimates of diabetes prevalence for 2013 and projections for 2035. Diabetes Res Clin Pract 2014 Feb;103(2):137-149. [doi: 10.1016/j.diabres.2013.11.002] [Medline: 24630390]
5. Ramachandran A. Know the signs and symptoms of diabetes. Indian J Med Res 2014 Nov;140(5):579-581 [FREE Full text] [Medline: 25579136]
6. Knowler WC, Barrett-Connor E, Fowler SE, Hamman RF, Lachin JM, Walker EA, Diabetes Prevention Program Research Group. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med 2002 Feb 07;346(6):393-403 [FREE Full text] [doi: 10.1056/NEJMoa012512] [Medline: 11832527]
7. Hopper I, Billah B, Skiba M, Krum H. Prevention of diabetes and reduction in major cardiovascular events in studies of subjects with prediabetes: meta-analysis of randomised controlled clinical trials. European journal of cardiovascular prevention and rehabilitation : official journal of the European Society of Cardiology, Working Groups on Epidemiology & Prevention and Cardiac Rehabilitation and Exercise Physiology 2011;186:813-823.
8. Ashra NB, Sprong R, Carter P, Davies MJ, Dunkley A, Gillies C, et al. A systematic review and meta-analysis assessing the effectiveness of pragmatic lifestyle interventions for the prevention of type 2 diabetes mellitus in routine practice.: Public Health England; 2015. URL: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/733053/PHE_Evidence_Review_of_diabetes_prevention_programmes-_FINAL.pdf [WebCite Cache ID 73jO54gVq]
9. Public Health England. Adult Dental Health Survey. In: Adult Dental Health Survey 2009. London: NHS Digital; May 12, 2013.
10. Type 2 diabetes: prevention in people at high risk.: NICE; 2018 Mar. URL: https://www.nice.org.uk/guidance/ph38 [WebCite Cache ID 73RPqXZRe]
11. Lalla E, Cheng B, Kunzel C, Burkett S, Ferraro A, Lamster I. Six-month outcomes in dental patients identified with hyperglycaemia: a randomized clinical trial. J Clin Periodontol 2015 Mar;42(3):228-235. [doi: 10.1111/jcpe.12358] [Medline: 25581313]
12. Genco RJ, Schifferle RE, Dunford RG, Falkner KL, Hsu WC, Balukjian J. Screening for diabetes mellitus in dental practices: a field trial. J Am Dent Assoc 2014 Jan;145(1):57-64. [doi: 10.14219/jada.2013.7] [Medline: 24379330]
13. Lalla E, Cheng B, Kunzel C, Burkett S, Lamster IB. Dental findings and identification of undiagnosed hyperglycemia. J Dent Res 2013 Oct;92(10):888-892. [doi: 10.1177/0022034513502791] [Medline: 23979781]
14. Creanor S, Millward BA, Demaine A, Price L, Smith W, Brown N, et al. Patients' attitudes towards screening for diabetes and other medical conditions in the dental setting. Br Dent J 2014 Jan;216(1):E2. [doi: 10.1038/sj.bdj.2013.1247] [Medline: 24413142]
15. Millward B, Creanor S, Demaine A, Brown N, Smith W, Creanor E. General dental practice patients' attitudes towards screening for diabetes and other medical conditions in the dental setting. Diabetic Medicine 2013;30:184. [doi: 10.1038/sj.bdj.2013.1247]
16. Bould K, Scott SE, Dunne S, Asimakopoulou K. Uptake of screening for type 2 diabetes risk in general dental practice; an exploratory study. Br Dent J 2017 Feb 24;222(4):293-296. [doi: 10.1038/sj.bdj.2017.174] [Medline: 28232690]
17. Moher D, Shamseer L, Clarke M, Ghersi D, Liberati A, Petticrew M, PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. Syst Rev 2015 Jan 01;4:1 [FREE Full text] [doi: 10.1186/2046-4053-4-1] [Medline: 25554246]
18. Cochrane Handbook for Systematic Reviews of Interventions.: The Cochrane Collaboration; 2011 Mar. URL: https://training.cochrane.org/handbook [WebCite Cache ID 73jOOTRZ5]
19. National Heart Lung and Blood Institute. URL: https://www.nhlbi.nih.gov/health-topics/study-quality-assessment-tools [accessed 2018-10-25] [WebCite Cache ID 73RPm4npQ]

Abbreviations

NDH: nondiabetic hyperglycemia

NHS: National Health Service
PROSPERO: prospective register of systematic reviews
T2DM: type 2 diabetes mellitus

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Protocol

Clients' Experiences With Internet-Based Psychological Treatments for Mental Disorders: Protocol for a Metasynthesis of Qualitative Studies

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Abstract

Background: Given the rise of internet-based treatments as an effective therapeutic tool for psychological disorders, it is necessary to carry out research that examines clients' experiences with this type of intervention. The qualitative methodology has been found to be useful for analyzing clients' perceptions in terms of facilitators and barriers, acceptability, and negative effects of internet-based treatments. However, a lack of integration of these primary studies has prevented their findings from being applied to new research and in clinical practice.

Objective: The objective of this paper is to describe the protocol for a metasynthesis of qualitative studies exploring the experiences of clients who underwent an internet-based treatment.

Methods: Elliot and Timulak's metasynthesis approach will be used to review and synthesize qualitative studies related to client experiences in terms of the barriers and facilitators they perceived when undergoing internet-based treatment. For each search string, the features in the Sample, Phenomenon of Interest, Design, Evaluation, Research type (SPIDER) tool will be considered. Electronic databases (PubMed, PsycINFO, and Web of Science) will be searched. Two independent reviewers will analyze the material in order to determine whether the eligibility criteria are fulfilled. Findings will make it possible to create a hierarchy of domains in terms of their relevance across all the primary studies. The data obtained from primary studies will be cross-analyzed using descriptive and interpretative procedures.

Results: The search strategy is currently being conducted. First results are expected to be submitted for publication in 2019.

Conclusions: We will develop conceptual framework of the barriers and facilitators perceived by clients and propose their implications and recommendations for clinical practice, research, and training.

Trial Registration: PROSPERO CRD42018079894; https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=79894 (Archived by WebCite at http://www.webcitation.org/73C6OtlS7).

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KEYWORDS

barriers; clients' experiences; facilitators; internet-based treatment; metasynthesis; qualitative

Introduction

Background

The high prevalence rates of psychological disorders are one of the main public health concerns in contemporary society [1,2]. Although well-established, effective psychological methods exist for the treatment of numerous disorders [3], a vast array of problems still persist, including relapse rates [4], dropout rates [5], iatrogenic and inert treatments [6], and the well-established gap between science and practice [7,8].

Specifically, the dissemination of evidence-based psychological treatments has been the subject of heated debate over the past decade [9]**.** The lack of economic resources, remote geographical settings, or the enduring the social stigma of psychological disorders is among the barriers preventing access to mental health treatment [10]**.**

In this scenario, internet-based treatments (IBTs) have emerged as a useful alternative to cope with the challenge of disseminating psychological treatments [11]. In recent years, these types of treatments have shown ample evidence of their efficacy and effectiveness for a wide range of psychological disorders and medical conditions. The most important aspect of IBTs is their potential to improve cost-effectiveness compared with face-to-face traditional therapy [12].

Early IBTs were computer-based but not delivered over the internet [13,14]. Current interventions are available over the internet and often recognized as internet-based therapies. Among the vast array of internet-based therapies or IBTs available, important differences among them must be mentioned: Some of these therapies are self-applied treatment protocols, which serve to reduce therapist support as much as possible and are sometimes even unguided. Other IBTs include some degree of therapist support, which can be delivered through emails, short message service text messages, phones calls, or videoconferences. Also, there are blended treatments, which are a combination of a self-applied IBTs and regular contact with a therapist at different points in time during the therapeutic process. Some studies also consider videoconferencing to be another kind of internet-based therapy that can be delivered through different devices, mainly computers [15,16]. Finally, smartphone-based interventions are becoming useful tools for improving access, and potentially the effectiveness, of treatments [17,18].

Apart from the numerous studies focusing on the extent to which IBTs are useful for providing psychological treatments, a considerable amount of research has also examined client experiences with these treatments. In particular, qualitative studies have been useful for analyzing clients' perceptions of a wide range of domains, including facilitators and barriers [19], acceptability [20], nonadherence [21], dropout [22], or negative effects [23] of IBTs. Nevertheless, the lack of integration of these primary studies has prevented their findings from being easily applied to new research or clinical practice.

In recent years, several developments within qualitative research have enhanced its quality standards. Moreover, the possibility of having tools to synthesize these studies may constitute a great leap forward. Metasynthesis makes it possible to draw conclusions from a wide range of primary studies that may focus on the same phenomenon from different perspectives using diverse qualitative methodologies in different contexts. Hence, metasynthesis can contribute to knowledge construction by revealing new insights from a detailed analysis of a broad range of findings [24]. Furthermore, these studies can identify research gaps, develop new theoretical and conceptual models, and provide evidence to further improve health interventions, in this case, psychological interventions [25].

As Timulak [26] explained, there are two kinds of metasyntheses: Those that aim to provide an assessment of the influence of a certain method on the results reported in primary studies and those that aim to increase knowledge about a particular phenomenon. This study follows the latter approach.

In addition, by drawing on the subjective and interpretative nature of qualitative research and not being merely aggregative, this type of synthesis can contribute to a more plausible understanding of reality and enhance its complexity (eg, by highlighting differences and discrepancies) [27].

Study Aims

The goal of this metasynthesis is to review qualitative research exploring the IBT experiences of clients with mental disorders. Furthermore, this study aims to synthesize and report these experiences to foster a deeper understanding of their experiences and improve the design of the next generation of IBTs. Our study takes into consideration client preferences that constitute 1 of the 3 legs incorporated by the American Psychological Association Presidential Task Force on Evidence-Based Practice [28]. Thus, new insights can emanate from such endeavor.

Methods

Study Registration

This metasynthesis was registered with the International Prospective Register of Systematic Reviews, registration number: CRD42018079894). The protocol was written according to the Enhancing Transparency in Reporting the Synthesis of Qualitative Research (ENTREQ statement) [27]. Instead, of using the Population, Intervention, Control and Outcomes (PICO) criteria, we used the Sample, Phenomenon of Interest, Design, Evaluation, Research type (SPIDER) tool, which was developed specifically for the synthesis of qualitative evidence [29].

Criteria for Study Inclusion

We will consider all primary qualitative studies examining the clients' experiences (eg, facilitators or barriers) of an IBT for adults (18-65 years) with a mental disorder disorders. We will consider "mental disorders" to be all those documented in the principal manuals of diagnosis, such as the Diagnostic and Statistical Manual of Mental Disorders 4th [30] or 5th edition [31] or the International Classification of Diseases 10th edition [32]. Medical conditions other than mental disorders will be excluded. To be included, a study needs to present a qualitative analysis following established methodological criteria (eg, a descriptive and interpretative approach), and the data should be

based on the reports (eg, interviews, focus groups) by participants who have undergone an IBT. In the case of mixed-methods studies, qualitative results will only be considered if they can be clearly separated from the quantitative data. Studies of completers and noncompleters will be considered, including all periods of follow-up. Additionally, eligible articles will be published in English and Spanish. There will be no restriction on the search period. As previously mentioned, all interventions delivered through web platforms or smartphone-based interventions (eg, Ecological Momentary Interventions) will be considered IBTs, regardless of the theoretical framework underlying the IBT itself.

Regarding the exclusion criteria, studies that do not follow qualitative data collection methods or do not use IBT as the intervention tool will not be included. Following Timulak's recommendations [26] for enhancing quality control, only published data will be considered. Hence, conference abstracts, unpublished manuscripts, or thesis dissertations will not be included. Moreover, studies not published in peer-reviewed journals will also be excluded.

Search Strategy

All articles will be identified through the following databases: PubMed, PsycINFO, and Web of Science. For each search string, the different aspects included in the SPIDER tool will be considered. In addition, back-tracking of references from relevant articles will also be searched for additional studies. We will also identify unpublished literature through Google searches with the same keywords and by contacting experts identified in the search of published literature.

Table 1 shows the SPIDER search strategy, and Multimedia Appendix 1 shows the PUBMED search strategy.

Selection of Studies

Two reviewers will complete all database searches, and the results obtained will be entered into Mendeley folders. All duplicates will be removed. Later, one reviewer will screen all the studies to discard irrelevant studies that may have been subject to inclusion. Next, two independent reviewers will screen all the remaining titles and abstracts to identify potentially relevant articles and then review the full texts of the relevant articles to determine eligibility. A third reviewer will resolve any discrepancies.

Quality Assessment

Two independent reviewers will assess the included studies following the Critical Appraisal Skills Programme checklist for qualitative research. This checklist allows qualitative research evidence to be appraised systematically, offering the reviewer guidance on study results, their validity, and their transferability [33]. Two independent reviewers will screen the final selection of primary studies, and a third senior reviewer (the last author of this study) will resolve any discrepancies.

Data Extraction

All reviewers on the research team will independently extract data for each study using an Excel template to include fundamental information such as author, year, aim of the study, number of participants, gender, setting or qualitative technique used. The whole study will be considered for the analysis, although the results and discussion sections will be given priority for the data extraction since they contain the core data in each study.

Table 1. Sample, Phenomenon of Interest, Design, Evaluation, Research type search strategy.

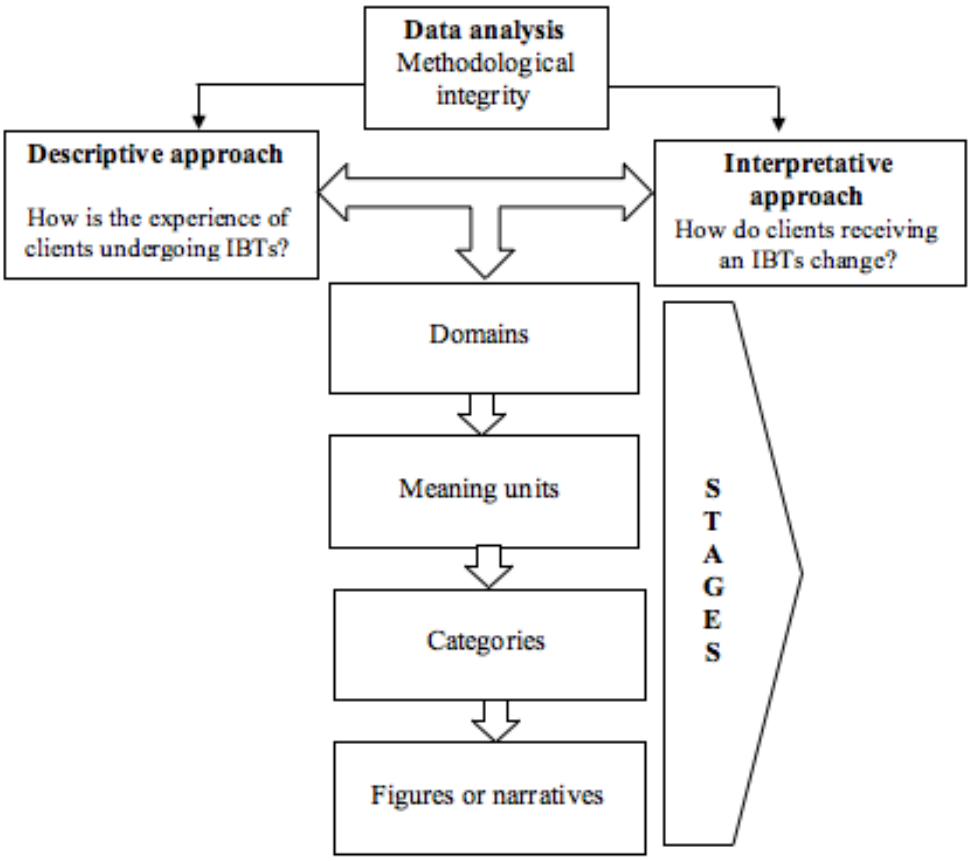
Content	Description	Examples of search terms
Sample	• Clients aged between18 and 65 years. • Clients with diagnosis of mental disorder by the Diagnostic and Statistical Manual of Mental Disorders or International Classification of Diseases undergoing IBT[a].	• "adult" OR "client'" OR "user'" OR "patient'." • "mental disorder" OR "psychological disorder."
Phenomenon of interest	• Clients' experiences or perceptions of a vast array of domains undergoing an IBT.	• "facilitators" OR "barriers" OR "acceptability" OR "adherence" OR "dropout" OR "negative effects." • "Internet" OR "Internet based treatments" OR "online treatments" OR "Internet interventions" OR "e-therapy" OR "web based" OR "self-applied" OR "blended" OR "computer-based" OR "smartphone based intervention."
Design	• Studies that allow the extraction of qualitative data.	• "Interviews" OR "focus groups" OR "questionnaire" OR "survey" OR "e-mail."
Evaluation	• Experiences, perspectives, insights, motivations or views of participants undergoing an IBT (outcome measures).	• "experience" OR "view" OR "opinion" OR "attitude" OR "perception" OR "belie*" OR "belief" OR "feeling."
Research type	• Qualitative studies or mixed-methods studies.	• "qualitative" OR "mixed method."

[a]IBT: internet-based treatment.

Data Analysis

Following the guidelines of Elliott and Timulak [34], we will adopt a descriptive and interpretative approach. This method makes it possible to include a more phenomenological perspective by first describing the primary studies in detail, then complementing this description with a hermeneutical perspective that goes beyond the given information to reach new conclusions. Specifically, this approach includes four stages in which the data analysis process is carried out. First, the collected data are ordered into domains, which represent high-order conceptualizations of the phenomenon. Second, meaning units are outlined that represent the smallest understandable piece of information from the data. Domains provide a conceptual and flexible framework for the data and can be modified by the researcher until they fit the data. Third, the meaning units are organized into categories and classified in the existing domains. The creation of categories is an interpretative process in which the researcher will strive to respect the data and use category labels close to the original language provided by the participants [35]. If there are similarities between the established categories, second-order categories could be organized. Finally, the results will be presented in different forms, such as figures or narratives, to better grasp the phenomena. We will ensure methodological integrity (in terms of fidelity and utility) by following the recommendations of Levitt, Motulosky, Wertz, Morrow, and Ponterotto [36]. Thus, the different considerations at both the data collection and data analysis levels will be fulfilled. All the researchers involved in the analytic process will have extensive experience in the use of technologies to deliver psychological treatments. Figure 1 shows the data analysis process that will be conducted. In total, 5 researchers (authors 1 to 5) will be in charge of the data analysis. Each researcher will develop a domain structure that will finally be discussed in an iterative process until a consensus among all the alternatives is met. To delineate meaning units, the final number of primary studies will be divided among the coders while still ensuring that every study will be coded by two researchers in order to guarantee methodological rigor. For this second step, an iterative process will also be conducted to reach a consensus. Additionally, through this iterative process, categories that capture the fundamental sense of the meaning units will be elaborated [26].

Figure 1. Methodological stages of the metasynthesis. IBT: internet-based treatment.



Results

The project was initiated in 2017 and searches were completed in 2018. Data analysis is currently under way and the first results are expected to be submitted for publication in 2019.

Discussion

Principal Findings

Although an abundance of qualitative studies has been published in recent years, few studies have attempted to synthesize the results. This synthesis is an essential step toward outlining more general conclusions about the experiences of clients undergoing IBTs. As long as available, IBTs do not differ much (at least in

their general features), the overall experiences can be consistently integrated. In particular, qualitative studies have focused on studying topics such as facilitators, barriers, acceptability, adherence, dropouts, and negative effects. This metasynthesis will more accurately weigh the extent to which different topics related to client experiences have been addressed, in addition to establishing taxonomy within each of these topics in order to foster its use in new research studies and in the clinical application of IBTs.

Our findings will make it possible to create a hierarchy of domains based on their relevance across all the primary studies. In this regard, a conceptual framework of the barriers and facilitators perceived by the clients will be developed. Implications and recommendations for clinical practice, research, and training will be suggested.

Potential Sources of Limitations

First and foremost, as in any other kind of review, the findings will depend on the quality of the primary studies included. Although there will be a particular emphasis on assessing the quality of the primary studies, it is a difficult task to accurately assess these kinds of studies. Moreover, there may be relevant studies in other languages that will not be included because only English and Spanish articles will be considered.

Furthermore, metasynthesis is a powerful tool for drawing overall conclusions from a certain topic. However, it may be subject to the potential underrepresentation of the richness of primary studies given that the material of analysis is not the raw data of each included study.

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Conflicts of Interest

None declared.

Multimedia Appendix 1

PubMed search string.

[PDF File (Adobe PDF File), 25KB - resprot_v7i11e183_app1.pdf]

References

1. Kessler RC, Petukhova M, Sampson NA, Zaslavsky AM, Wittchen H. Twelve-month and lifetime prevalence and lifetime morbid risk of anxiety and mood disorders in the United States. Int J Methods Psychiatr Res 2012 Sep;21(3):169-184 [FREE Full text] [doi: 10.1002/mpr.1359] [Medline: 22865617]
2. Olesen J, Gustavsson A, Svensson M, Wittchen H, Jönsson B, CDBE2010 SG, et al. The economic cost of brain disorders in Europe. Eur J Neurol 2012 Jan;19(1):155-162. [doi: 10.1111/j.1468-1331.2011.03590.x] [Medline: 22175760]
3. Nathan P, Gorman J. A guide to treatments that work. 4th edition. New York: Oxford University Press; 2015:9780199342211.
4. Steinert C, Hofmann M, Leichsenring F, Kruse J. What do we know today about the prospective long-term course of social anxiety disorder? A systematic literature review. J Anxiety Disord 2013 Oct;27(7):692-702. [doi: 10.1016/j.janxdis.2013.08.002] [Medline: 24176803]
5. Swift JK, Greenberg RP. A treatment by disorder meta-analysis of dropout from psychotherapy. Journal of Psychotherapy Integration 2014;24(3):193-207. [doi: 10.1037/a0037512]
6. Lilienfeld SO. Psychological Treatments That Cause Harm. Perspect Psychol Sci 2007 Mar;2(1):53-70. [doi: 10.1111/j.1745-6916.2007.00029.x] [Medline: 26151919]
7. Beutler LE, Williams RE, Wakefield PJ, Entwistle SR. Bridging scientist and practitioner perspectives in clinical psychology. Am Psychol 1995 Dec;50(12):984-994. [Medline: 8561382]
8. Castonguay L, Barkham M, Lutz W, McAleavey A. Practice-oriented research: Approaches and application. In: Lambert MJ editor. Bergin and Garfield?'s handbook of psychotherapy and behavior change. 6th ed. New York: Wiley; 2013:85-133.
9. McHugh RK, Barlow DH. The dissemination and implementation of evidence-based psychological treatments. A review of current efforts. Am Psychol 2010;65(2):73-84. [doi: 10.1037/a0018121] [Medline: 20141263]
10. Kazdin AE, Blase SL. Rebooting Psychotherapy Research and Practice to Reduce the Burden of Mental Illness. Perspect Psychol Sci 2011 Jan;6(1):21-37. [doi: 10.1177/1745691610393527] [Medline: 26162113]
11. Andersson G, Titov N. Advantages and limitations of Internet-based interventions for common mental disorders. World Psychiatry 2014 Feb;13(1):4-11 [FREE Full text] [doi: 10.1002/wps.20083] [Medline: 24497236]
12. Andersson G. Internet-Delivered Psychological Treatments. Annu Rev Clin Psychol 2016;12:157-179. [doi: 10.1146/annurev-clinpsy-021815-093006] [Medline: 26652054]

13. Botella C, Hofmann SG, Moscovitch DA. A self-applied, Internet-based intervention for fear of public speaking. J Clin Psychol 2004 Aug;60(8):821-830. [doi: 10.1002/jclp.20040] [Medline: 15241810]
14. Marks IM, Kenwright M, McDonough M, Whittaker M, Mataix-Cols D. Saving clinicians' time by delegating routine aspects of therapy to a computer: a randomized controlled trial in phobia/panic disorder. Psychol Med 2004 Jan;34(1):9-17. [Medline: 14971623]
15. Berger T. Internet-based psychotherapy treatments. 2014 URL: http://societyforpsychotherapy.org/Internet-based-psychotherapy-treatments/ [accessed 2018-09-27] [WebCite Cache ID 72kaBjy8L]
16. Berger T. The therapeutic alliance in internet interventions: A narrative review and suggestions for future research. Psychother Res 2017 Sep;27(5):511-524. [doi: 10.1080/10503307.2015.1119908] [Medline: 26732852]
17. Cuijpers P, Kleiboer A, Karyotaki E, Riper H. Internet and mobile interventions for depression: Opportunities and challenges.Depress Anxiety. Depression and Anxiety 2017;34(7):569-602. [doi: 10.1002/da.22641]
18. Firth J, Torous J, Nicholas J, Carney R, Pratap A, Rosenbaum S, et al. The efficacy of smartphone-based mental health interventions for depressive symptoms: a meta-analysis of randomized controlled trials. World Psychiatry 2017;16(3):287-298.
19. Roberge P, Hudon C, Pavilanis A, Beaulieu M, Benoit A, Brouillet H, et al. A qualitative study of perceived needs and factors associated with the quality of care for common mental disorders in patients with chronic diseases: the perspective of primary care clinicians and patients. BMC Fam Pract 2016 Dec 13;17(1):134 [FREE Full text] [doi: 10.1186/s12875-016-0531-y] [Medline: 27620166]
20. Richards D, Murphy T, Viganó N, Timulak L, Doherty G, Sharry J, et al. Acceptability, satisfaction and perceived efficacy of “Space from Depression” an internet-delivered treatment for depression. Internet Interv 2016 Sep;5:12-22 [FREE Full text] [doi: 10.1016/j.invent.2016.06.007] [Medline: 30135802]
21. Johansson O, Michel T, Andersson G, Paxling B. Experiences of non-adherence to Internet-delivered cognitive behavior therapy: A qualitative study. Internet Interventions 2015 May;2(2):137-142. [doi: 10.1016/j.invent.2015.02.006]
22. Fernández-Álvarez J, Díaz-García A, González-Robles A, Baños R, García-Palacios A, Botella C. Dropping out of a transdiagnostic online intervention: A qualitative analysis of client's experiences. Internet Interventions 2017 Dec;10:29-38. [doi: 10.1016/j.invent.2017.09.001]
23. Rozental A, Boettcher J, Andersson G, Schmidt B, Carlbring P. Negative effects of internet interventions: a qualitative content analysis of patients' experiences with treatments delivered online. Cogn Behav Ther 2015;44(3):223-236. [doi: 10.1080/16506073.2015.1008033] [Medline: 25705924]
24. Sandelowski M, Docherty S, Emden C. Qualitative metasynthesis: issues and techniques. Res. Nurs. Health 1997;20:365-371. [doi: 10.1002/(SICI)1098-240X(199708)20:4<365::AID-NUR9>3.0.CO;2-E]
25. Schreiber R, Crooks D, Stern P. Completing a qualitative project: Details and dialogue. In: Morse JM editor. Thousand Oaks, CA: Sage; 1997:311-326.
26. Timulak L. Meta-analysis of qualitative studies: a tool for reviewing qualitative research findings in psychotherapy. Psychother Res 2009 Jul;19(4-5):591-600. [doi: 10.1080/10503300802477989] [Medline: 19034804]
27. Tong A, Flemming K, McInnes E, Oliver S, Craig J. Enhancing transparency in reporting the synthesis of qualitative research: ENTREQ. BMC Med Res Methodol 2012;12:181 [FREE Full text] [doi: 10.1186/1471-2288-12-181] [Medline: 23185978]
28. APA Presidential Task Force on Evidence-Based Practice. Evidence-based practice in psychology. Am Psychol 2006;61(4):271-285. [doi: 10.1037/0003-066X.61.4.271] [Medline: 16719673]
29. Cooke A, Smith D, Booth A. Beyond PICO: the SPIDER tool for qualitative evidence synthesis. Qual Health Res 2012 Oct;22(10):1435-1443. [doi: 10.1177/1049732312452938] [Medline: 22829486]
30. American Psychiatry Association. Diagnostic Statistical Manual of Mental Disorders (DSM-IV-TR), 4th Edition. Arlington, VA: American Psychiatric Association; 2000.
31. American Psychiatry Association. Diagnostic Statistical Manual of Mental Disorders DSM-5, Fifth Edition. Arlington, Va: American Psychiatric Publishing; 2013:18.
32. World Health Organization. International Classification of Diseases. 2016. URL: http://www.who.int/classifications/icd/en/ [accessed 2018-09-27] [WebCite Cache ID 72kbPwJ7N]
33. Critical Appraisal Skills Programme (CASP). Qualitative research checklist. 2013 URL: https://casp-uk.net/ [accessed 2018-09-27] [WebCite Cache ID 72kbXSK4H]
34. Elliott R, Timulak L. Descriptive interpretive approaches to qualitative research. In: Miles J, Gilbert P, editors. Gilbertditors. A handbook of research methods in clinical and health psychology. Oxford, UK: Oxford University Press; 2005.
35. Hill CE, Thompson BJ, Williams EN. A Guide to Conducting Consensual Qualitative Research. The Counseling Psychologist 2016 Jun 30;25(4):517-572. [doi: 10.1177/0011000097254001]
36. Levitt HM, Motulsky SL, Wertz FJ, Morrow SL, Ponterotto JG. Recommendations for designing and reviewing qualitative research in psychology: Promoting methodological integrity. Qualitative Psychology 2017;4(1):2-22. [doi: 10.1037/qup0000082]

Abbreviations

IBT: internet-based treatment
SPIDER: Sample, Phenomenon of Interest, Design, Evaluation, Research type

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Protocol

Parental Activation and Obesity-Related Health Behaviors Among a Racially and Ethnically Diverse Population of Low-Income Pediatric Patients: Protocol for a Cross-Sectional Survey Study

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Abstract

Background: Despite a recent decline in the obesity prevalence among preschool-aged children, obesity remains disproportionately high among children from low-income racial or ethnic minority families. Promoting healthy lifestyles (eg, obesity-preventative behaviors) in primary care settings is particularly important for young children, given the frequency of preventative health visits and parent-provider interactions. Higher adoption of specific health behaviors is correlated with increased patient activation (ie, skill, confidence, and knowledge to manage their health care) among adults. However, no published study, to date, has examined the relationship between parental activation and obesity-related health behaviors among young children.

Objective: The goal of this study is to measure parental activation in low-income parents of preschoolers in 2 large health systems and to examine the association with diet, screen-time, and physical activity behaviors.

Methods: We will conduct a cross-sectional study of parents of preschool-aged patients (2-5 years) receiving primary care at multiple clinic sites within 2 large health care systems. Study participants, low-income black, Hispanic, and white parents of preschool-aged patients, are being recruited across both health systems to complete orally administered surveys.

Results: Recruitment began in December 2017 and is expected to end in May 2018. A total of 267 low-income parents of preschool-aged children have been enrolled across both clinic sites. We are enrolling an additional 33 parents to reach our goal sample size of 300 across both health systems. The data analysis will be completed in June 2018.

Conclusions: This protocol outlines the first study to fully examine parental activation and its relationship with parent-reported diet, physical activity, and screen-time behaviors among low-income preschool-aged patients. It involves recruitment across 2 geographically distinct areas and resulting from a partnership between researchers at 2 different health systems with multiple clinical sites. This study will provide new knowledge about how parental activation can potentially be incorporated as a strategy to address childhood obesity disparities in primary care settings.

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KEYWORDS

activation; parent; child; health behaviors; obesity; primary care

Introduction

Racial and ethnic minority preschoolers (aged 2-5 years) are disproportionately affected by obesity and are, consequently, at higher risk for obesity-related health outcomes, including adult obesity, diabetes, and cardiovascular disease [1,2]. Effective obesity prevention and treatment programs in clinical settings are a key component of multisector efforts to halt and reverse the childhood obesity epidemic [3]. The American Academy of Pediatrics recommends that obesity screening and healthy weight counseling be integrated into all pediatric well-child visits beginning in infancy and that the counseling include promotion of a healthful diet and developmentally appropriate physical activity behaviors [4]. For young children, this includes paying particular attention to assessing feeding, screen-time, and physical activity-related behaviors and providing anticipatory guidance and counseling [4].

A healthful diet and physical activity behaviors and the adherence to physician recommendations have been linked to patient activation among adults [5,6]. Patient activation refers to skill, confidence, and knowledge in managing one's health [7]. Research suggests that racial or ethnic minorities have lower activation than white individuals [8]. However, most research in this field focuses on the activation in adults regarding their *own* health.

In spite of the existing evidence base supporting a linkage between the adult patient activation and positive health-related behaviors, research exploring the relationship between parents' activation on behalf of their children's health and elucidating the potential mechanisms underscoring these relationships is lacking. Describing the relationship between parental activation and child healthful diet and physical activity behaviors is informative to the development of interventions utilizing parental activation to address disparities in obesity among young primary care patients.

The aims of this project are to examine differences in parental activation by race or ethnicity and explore the relationship between parental activation and parent-reported diet, physical activity, and screen-time behaviors. We hypothesize that the activation will be lower among black and Hispanic parents versus white parents and that parental activation will be positively associated with healthful diet, screen-time, and physical activity behaviors among young primary care patients.

Methods

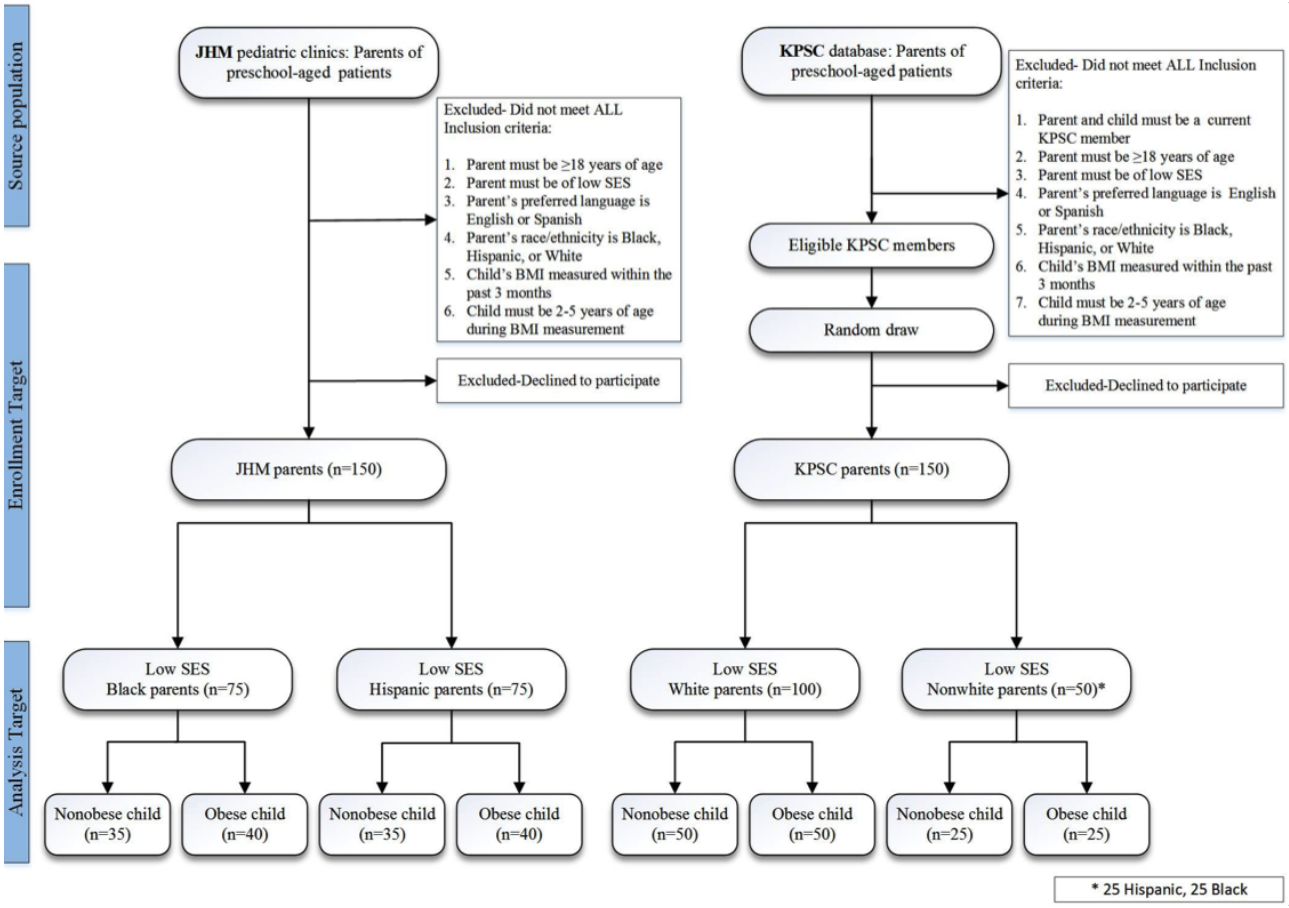
Study Population and Settings

Study participants are being recruited from 2 different health systems, Johns Hopkins Medicine (JHM) and Kaiser Permanente Southern California (KPSC). The JHM pediatric primary care clinics are located in Baltimore, MD, and serve a predominant low-income, black, and Hispanic patient population. Kaiser Permanente, the largest integrated health care system in Southern California, serves a predominantly Hispanic and socioeconomically diverse pediatric population [9,10]. The obesity prevalence and disparities among preschoolers receiving care at KPSC pediatric primary care clinics mirror national trends [11]. About 13.01% (18,315/140,733) of KPSC preschoolers are obese. At this very young age, Hispanic and black preschoolers are more likely to be obese than their non-Hispanic white counterparts (12,703/78,703, 16.14%, and 1340/11,162, 12.01%, respectively, vs 2055/25,967, 7.91%) [11]. At JHM, the pattern for obesity among preschoolers is similar, specifically among young Hispanic patients; 23.3% (211/904) of preschool-aged Hispanic patients are obese compared with 14.1% (35/249) of white patients [12].

Recruitment Strategies

Eligible participants are being identified from the electronic medical records (EMRs) at both sites (Figure 1). Parents whose preferred health care language is English or Spanish are eligible to participate if they are (1) aged ≥18 years; (2) of low socioeconomic status (defined by the receipt of Medicaid insurance); (3) a parent of a child aged 2-5 years with height and weight measured in the past 3 months; and (4) black, Hispanic, or white by self-report. From the eligible KPSC source population, lists of potential participants were created in 2 waves by randomly selecting a subset of eligible patients through the EMR. Specifically, an initial random sample of 300 children (200 white and 100 nonwhite) was selected, which consisted of 50% (150/300) nonobese children and 50% (150/300) obese children. The random selection was performed while applying a normal distribution centered at the 50th percentile of body mass index (BMI)-for-age for nonobese and the 97th percentile for obese children. Given the high prevalence of overweight and obesity in this population, the random selection of normally distributed BMIs around the 50th and 97th percentile was chosen to avoid 2 groups of children clustering around the obesity cutoff of the 95th percentile. A second random draw of 175 (100 white, 50 black, and 25 Hispanic children) from the prior sample was then conducted. Oversampling was conducted on the basis of prior response rates to achieve the final intended sample size of 150 children, as indicated in Figure 1. At KPSC, introduction emails were sent to invite randomly selected parents to participate, and follow-up phone calls were conducted to complete surveys. At JHM sites, a convenience sample of low socioeconomic status parents of preschoolers presenting for care is identified based on the EMR review and recruited in real-time during clinic visits to participate in a survey. We will collect data from parents of nonobese (defined as normal weight and overweight: BMI-for-age percentile of 5th-85th) and obese (BMI-for-age percentile ≥95th) children. Because the majority of preschool-aged children will be normal weight, we oversampled parents of children who are overweight or obese. Figure 1 presents the sampling strategy for both clinical sites.

Figure 1. Study design and recruitment targets. JHM: Johns Hopkins Medicine; KPSC: Kaiser Permanente Southern California; SES: socioeconomic status; BMI: body mass index.



Data Collection

Surveys are administered in the preferred language of participants (English or Spanish). Surveys will be conducted by telephone at KPSC sites and in-person at JHM sites. The following clinical and sociodemographic data will be collected from children's EMR: most recent weight, height, BMI or BMI percentile, age, gender, race, ethnicity, and insurance type. The child EMR data are linked with the parental survey data at both sites. Study data are being collected and managed across sites using Research Electronic Data Capture (REDCap) electronic data capture tools hosted at John's Hopkins Medicine [13]. REDCap is a secure, Web-based app designed to support data capture for research studies, providing (1) an intuitive interface for validated data entry; (2) audit trails for tracking data manipulation and export procedures; (3) automated export procedures for seamless data downloads to common statistical packages; and (4) procedures for importing data from external sources [13]. Table 1 provides a summary of the survey and EMR data currently being collected.

Measures and Statistical Analysis Plan

Parental activation concerning their child's health is the primary study outcome and is being assessed using the Parent-Patient Activation Measure (Parent-PAM), a standardized 13-item survey adapted from the well-validated adult Patient Activation Measure (PAM) [7,14]. The Parent-PAM has high internal consistency and reliability among low-income Spanish and English-speaking patients and assesses parents' knowledge, confidence, and willingness to act concerning their child's health [14,15]. The Parent-PAM is scored on a Likert scale, and responses are scored on a scale from 0 to 100, with higher scores corresponding to higher activation [14].

Secondary study outcomes are as follows: parent-reported feeding, screen-time, and physical activity behaviors. Parents' child feeding behaviors will be measured using questionnaires assessing the parental report of feeding sugar-sweetened beverages, fruits and vegetables, and fast food. The survey includes items adapted from the Timing and Frequency of Infant Sugar-Sweetened Beverage Consumption Questionnaire and the Preschool-aged Children's Physical Activity Questionnaire, which includes measures of screen time [16,17]. Because a prior study found that the parent self-activation was associated with parental activation concerning their child's health [18], parent self-activation is being measured using the PAM. Furthermore, given the correlation between parent self-activation and activation on behalf of their child's health, study participants will be randomly assigned to 1 of 2 groups with the alternating ordering of the PAM and related Parent-PAM to minimize order bias in the survey. Multimedia Appendix 1 shows a copy of the survey.

Table 1. Collection of electronic medical records and survey data by study site.

Measurement or collection method	Site	
	Johns Hopkins Medicine	Kaiser Permanente Southern California
Surveys		
Parental activation	✓	✓
Parent self-activation	✓	✓
Child sociodemographic[a]	✓	✓
Parent sociodemographic[a]	✓	✓
Parent feeding, screen-time and physical activity behaviors	✓	✓
Parent height and weight	✓	✓
Parent health literacy	✓	✓
Parent preferred language (medical care)	✓	✓
Parent English language proficiency	✓	✓
Parent nativity and immigrant generational status	✓	✓
Electronic medical records		
Child height, weight, or body mass index or body mass index percentile	✓	✓
Child sociodemographics[a]	✓	✓
Child medical insurance	✓	✓
Child health status	✓	✓
Parent medical insurance[b]	N/A[c]	✓
Parent body mass index or body mass index percentile[b]	N/A	✓
Parent sociodemographics[a,b]	N/A	✓

[a]Sociodemographic data collected from surveys and electronic medical records: race and ethnicity, gender, age, educational attainment, employment status, marital status, household income level, neighborhood income, and neighborhood education (determined on the basis of geocoding of addresses and census block information for Kaiser Permanente Southern California site only).

[b]Data not collected from electronic medical records at Johns Hopkins Medicine site.

[c]N/A: not applicable.

Covariates for parents and preschoolers will be included in analyses as follows: (1) parent self-activation (measured using the PAM), parental health care language, health literacy, nativity and immigrant generational status, English language proficiency, race or ethnicity, age, gender, educational attainment, employment status, self-reported height and weight, and study site (JHM or KPSC) and (2) child race or ethnicity, gender, age, health insurance, health status, and BMI.

Descriptive statistics for all variables, including the mean, median, SDs, and frequencies, will be calculated prior to conducting the primary analyses. The Pearson chi-square test or Fisher exact test (in cases of sparse data) for categorical variables and the analysis of variance or the Kruskall-Wallis test for continuous variables will be calculated to assess differences between parental activation scores.

Multivariable regression analyses will be used to test all hypotheses, adjusted for key covariates, including study site. We will consider all covariates as potential candidate variables and will create the final models based on the best fit using the Bayesian information criterion, the corrected Akaike information criterion, and residual analysis. In addition, descriptive analyses will be performed to explore if there are differences by all variables by study site.

To guide our sample size and power estimates for aim 1, we used available data from previously published data in the adult patient activation literature. We estimate a 20% difference in activation levels between racial or ethnic minority and white parents [8]. Assuming a fixed sample size of 300 parents with equal numbers of black, Hispanic, and white parents, we will have 96% power respectively to detect a statistically significant difference ($P<.05$) in parental activation for Hispanic versus white parents.

Ethics and Consent

The study received approval from the Johns Hopkins' Institutional Review Board, as well as KPSC's Institutional Review Board. Informed oral consent is being obtained from all participants. Participants are free to withdraw from the study at any time and can refuse to answer any question.

Results

Recruitment for the study has commenced at both clinical sites in December 2017. Study enrollment is expected to end by May 2018, and the data analysis is expected to commence in May 2018. Figure 1 provides details on enrollment and recruitment targets.

Discussion

Expected Results and Future Directions

Upon completion of this study, we anticipate the following results: parental activation scores for the overall study sample, by clinical site (KPSC vs JHM), and by race or ethnicity (white, Hispanic, and black), noting any detected differences between racial or ethnic subgroups. Additionally, we will have results of analyses testing the association between parental activation and parent-reported healthful diet, physical activity, and screen-time behaviors. Our findings will inform the planning of a larger study. Specifically, if as anticipated, we find a positive relationship between parental activation and obesity-preventative behaviors, we will utilize these findings to guide the development of a primary care-based intervention targeting increasing parental activation to promote healthful diet, screen-time, and physical activity behaviors among low-income preschool-aged children.

Study Rigor and Reproducibility

To address rigor and reproducibility, a mixed study design is being used—one that incorporates EMR-guided convenience sampling (JHM) and a randomized approach to participant selection (KPSC). The advanced integrated EMR system used by KPSC allows for greater recruitment precision in this study. In addition, we are using the randomization of survey activation measure ordering as a key strategy to minimize survey bias, given the correlation with parent self-activation and parental activation. Such study design approaches improve the level of rigor realistically possible in a study that mimics the real-world clinical recruitment. To promote study reproducibility, we will make every effort to give complete, detailed descriptions of methods and analyses in future publications, given that wide dissemination is a key goal of the project. Details of the recruitment process, participant demographics, and factors for potential response heterogeneity will be published and made available for future replication in other settings.

Limitations

We acknowledge some limitations of this study. This study uses convenience sampling to recruit participants from the JHM study site. While this sampling strategy is the most practical and feasible recruitment mechanism at this particular site, we recognize that nonrandomized convenience sampling may introduce selection bias; to explore this, we will conduct a comparative analysis of study participants' characteristics (using demographic and electronic health record data) across the 2 sites. In addition, we will compare study participants to the general population of 2-5-year-old patients at each site to further assess the extent to which study participants are representative of the overall clinic population with respect to demographic characteristics [12]. This comparative analysis will focus on the characteristics that are most likely to be associated with the exposures and outcomes of interests (eg, child BMI distribution, number of clinic visits in a 12-month period).

Furthermore, we will explore if there are any between-site differences in our results, as described in the Methods section. Another limitation of this study is the inability to capture information of other sample characteristics that may be associated with parental activation and obesity-related health behaviors. These factors include the parental perception of the health care system, neighborhood access to healthful food items, and residential proximity to outdoor play space. Future research should explore the influence of additional parent- and neighborhood-level factors on parental activation and its relationship with obesity-related health behaviors.

Conclusions

This protocol represents the first description of parental activation and its potential association with diet, screen-time, and physical activity behaviors among low-income, racial or ethnically diverse preschool-aged children in primary care settings. Delineation of parental activation among this population and understanding the relationship between parental activation and children's diet, screen-time, and physical activity behaviors can guide the development of targeted approaches to clinic-based obesity management programs.

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Conflicts of Interest

None declared.

Multimedia Appendix 1

Copy of Study Survey.

[PDF File (Adobe PDF File), 88KB - resprot_v7i11e182_app1.pdf]

References

1. Ogden CL, Carroll MD, Kit BK, Flegal KM. Prevalence of obesity and trends in body mass index among US children and adolescents, 1999-2010. JAMA 2012 Feb 1;307(5):483-490. [doi: 10.1001/jama.2012.40] [Medline: 22253364]
2. Wang Y, Beydoun MA. The obesity epidemic in the United States--gender, age, socioeconomic, racial/ethnic, and geographic characteristics: a systematic review and meta-regression analysis. Epidemiol Rev 2007;29:6-28. [doi: 10.1093/epirev/mxm007] [Medline: 17510091]
3. Committee on Accelerating Progress in Obesity Prevention; Food and Nutrition Board; Institute of Medicine. In: Glickman D, Parker L, Sim LJ, Del Valle Cooke H, Miller EA, editors. Accelerating progress in obesity prevention: solving the weight of the nation. Washington, DC: National Academies Press; May 2012.
4. Bright Futures Guidelines for Health Supervision of Infants, Children & Adolescents,Promoting Healthy Weight. Available at: Accessed April 25, 2018 URL: https://brightfutures.aap.org/materials-and-tools/guidelines-and-pocket-guide/Pages/default.aspx
5. Hibbard JH, Greene J. What the evidence shows about patient activation: better health outcomes and care experiences; fewer data on costs. Health Aff (Millwood) 2013 Feb;32(2):207-214. [doi: 10.1377/hlthaff.2012.1061] [Medline: 23381511]
6. Greene J, Hibbard JH, Sacks R, Overton V, Parrotta CD. When patient activation levels change, health outcomes and costs change, too. Health Aff (Millwood) 2015 Mar 1;34(3):431-437. [doi: 10.1377/hlthaff.2014.0452] [Medline: 25732493]
7. Hibbard JH, Stockard J, Mahoney ER, Tusler M. Development of the Patient Activation Measure (PAM): conceptualizing and measuring activation in patients and consumers. Health Serv Res 2004 Aug;39(4 Pt 1):1005-1026 [FREE Full text] [doi: 10.1111/j.1475-6773.2004.00269.x] [Medline: 15230939]
8. Cunningham PJ, Hibbard J, Gibbons CB. Raising low 'patient activation' rates among Hispanic immigrants may equal expanded coverage in reducing access disparities. Health Aff (Millwood) 2011 Oct;30(10):1888-1894 [FREE Full text] [doi: 10.1377/hlthaff.2009.0805] [Medline: 21976331]
9. Koebnick C, Coleman KJ, Black MH, Smith N, Der-Sarkissian JK, Jacobsen SJ, et al. Cohort profile: the KPSC Children's Health Study, a population-based study of 920 000 children and adolescents in southern California. Int J Epidemiol 2012 Jun;41(3):627-633 [FREE Full text] [doi: 10.1093/ije/dyq252] [Medline: 21257603]
10. Koebnick C, Langer-Gould AM, Gould MK, Chao CR, Iyer RL, Smith N, et al. Sociodemographic characteristics of members of a large, integrated health care system: comparison with US Census Bureau data. Perm J 2012;16(3):37-41 [FREE Full text] [Medline: 23012597]
11. Koebnick C, Mohan YD, Li X, Young DR. Secular Trends of Overweight and Obesity in Young Southern Californians 2008-2013. J Pediatr 2015 Dec;167(6):1264-71.e2. [doi: 10.1016/j.jpeds.2015.08.039] [Medline: 26421485]
12. Showell N, Cole KW, Johnson K, DeCamp LR, Bair-Merritt M, Thornton RLJ. Neighborhood and Parental Influences on Diet and Physical Activity Behaviors in Young Low-Income Pediatric Patients. Clin Pediatr (Phila) 2017 Nov;56(13):1235-1243 [FREE Full text] [doi: 10.1177/0009922816684599] [Medline: 28024417]
13. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)--a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform 2009 Apr;42(2):377-381 [FREE Full text] [doi: 10.1016/j.jbi.2008.08.010] [Medline: 18929686]
14. Insignia Health. Patient Activation Measure. URL: https://www.insigniahealth.com/products/pam-survey [accessed 2018-09-20] [WebCite Cache ID 72ZmMRRIN]
15. DeCamp LR, Leifheit K, Shah H, Valenzuela-Araujo D, Sloand E, Polk S, et al. Cross-cultural validation of the parent-patient activation measure in low income Spanish- and English-speaking parents. Patient Educ Couns 2016 Dec;99(12):2055-2062 [FREE Full text] [doi: 10.1016/j.pec.2016.07.003] [Medline: 27444234]
16. Taveras EM, Gortmaker SL, Hohman KH, Horan CM, Kleinman KP, Mitchell K, et al. Randomized controlled trial to improve primary care to prevent and manage childhood obesity: the High Five for Kids study. Arch Pediatr Adolesc Med 2011 Aug;165(8):714-722 [FREE Full text] [doi: 10.1001/archpediatrics.2011.44] [Medline: 21464376]
17. Dwyer GM, Hardy LL, Peat JK, Baur LA. The validity and reliability of a home environment preschool-age physical activity questionnaire (Pre-PAQ). Int J Behav Nutr Phys Act 2011 Aug 04;8:86 [FREE Full text] [doi: 10.1186/1479-5868-8-86] [Medline: 21813025]
18. Pennarola BW, Rodday AM, Mayer DK, Ratichek SJ, Davies SM, Syrjala KL, HSCT-CHESS Study. Factors associated with parental activation in pediatric hematopoietic stem cell transplant. Med Care Res Rev 2012 Apr;69(2):194-214 [FREE Full text] [doi: 10.1177/1077558711431460] [Medline: 22203645]

Abbreviations

BMI: body mass index
EMR: electronic medical record
JHM: Johns Hopkins Medicine
KPSC: Kaiser Permanente Southern California
PAM: Patient Activation Measure

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Protocol

Assessing and Improving the Use of Online Information About Child Development, Education, Health, and Well-Being in Low-Education, Low-Income Parents: Protocol for a Mixed-Methods Multiphase Study

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Abstract

Background: This study is born from a partnership between Web editors of *Naître et grandir* (N&G) and *AboutKidsHealth* (AKH) and researchers who developed and validated the Information Assessment Method (IAM). N&G and AKH are popular Canadian websites with high-quality comprehensive information about child development, education, health, and well-being. IAM allows parents to assess online information and provide feedback to Web editors. High-quality online consumer health information improves knowledge, self-efficacy, and health. However, low-socioeconomic status (SES) parents underuse N&G and IAM, despite these parents being more likely to report decreased worries and increased confidence as outcomes from N&G information.

Objective: The study is aimed to improve low-SES parents' use of online child information and interaction with Web editors and explore subsequent health outcomes for parents and children.

Methods: Multiphase mixed-methods design. Our general approach is centered on organizational participatory research. In phase 1, we will conduct a qualitative interpretive study to identify barriers and facilitators to using N&G information and to interacting with N&G editors via IAM; interview more than 10 low-SES parents about their experience with N&G and IAM and more than 10 nonusers of N&G and IAM; and use thematic analysis to identify main barriers and facilitators. In phase 2, we will integrate parents' views (phase 1 findings) in N&G and IAM and implement a new version: IAM+N&G+. In phase 3, we will conduct a quantitative prospective longitudinal study (pre-/postimplementation monitoring of knowledge use and outcomes). We will compare the use of original (IAM and N&G) and new (IAM+ and N&G+) versions using Google Analytics variables, IAM variables, a material and social deprivation index, and demographics. We anticipate increased use post implementation (linear mixed modeling). In phase 4, we will conduct a qualitative descriptive study on outcomes of information use. We will interview

more than 30 low-SES parents who receive and rate the N&G+ newsletter using IAM+ and analyze data in the form of life histories to describe how parents and children experience perceived outcomes.

Results: The project was funded in 2017 by the Canadian Institutes of Health Research and received an ethics approval by the McGill University's institutional review board. Data collection for phase 1 was completed in 2018. Phases 2 to 4 will be conducted until 2020. Findings from this study will also be used to develop a free toolkit, useful to all Web editors, with recommendations for improving health information for low-SES persons and interactions with them using IAM.

Conclusions: The results of this study will provide a deep understanding of how low-SES parents use online child information and interact with Web editors. Following the implementation of IAM+N&G+, results will also elucidate subsequent health outcomes for low-SES parents and children after interaction with Web editors has been optimized.

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KEYWORDS

consumer health information; information technology; primary health care; knowledge translation; literacy; vulnerable populations

Introduction

Rationale

Early life experience is a determinant of social inequalities in physical, mental, and social well-being [1-6]. Children living in poverty are more likely to suffer from developmental and health problems, and childhood interventions can decrease incidence and prevalence of these problems [7-12]. The proposed project is aimed to assess and improve a childhood intervention: the *Naître et grandir* (N&G) website and newsletter on child development, education, health, and well-being, which includes the Information Assessment Method (IAM) that allows N&G readers to continuously assess, and subsequently the N&G editors to improve, the content shared on the N&G website and newsletter.

Parents with low education and low income, hereafter referred to as parents with low socioeconomic status (SES), typically have a low literacy level (limited ability to acquire, understand, evaluate, and use written information). Low parental literacy level is particularly detrimental to child health: a low literacy level is associated with worse health status, difficulties accessing health care, and poorer preventive health behavior and self-management of health problems [13-23].

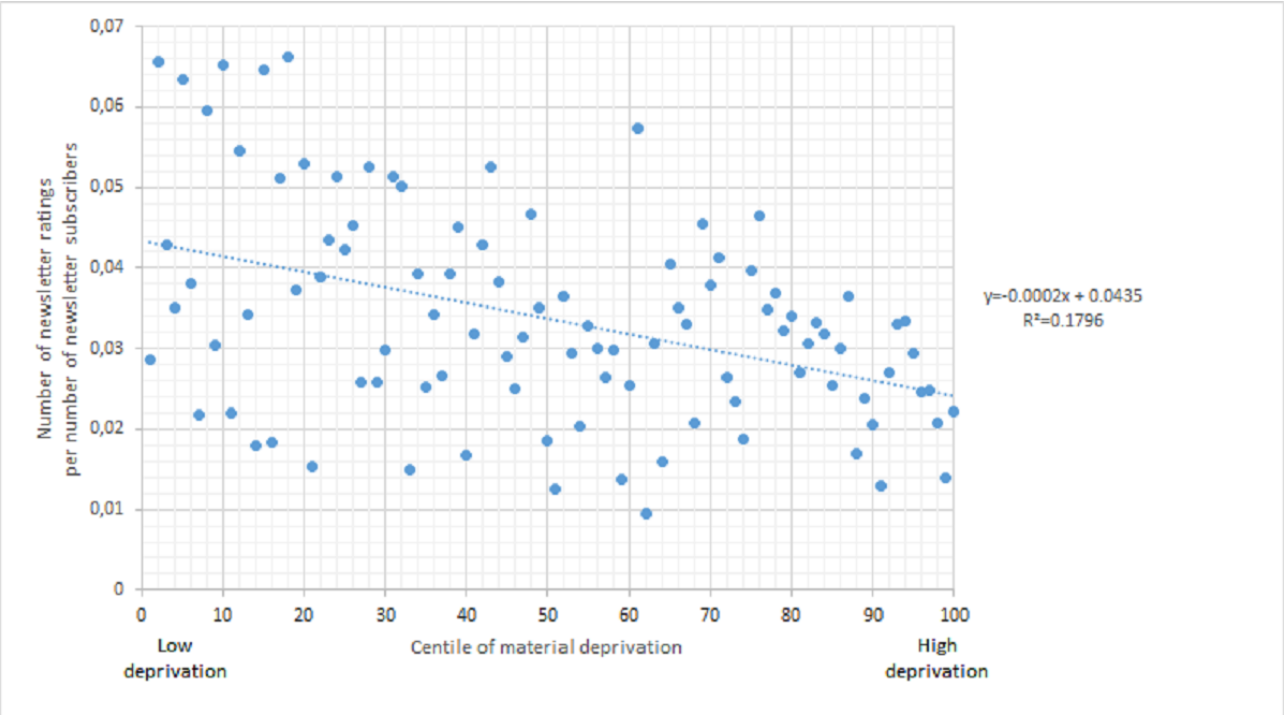
Education and income are the most important SES indicators, and together, they are strongly associated with child health status [24,25]. According to research on information-seeking behavior, parents with low SES have greater information needs than parents with high SES [26]. The use of high-quality online information can improve quality of life and have positive family, economic, and social impacts on low-SES parents, including refugee and homeless parents [27-31]. High-quality information and literacy-related interventions can reduce unnecessary calls and visits to health professionals, increase knowledge and self-efficacy, and improve health [16-19,32-47].

N&G [48] is a website independent from industry funding that provides high-quality information (based on research syntheses and validated by experts) on child development, education, health, and well-being. N&G users can access hundreds of information pages (1 page per topic) that are organized in age group categories, ranging from pregnancy to the age of 8 years. N&G also produces a weekly newsletter to support parents, including those with a low literacy level, having children under the age of 8 years.

N&G partnered with investigators from McGill University to validate and implement the IAM to continuously assess and improve content shared on the N&G website and newsletter [49-53]. In line with the Canadian Institutes of Health Research (CIHR)'s definitions [54], the IAM is a knowledge translation tool for monitoring N&G information use, and its impact on parents is measured by expected health/well-being benefits. It is also fostering parent engagement by enabling parents to interact with N&G editors by providing feedback on the information content. The IAM questionnaire includes 7 questions (with clickable answers and 2 comment boxes), allowing users to rate on the situational relevance, cognitive/affective impact, intention to use and expected benefits of specific information content (N&G information page), and write comments.

During our pilot phase (September 1, 2014, to August 31, 2016), we collected 34,021 IAM ratings (completed IAM questionnaires) from parents, relatives, and professionals (education, health, and social services) who read N&G content. In line with studies on social inequalities in Web information use [55-61], the statistical analysis of these ratings revealed a social gradient: low-SES parents underuse N&G and the IAM (Figure 1). Results also indicated that low-SES parents are more likely to report decreased worries and increased confidence as a result of using N&G information [50]. There is a need to understand this gradient to improve N&G content and reach low-SES parents and a need to explore how the use of knowledge translates into health and well-being outcomes for low-SES parents and children.

Figure 1. Social gradient in assessing *Naître et grandir* (N&G) information with Information Assessment Method (IAM). A dot represents the total number of IAM ratings completed by all N&G newsletter subscribers living within the postal code areas of a Canadian centile of Material Deprivation. There is a negative linear relationship as areas with higher deprivation have a lower proportion of newsletter ratings/subscribers. The correlation coefficient is −.42 (*P*<.001).



Goal and Objectives

This study (research protocol) has been recently funded by CIHR. As per CIHR's definition of knowledge translation ("making people aware of knowledge and facilitating knowledge use to improve health") [62], our goal is to improve how low-SES parents engage with and use online information about child development, education, health, and well-being; learn how this format for knowledge sharing translates to improved health and well-being outcomes for low-SES parents and their children; and explore their interaction with Web editors to influence content (responsible for websites' content). On the basis of the N&G team's (the director and 2 coordinators) questions and using the Knowledge-to-Action framework [63], we determined 4 research objectives:

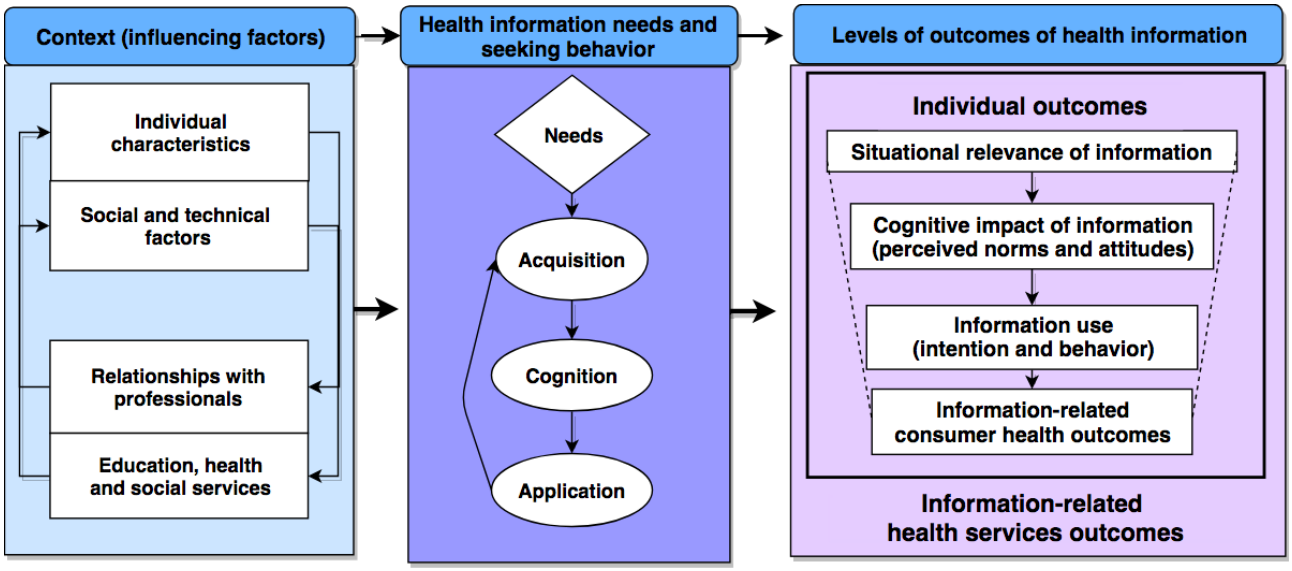
- Objective 1: Identify low-SES parents' views on barriers and facilitators to accessing, understanding, and using N&G information content and to interacting with N&G editors via the IAM.
- Objective 2: Adapt N&G content/functions and the IAM tool (user-centered design) to reduce barriers and optimize facilitators identified in phase 1 and implement new versions labeled N&G+ and IAM+.
- Objective 3: Evaluate whether N&G+ and IAM+ result in a higher proportion of low-SES parents engaging with the N&G site and the content provided and interacting with editors via the IAM.
- Objective 4: Describe how expected health and well-being benefits of N&G+ information use (reported via IAM+) are experienced by parents with low SES and their children.

Systematic Literature Review and Theoretical Model

The nominated principal investigator (NPI) led a CIHR-funded systematic review and proposed a comprehensive harmonized typology of (1) outcomes associated with the use of online consumer health information and (2) conditions (network and resources) leading to these outcomes [64-67]. A total of 68 studies were analyzed using framework synthesis [68,69]. This synthesis was based on an initial framework derived from information studies [49,70-78] and led to propose an innovative theoretical model (Figure 2) [66,67]. This model includes positive and negative health outcomes of online consumer health information in a primary care context and is (information) consumer oriented.

The model comprises 13 main concepts (42 factors and outcomes) and will be used in this study to inform data collection and analysis, for example, the phase 1 qualitative interview guide and interpretive thematic analysis. The model will contribute to establish a chain of evidence linking ultimate outcomes of information (such as health outcomes), intermediary outcomes (such as cognitive impact of information), and conditions associated with outcomes (information needs and seeking behaviors and contextual factors).

Figure 2. Theoretical model.



Outcomes

The model includes an organizational level of information outcome (eg, increased or decreased use of health services) and 4 individual levels of outcomes of information. The latter outcomes reflect how information is valuable from the consumer's perspective: situational relevance, cognitive impact, use of information (conceptual, legitimating, instrumental, and symbolic use), and subsequent health and well-being outcomes.

Conditions

The model includes conditions associated with outcomes of information in relation to a specific situation: a particular information object is acquired or delivered (eg, a Web page or a newsletter) in a particular situation (eg, before or during or after an encounter with someone) directly or with help from a relative or a professional. The main conditions are information needs and seeking behaviors; individual characteristics (such as electronic health literacy); social and technical factors (such as social networks); relationships with professionals (such as teachers, clinicians, and social workers); and access to education, health, and social services. The first phase of this study will specifically look into conditions experienced by low-SES parents, such as media competence.

Direct acquisition of online information depends on an impetus to search (motivation), momentary internet connection, internet search skills, and one's ability to understand the content that may or may not be adapted to their individual literacy level [79-81]. Approximately 95% of parents of preschool children have direct individual access to the internet in Quebec [61], and parents can also access it at office workplaces and public libraries [79-81]. Literacy level is generally defined as the degree to which a person has the ability to "acquire, understand, evaluate, and use information" needed to obtain services and make appropriate decisions [23]. Computer literacy, information literacy, and health literacy are interdependent (eg, a person with a low literacy level has a low level of health literacy). Culture is central in literacy, and one's literacy level depends on one's ability to understand systems of symbols from one's own culture or a dominant culture and language, for example, immigrants and refugees may have a higher literacy level in their country of origin compared with their adoptive country [23]. As mentioned in our model, the literacy level is *situational* and *contextual*, given that a social network can compensate for an individual's low literacy level.

Mediated (by someone else) acquisition of information is very common. The absence of an individual connection 24/7 is no longer the primary barrier to seeking health information [80]; for example, our pilot data show that 18.1% of IAM ratings concerned N&G information seeking for someone else's child (eg, relative's, friend's, neighbor's, or client's child). Even homeless parents or recent immigrants and refugees can acquire online consumer health information directly or mediated by their social network, including community organizations; public libraries; and education, health, and social services [23,27-31]. Indeed, information studies show that consumers combine mediated information with direct acquisition of online health information, the latter allowing them to probe information provided by professionals [64-67]. For analytical purpose, we conceive these combinations as the interpenetration of social systems centered on communicative action, for example, the health system (mediated access) and a consumer parent system (direct access and mediated access via their social network) [82-85].

Significance

Our project focuses on all Canadian parents with low SES who acquire (direct or mediated) online information about child development, education, health, and well-being. In Canada, 42% of nonelderly adults [16,17] and 15% of children live in low-income households [86]. In Quebec, 36% of parents report living in poverty [87]. The demand for information is very high, resulting in frequent internet searches; for example, parents search the internet for child-related information on average 1.3 times per week in Quebec, and 73% of parents report that the internet constitutes their first-line source of parenting information [88].

Table 1. Main features of *Naître et grandir* and *AboutKidsHealth*.

Main features	*Naître et grandir* [48]	*AboutKidsHealth* [94]
Website annual traffic	24 million worldwide visits	16.8 million worldwide visits
Information	Developmental, educational, health, and well-being information about children aged under 8 years	Health information about children aged under 19 years
Language	French	English, French, and 10 other languages
Targeted audience	Parents, relatives, and caregivers	Parents, relatives, and caregivers and health professionals

Specifically, our project is important for about half the population of parents of children under 19 years, namely, parents with a low literacy level. Low literacy is a major concern in Canada [16,17,19,20,23]. Results of the 2011 to 2012 survey of a representative sample of 25,267 Canadian parents aged 16 to 65 years showed that 49% of parents have a low literacy level: [89,90] they have difficulty finding, understanding, and using information presented in a dense or lengthy text; navigating complex digital texts; interpreting and evaluating information (constructing meaning); and disregarding irrelevant or inappropriate content when there is competing information (including when correct content is more prominent). Furthermore, our results may help any parent who faces a transitory low literacy level because of a stressful situation. This interdependence between information and emotion is well established in the information literature [91,92].

Our project nevertheless does not focus on the few *information-poor* parents without access (direct or mediated) to online information. In the United States, only 1% of 18- to 29-year olds did not use the internet in 2015 [93]. The Quebec 2015 survey of a representative sample of 23,693 parents of preschool children showed that only 1.5% of parents never know where to find child information [61]. According to information studies, the *information-poor* parents (1) perceive themselves as persons who cannot be helped, (2) adopt self- or group-protective behaviors, (3) are secretive and mistrust others, and (4) consider exposure to information as a risk (harm outweighing benefits) [30].

Our project engages a partnership between N&G and *AboutKidsHealth* (AKH) [94], both popular comprehensive Web-based resources (Table 1). Both resources contain text with a readability level below high school (this level may be higher for disease-related information), visual illustrations, and complementary simple illustrative videos. For each Web page, an audio help system highlights words as they are spoken. In 2016, our librarian did an environmental scan of Canadian parental websites and found multiple specialized resources but only 12 comprehensive resources (including N&G and AKH).

Although this study is a priority in a Canadian context, our results can be important to and applied by all Web editors who provide health information, thereby benefitting all adults with a low literacy level (not only parents). For example, Health Canada policies recommend funding projects that aim to improve access to, and conduct research on, information for Canadians with a low literacy level [23]. Information systems are key components of health systems and crucial to meet human rights and the democratic right to know and communicate [31,95-100]. Among adults, the most frequent searches for information are about health [101]. The demand for high-quality low-literacy health information is, hence, very high.

Methods

Organizational Participatory Research Approach

Our project uses an organizational participatory research (OPR) approach. OPR is a form of integrated knowledge translation that blends action research and organizational learning to undertake research with organizations and improve practice [102-107]. N&G (organization) proposed the research questions and will participate in all research steps. The NPI has OPR experience and expertise. The NPI led a CIHR-funded systematic review on OPR key processes and outcomes [107]. A steering committee composed of the NPI, the coprincipal investigator, the partner (principal knowledge user), another knowledge user (AKH), and 2 low-SES parents will meet before and after each phase for planning and interpreting results, respectively. All team members will be consulted and have the opportunity to influence the steering committee's decision making.

Methodology and Methods

A mixed-methods multiphase design will be used [108,109]. Ethical approval has been recently obtained from the institutional review board (IRB) of the Faculty of Medicine at McGill University (IRB#A10-E69-17B). Phases 1, 3, and 4 will be informed by our theoretical model (Figure 2).

Phase 1 (Objective 1): Identify Barriers and Facilitators to Use Naître et Grandir and Interact With Editors Via Information Assessment Method

Design

We will conduct an exploratory qualitative interpretive study to have a better understanding of barriers and facilitators in using N&G and interacting with editors via IAM [110]. Qualitative research is appropriate as it provides in-depth descriptions from the stakeholders' viewpoint and helps researchers to understand their constitutive elements and variants [111].

Setting and Participants

Participants will be 20 users and 20 nonusers of IAM and N&G (additional participants will be recruited to achieve data saturation). First, users will be recruited among low-SES parents who indicate that they agree to be contacted when they complete an IAM questionnaire on N&G and who have used N&G and IAM at least once. N&G will send the group an invitation to participate in a research project via an email containing the

research team's full identification and contact information. The research team will only communicate with N&G users who responded with an interest to participate in the research project via email or phone. Eligible parents will have no high school diploma and have an annual family income lower than Can $40,000 (Quebec poverty line). Second, nonusers (10 who never used the IAM and 10 who never used N&G) will be recruited by a principal investigator (CL) and a collaborator (GD, N&G Director) who work with community organizations for parents with low SES.

Data Collection

A research assistant having experience in qualitative interviews with low-SES persons will conduct individual 60-min semistructured face-to-face interviews at the location of each participant's choice. In line with sociological and information studies [112,113], interviews will explore how participants experience, conceptualize, perceive, and understand aspects of N&G information and the IAM. The interview guide will consist of open-ended questions addressing the participants' routines in terms of internet use (both for their personal and children's development information needs), their experience in the use of IAM and N&G's information, the facilitating aspects of N&G and IAM, perceived barriers in their experience, and suggestions to improve the N&G website and IAM. On the basis of the theoretical model, the interview guide will be developed in a simplified language with input from team members and the steering committee. We will conduct 2 pilot interviews to ensure the questions are comprehensible for the participants. The recruited respondents will receive Can $20 as compensation for their time. In addition to the research assistant's observation notes, interviews will be audio recorded and transcribed verbatim.

Data Analysis

Two principal investigators (PP and CL) have experience in qualitative research and 1 (CL) has experience in qualitative research with populations in situations of vulnerability. With the research assistant and a research trainee, they will read notes and interviews and meet regularly to build memos (meeting minutes with arguments for and against each analytical decision, as rigor is mainly based on researchers' reflexivity in this design [110]), case summaries, and themes (definitions and key examples) using hybrid deductive-inductive thematic analysis [114,115]. The research assistant will manage the analysis using specialized software (NVivo11). Themes will be derived from our theoretical model (Figure 2; deductive coding) and emerge from the data (inductive coding). Major themes will be barriers and facilitators. For each type of participant (user/nonuser), additional parents will be recruited up to saturation (no new parents' views of barrier or facilitator). Then, we will harmonize themes [116]. For each theme and definition, we will identify terms, confirm the usage of these terms in reference documents, distinguish correct from incorrect usage, and retain terms that facilitate unambiguous communication. This will lead us to classify, group, and clarify barriers and facilitators in a coherent taxonomy, which will be reviewed by team members and the steering committee. Findings will provide recommendations for improving IAM and N&G.

Phase 2 (Objective 2): Improve Naître et Grandir and Information Assessment Method

Two team members (FL and GD) are head directors of the N&G website and will lead this phase. Phase 1 findings will inform the production and implementation of IAM+N&G+ (user-centered design). This version will integrate the perspectives of low-SES parents, the steering committee, research team members, and N&G staff on how to overcome barriers and optimize facilitators. Production of this version will be planned with 2 Web editors and 2 Web engineers from the N&G team. According to Web engineers, 6 months is an ample time frame for production and beta testing. All necessary resources at N&G will be made available to implement IAM+N&G+. Two half-day meetings with principal investigators and N&G staff have been deemed sufficient to plan changes with editors and engineers. The N&G Director stated that she will implement what will be requested by the phase 1 participants, as her mandate (N&G mission) is to specifically address information needs of parents with low SES. For their part, AKH will redesign their website, integrate phase 1 results in this study, and implement IAM+.

Phase 3 (Objective 3): Evaluate Use of Information Assessment Method+ Naître et Grandir+, Information Use, and Benefits

Design

We will conduct a quantitative prospective longitudinal study to evaluate the impact of the intervention (IAM+N&G+).

Setting

Weekly numbers of N&G sessions and IAM ratings will be monitored over 2 years. A session starts when someone opens a Web page and ends when the person (or a relative with the same IP address) does not use the website for more than 30 min. For each quintile of SES, data will be collected for 9 months preimplementation (IAM/N&G) and 9 months postimplementation (IAM+N&G+). To avoid bias related to the *novelty effect*, data collected in the 3 months immediately following the implementation will be excluded from the analysis. The chosen periods also ensure seasonal comparability of the collected outcome data (before and after intervention).

Participants

All N&G readers and IAM raters across Canada will participate.

Measurement

N&G and McGill already use Google Analytics, an objective and reliable automatic data collection of N&G readers' demographic characteristics and website use behavior (based on javascript codes in each Web page) [117-120]. IAM raters' demographic data are collected with a questionnaire (linked to an anonymized identifier). The validated IAM questionnaire [53] collects self-reported information use and subsequent expected health/well-being benefits for parents and their child.

Table 2. Types of outcomes monitored weekly.

Type	Outcome	Description and data source
A1	N&G[a] sessions	Weekly number of unique sessions (Google Analytics)
A2	N&G read	Weekly proportion of sessions with at least 1 page entirely read (Google Analytics)
A3	IAM[b] ratings	Weekly number of IAM questionnaires submitted
B1	N&G mediated	Weekly proportion of IAM ratings information used for the child of someone else
B2	N&G used	Weekly proportion of IAM ratings information used for oneself and one's child
C	Expected benefits	Weekly proportion of IAM ratings expected health or well-being benefit for a parent and child, including at least 1 of the following self-perceived benefits (IAM choices of response): improvement of the health or well-being of a child, being less worried, prevention of a problem or the worsening of a problem, handling a problem, and being more confident to decide something with someone else

[a]N&G: *Naître et grandir*.

[b]IAM: Information Assessment Method.

Outcomes

In line with CIHR knowledge translation guidance [54], 3 types of outcomes will be considered weekly (Table 2): (A) N&G and IAM use, (B) self-reported N&G information use, and (C) subsequent expected benefits.

Covariates

The main predictor will be participants' SES as determined by the Quebec Index of Material and Social Deprivation, a validated ecological measure of the (education, income, and employment) disadvantage of a given geographic area (postal code) [121,122]. For each session, an index will be automatically assigned using (1) the reported postal code and the Canadian Deprivation Index Assignment Program (CDIAP) of the Public Health Agency of Canada when the data source is IAM and (2) the postal code matched to the session geotag via the "Dissemination Area Boundary File" of Statistics Canada and the CDIAP when the data source is Google Analytics. This will allow for the identification of low-SES participants (highest quintile of material and social deprivation). Using Google Analytics, participants' demographic variables that will be considered in all analyses are age, gender, rural/urban location, and province. In addition, Web page–specific variables will be included to assess potential confounding and effect modifications. For each session, the type of device (Google Analytics: phone, tablet or laptop, and desktop), the audio-guide use (Google Analytics: yes or no), and the readability score of pages entirely read (automatic extraction and measurement using a text classifier validated for French) [123] will be collected.

Study Size

On the basis of our 2-year pilot data (2014/09-2016/08), we anticipate about 5 million N&G sessions and 15,000 IAM ratings from Canadian participants during each period (pre- and postimplementation).

Anticipated Results

The IAM+N&G+ will result in an increase of all outcomes (N&G and IAM use, self-reported N&G information use, and subsequent expected health and well-being benefits for parents and children such as *decreased worries* and *health improvement*, respectively).

Statistical Analysis

Linear mixed modeling will integrate spatial analytics (geomatics) and account for the clustered nature of the data. The pre/post status, the SES quintile of deprivation, and potentially confounding variables will be included as fixed-effects covariates. The inference model will incorporate random effect terms for individual variables and Web page–specific variables. For each outcome, an interaction term of the SES quintile of deprivation and the pre/post status will be included to assess the pre/post change for each quintile. Estimated regression coefficients and variance parameters will be reported along with appropriate confidence intervals.

Phase 4 (Objective 4): Describe Parent and Child Outcomes of Naître et Grandir+ Information Use

Design

We will conduct a qualitative interpretive study to generate an in-depth description of parent and child outcomes from the parents' perspective [124]. On the basis of our systematic review [66,67], we anticipate 3 types of parent outcomes (decreased worries, increased confidence, and self-management) and 2 types of child outcomes (prevented problem and improved development, health, and well-being). Our pilot data (34,021 IAM ratings) also suggest parents rarely report potential negative consequences of using information, for example, vaccine adverse effect (n=183; 0.5%). In outcomes research, qualitative methods are appropriate for exploring complex outcomes from the stakeholders' perspective, such as life experiences [111,125-131]. In our study, information can influence parent decision making, but the relationship between information and decision is not simple. Our qualitative study will (1) identify causal events, (2) map them in a complex causal network, and (3) build a chronological chain of qualitative evidence between N&G information and a parents' decision that affects knowledge, attitude, or behavior [131,132].

Participants

Participants who received the N&G+ newsletter, used IAM+ at least once, have agreed to be contacted for research, and live in a high deprivation area will be approached for recruitment. The recruitment procedure will be the same as for phase 1. In 2015, more than 24,000 families received, upon request, the weekly

newsletter. We will begin by recruiting 30 parents (and continue recruitment, as needed, to achieve data saturation) who report, via IAM+, positive health and well-being outcomes and/or potential negative consequences of information (prioritizing those who live in the areas of highest deprivation). As we are looking for individual stories for about 6 types of outcomes (some less frequently reported than others), data saturation may not be reached with fewer than 50 participants [111,133-135].

Data Collection

The research assistant having experience in qualitative interviews with low-SES persons will conduct 60-min face-to-face interviews to elicit participants' IAM+ ratings. The interview guide will be based on our theoretical model (Figure 2) and input from team members and the steering committee. To stimulate recall (memory), the interviewee will be given the list of recent texts they rated and their ratings. For each newsletter, the research assistant will ask open questions regarding what happened to them and/or their children that led them to report an expected outcome (positive or negative). Participants will be interviewed twice 3 months apart to increase the number of described outcomes and avoid fatigue of long interviews. Participants will receive Can $20 per interview as compensation for their time. In addition to the research assistant's observation notes, interviews will be audio recorded and transcribed verbatim.

Data Analysis

Two principal investigators (PP and CL) have experience in qualitative research. With the research assistant, a collaborator anthropologist having expertise in life histories (MB) and a research trainee will read notes and interviews and meet regularly. For each case (information used with at least 1 outcome experienced by a parent and a child), they will interpret the data in the form of a *small story* [112,136-138]. This method allows researchers to describe a person's individual experience (including all perceived influences) and helps the researcher understand the individual's attitude and behavior [33]. In research meetings, 2 questions will be answered through recorded discussion of arguments for and against each analytical decision (rigor based on sharing reflexivity): is the case story clear? and are the causal network and chain of evidence trustworthy? Disagreements about clarity and trustworthiness of case stories will be resolved with 3 other team members having experience in qualitative research (Bouthillier, Thoër, and Smythe). Case stories will be reviewed by all team members and the steering committee. This may detect issues and result in the principal investigators and research assistant revising parts of their analysis.

Anticipated Results

This will generate up to 10 case stories per outcome type, being the first in-depth qualitative description of low-SES parents' perspective on outcomes of online child information use.

Results

The project was funded in 2017 by the CIHR and received an ethics approval by the McGill University's IRB. Data collection for phase 1 was completed in 2018. Phases 2 to 4 will be completed by 2020. Findings from this study will be used to develop a free toolkit, useful to all Web editors, with recommendations for improving health information for low-SES persons and interactions with them using IAM. Results will be published in peer-reviewed journals and presented at national and international scientific conferences.

Discussion

Direct Impact on *Naître et grandir* and *AboutKidsHealth*

Any improvement of knowledge translation tools and websites such as IAM, N&G, and AKH can have an important impact as it affects a large population of individuals with a low literacy level. In fact, the effectiveness of childhood education interventions has been demonstrated repeatedly [16-19,23,27-47]. In our 2-year pilot data, parents expected health and well-being benefits (for themselves or their child) from using N&G information in 65.4% of all IAM ratings (n=34,021) [50]. In accordance with knowledge translation and implementation research [62], we will not replicate effectiveness studies and rather focus on improving interventions that work.

Our project can improve engagement (number of visits) with websites providing high-quality low literacy information; in turn, online parenting information improves parents' knowledge, attitudes, and behaviors [139-145]. Given our integrated knowledge translation (participatory research) approach, N&G and AKH will adapt their content for low-SES users as we generate results. In addition, IAM+ will better support low-SES parents' interactions with Web editors and empowerment. Thus, our results can immediately benefit millions of information users with a low literacy level (children's parents and relatives), for example, in Canada (Table 3).

IAM+N&G+ can be seen as an innovative intervention that complements traditional literacy programs (eg, family literacy classes). Indeed, interventions that somewhat compensate for a low literacy level can greatly improve parents' and children's health and well-being [23]. Thus, our results can have a positive impact on 55% of the Canadian working age, those who have a low level of *health literacy* and need compensatory help to manage their health [23,89,90].

Specifically, IAM+N&G+ can help Canadians in francophone minority communities, as 500,000 annual N&G website visits originate from them. Research with these communities is very underfunded, thus a CIHR priority [146]. As stated in the October 2016 report of the Commissioner of Official Languages [147], early childhood development in these communities *is hindered by a lack of resources*, and *the absence of specific funding* has left them *vulnerable and often incapable of meeting their needs*.

Table 3. Targeted population in Canada.

Across Canada	IAM[a] *Naître et grandir* (new version)	IAM *AboutKidsHealth* (new version)
Families[b]	1.3 million families have French as mother tongue (couples with children and single-parent families with at least 1 child)	5.8 million families (couples with children and single-parent families with at least 1 child)—all languages
Children's parents and relatives[b]	2.8 million adults aged 20 to 69 years have a low literacy level (and French as mother tongue)	12 million adults aged 20 to 69 years have a low literacy level
Website visits from Canada	8.3 million[c] visits in 2015 mainly from Quebec (7.8 million), Ontario (304,000), and New Brunswick (70,000)	1.5 million visits in 2015 mainly on Web pages in English (58%), French (16%), Spanish (14%), and Arabic (5%)

[a]IAM: Information Assessment Method.

[b]Statistics Canada 2015.

[c]76% of parents of children aged under 8 years consult *Naître et grandir* in Quebec (on average 1.3 times per week).

Potential Impact Beyond *Naître et grandir* and *AboutKidsHealth*

Results will inform the development of an open access online tool kit on how to adapt websites and IAM+ for a low literacy audience (a growing consideration of many Web editors). The tool kit will be designed to be generalizable to all types of online consumer health information in Canada. It will include guidance with 3 main messages: (1) how to produce simple information in lay language with audio and visual content, (2) how to better interact with low-SES persons using IAM+, and (3) how to use consumers' IAM+ ratings and feedback to continuously optimize information content. The tool kit will be freely available to any Web editor via the Quebec SPOR-SUPPORT Unit and IAM websites. The NPI has experience in developing tools and leads the method development platform of the Quebec SPOR-SUPPORT Unit.

Our primary knowledge translation goal for knowledge user audiences will be to raise awareness about our main messages and drive attention to the tool kit. A secondary knowledge translation goal will be to support the implementation of the toolkit by Web editors. Knowledge users will disseminate our work in multiple Canadian organizations. As per reviews on scaling up [148-150], we will update our 2016 environmental scan and contact all Canadian websites targeting parents. A specialized librarian (collaborator) will reach additional health websites through librarian listservs and peer networks. Team members will raise general awareness for the tool kit and deliver our main messages to a variety of academic and nonacademic knowledge user audiences via a range of knowledge translation strategies (conference presentations, open access peer-reviewed publications, plain language summaries and grey literature, social media, and networks). Multiple knowledge translation channels will be used including Twitter (@UniteSoutien) and websites such as the Quebec SPOR-SUPPORT Unit and the IAM websites [151,152].

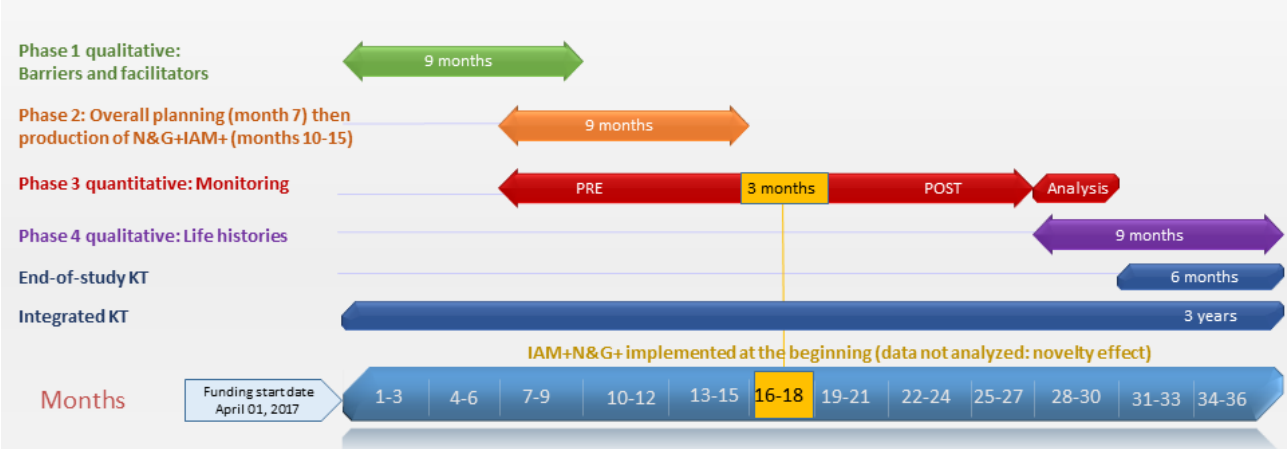
Contribution to Scientific Knowledge

Our project will advance knowledge on the value of online information for, and interaction with, low-SES persons to strengthen health systems. On the one hand, this project is the first to systematically explore health and well-being outcomes for low-SES parents and children associated with parenting information websites. Most studies focus on discussion forums that can be intimidating to low-SES parents [140,142,143,153,154]. On the other hand, many studies concern relational marketing and website feedback buttons [52,155-158], but we know of none that addresses interactions between low-SES persons and Web editors (such as interaction through IAM+).

Timeline and Potential Challenges

Overall, 3 years will be needed to complete this project (Figure 3). Our phases are simple and well defined, and our planning is realistic. In phases 1 and 4, we anticipate no recruitment difficulties. Many parents have already agreed to be contacted for research, and N&G will facilitate the recruitment. Phase 2 is feasible, and the deliverables are realistic given that N&G has already implemented IAM, McGill and N&G have a strong OPR partnership, and N&G is committed to implementing IAM+N&G+. In phase 3, the large number of N&G readers guarantee a large sample. To control for potential seasonal variation in the number of sessions pre- and postimplementation, monitoring will be conducted during the same seasons. To control for contextual changes, variables such as type of device, age, gender, and location are covariates. We have opted for a prospective longitudinal study as monitoring is embedded in N&G routines. In addition, although randomization would provide a higher level of evidence, it was considered unethical to randomly assign low-SES parents to N&G+ or N&G information and impractical for such a popular website (contamination bias) [159]. Moreover, 3 typical potential sources of biases in longitudinal designs may not affect our study: the use of proportions will control for historical events, there will be no *respondent fatigue* as our 2-year pilot data showed that the monthly number of IAM raters is stable, and the social desirability bias will affect pre- and postimplementation periods in a similar manner.

Figure 3. Study timeline. N&G: *Naître et grandir*; KT: knowledge translation; IAM: Information Assessment Method.



Considering the commitment, expertise, and networks of our team, we expect no major challenges. This project is highly facilitated by the participatory research approach (a form of integrated knowledge translation). In addition, it is sustainable as our results will be applied and sustained by 2 longstanding organizations. N&G is fully funded since 1998 by the Lucie et André Chagnon Foundation (one of the largest philanthropic agencies in Canada) and is a priority of this foundation. AKH is owned by the Hospital for Sick Children (Toronto) and is fully funded since 2004 by multiple maternal and child health agencies.

Conclusions

The results of this study will provide a deep understanding of how low-SES parents use online child information and interact with Web editors. Following the implementation of IAM+N&G+, results will also elucidate subsequent health outcomes for low-SES parents and children after interaction with Web editors have been optimized. Thus, our results can immediately benefit millions of information users, children's parents and relatives in particular, with a low literacy level.

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Conflicts of Interest

None declared.

References

1. Marmot MG. Understanding social inequalities in health. Perspect Biol Med 2003 Jan;46(3 Suppl):S9-23. [doi: 10.1353/pbm.2003.0070] [Medline: 14563071]
2. Whitehead M. A typology of actions to tackle social inequalities in health. J Epidemiol Community Health 2007 Jun;61(6):473-478 [FREE Full text] [doi: 10.1136/jech.2005.037242] [Medline: 17496254]
3. Bardsley M, Morgan D. Inequalities in maternal and early child health: Priorities for London. Measuring Inequalities in the Health of Mothers and Children. Briefing Paper 1. London: Department of Health; 2000.
4. Siegrist J, Marmot M, editors. Social inequalities in health. Oxford: Oxford University Press; 2006.
5. Warwick-Booth L. Social inequality. London: Sage; 2013.
6. Grabb E, Guppy N. Social inequality in Canada. Don Mills: Pearson Prentice Hall; 2008.
7. Brooks-Gunn J, Duncan GJ. The effects of poverty on children. Future Child 1997;7(2):55-71. [Medline: 9299837]
8. McLeod J, Shanahan MJ. Poverty, parenting, and children's mental health. Am Sociol Rev 1993 Jun;58(3):351-366. [doi: 10.2307/2095905]
9. Curtis LJ, Dooley MD, Lipman EL, Feeny DH. The role of permanent income and family structure in the determination of child health in Canada. Health Econ 2001 Jun;10(4):287-302. [doi: 10.1002/hec.591] [Medline: 11400252]
10. Michl LC, Handley ED, Rogosch F, Cicchetti D, Toth SL. Self-criticism as a mechanism linking childhood maltreatment and maternal efficacy beliefs in low-income mothers with and without depression. Child Maltreat 2015 Nov;20(4):291-300 [FREE Full text] [doi: 10.1177/1077559515602095] [Medline: 26318693]

11. Health Inequalities Unit. Tackling health inequalities. London: Department of Health; 2008. URL: http://webarchive.nationalarchives.gov.uk/20031221005110/http://www.doh.gov.uk/healthinequalities/programmeforaction/programmeforaction.pdf [WebCite Cache ID 736bzNftU]
12. Raphael D. Poverty, income inequality, health in Canada. In: Social determinants of health: Canadian perspectives. Toronto: Canadian Scholars' Press; 2016:218-239.
13. Bennett IM, Chen J, Soroui JS, White S. The contribution of health literacy to disparities in self-rated health status and preventive health behaviors in older adults. Ann Fam Med 2009;7(3):204-211 [FREE Full text] [doi: 10.1370/afm.940] [Medline: 19433837]
14. Easton P, Entwistle V, Williams B. Health in the 'hidden population' of people with low literacy. A systematic review of the literature. BMC Public Health 2010 Aug 05;10:459 [FREE Full text] [doi: 10.1186/1471-2458-10-459] [Medline: 20687946]
15. Institute of Medicine. Health literacy. Washington: The National Academy Press; 2004.
16. Canadian Council on learning. Health literacy in Canada. Ottawa: Canadian Council on Learning; 2008.
17. Rootman I, Gordon-El-Bihbety D. A vision for a health literate Canada. Ottawa: Canadian Public Health Association; 2008.
18. Smith S, Duman M. The state of consumer health information: an overview. Health Info Libr J 2009 Dec;26(4):260-278 [FREE Full text] [doi: 10.1111/j.1471-1842.2009.00870.x] [Medline: 19930474]
19. Clement S, Ibrahim S, Crichton N, Wolf M, Rowlands G. Complex interventions to improve the health of people with limited literacy: a systematic review. Patient Educ Couns 2009 Jun;75(3):340-351. [doi: 10.1016/j.pec.2009.01.008] [Medline: 19261426]
20. Benigeri M, Pluye P. Shortcomings of health information on the internet. Health Promot Int 2003 Dec;18(4):381-386. [Medline: 14695369]
21. Or C, Karsh BT. A systematic review of patient acceptance of consumer health information technology. J Am Med Inform Assoc 2009;16(4):550-560 [FREE Full text] [doi: 10.1197/jamia.M2888] [Medline: 19390112]
22. Weightman AL, Morgan HE, Shepherd MA, Kitcher H, Roberts C, Dunstan FD. Social inequality and infant health in the UK: systematic review and meta-analyses. BMJ Open 2012;2(3) [FREE Full text] [doi: 10.1136/bmjopen-2012-000964] [Medline: 22700833]
23. McNichol BR, Rootman I. Literacy and Health Literacy: New Understandings about Their Impact on Health. In: Raphael D, editor. Social Determinants of Health: Canadian Perspectives. Toronto: Canadian Scholars' Press; 2016:261-290.
24. Feinstein L, Sabates R, Anderson T, Sorhaindo A, Hammond C. What are the effects of education on health? 2006 Presented at: Symposium Measuring Effects of Education on Health; March 23-25, 2006; Copenhagen URL: http://www.oecd.org/education/innovation-education/37425753.pdf
25. Mikkonen J, Raphael D. Social determinants of health: The Canadian facts. Toronto, Canada: York University School of Health Policy and Management; 2010.
26. Case D. Looking for information. London: Academic Press; 2002.
27. Lloyd A, Anne Kennan M, Thompson K, Qayyum A. Connecting with new information landscapes: information literacy practices of refugees. J Doc 2013 Jan 11;69(1):121-144. [doi: 10.1108/00220411311295351]
28. Knapp C, Madden V, Wang H, Sloyer P, Shenkman E. Internet use and eHealth literacy of low-income parents whose children have special health care needs. J Med Internet Res 2011 Sep 29;13(3):e75 [FREE Full text] [doi: 10.2196/jmir.1697] [Medline: 21960017]
29. Hersberger J. Are the economically poor information poor? Does the digital divide affect the homeless and access to information? Can J Inform Lib Sci 2003;27(3):45-63 [FREE Full text]
30. Chatman EA. The impoverished life-world of outsiders. J Am Soc Inf Sci 1996 Mar;47(3):193-206. [doi: 10.1002/(SICI)1097-4571(199603)47:3<193::AID-ASI3>3.0.CO;2-T]
31. Britz JJ. To know or not to know: a moral reflection on information poverty. J Inf Sci 2016 Jul;30(3):192-204. [doi: 10.1177/0165551504044666]
32. Zamaria C, Fletcher F. Canada online! : the internet, media and emerging technologies : uses, attitudes, trends and international comparisons, year two highlights, 2007. Toronto: Ryerson University; 2008.
33. Baker DW, Wolf MS, Feinglass J, Thompson JA, Gazmararian JA, Huang J. Health literacy and mortality among elderly persons. Arch Intern Med 2007 Jul 23;167(14):1503-1509. [doi: 10.1001/archinte.167.14.1503] [Medline: 17646604]
34. Coulter A. Patient engagement--what works? J Ambul Care Manage 2012;35(2):80-89. [doi: 10.1097/JAC.0b013e318249e0fd] [Medline: 22415281]
35. Dwyer D, Liu H. The impact of consumer health information on the demand for health services. Q Rev Econ Fin 2013 Feb;53(1):1-11. [doi: 10.1016/j.qref.2012.11.002]
36. Edwards M, Davies M, Edwards A. What are the external influences on information exchange and shared decision-making in healthcare consultations: a meta-synthesis of the literature. Patient Educ Couns 2009 Apr;75(1):37-52. [doi: 10.1016/j.pec.2008.09.025] [Medline: 19036550]
37. Kickbusch I. Health literacy: addressing the health and education divide. Health Promot Int 2001 Sep;16(3):289-297. [Medline: 11509466]

38. Lee CJ. Does the internet displace health professionals? J Health Commun 2008;13(5):450-464. [doi: 10.1080/10810730802198839] [Medline: 18661387]
39. Parsons S, Winterbottom A, Cross P, Redding D. The quality of patient engagement and involvement in primary care. London: The King's Fund; 2010. URL: https://www.picker.org/wp-content/uploads/2014/10/The-quality-of-patient-engagement...-primary-care.pdf [WebCite Cache ID 736evLhiM]
40. Renahy E, Chauvin P. Internet uses for health information seeking: a literature review. Rev Epidemiol Sante Publique 2006 Jun;54(3):263-275. [Medline: 16902386]
41. Wasson JH, Forsberg HH, Lindblad S, Mazowita G, McQuillen K, Nelson EC. The medium is the (health) measure: patient engagement using personal technologies. J Ambul Care Manage 2012;35(2):109-117. [doi: 10.1097/JAC.0b013e31824a235e] [Medline: 22415284]
42. Wagner TH, Hu TW, Hibbard JH. The demand for consumer health information. J Health Econ 2001 Nov;20(6):1059-1075. [Medline: 11758048]
43. Tu HT, Cohen GR. Striking jump in consumers seeking health care information. Track Rep 2008 Aug(20):1-8. [Medline: 18770913]
44. Fox S, Duggan M. Health Online 2013. Washington, DC: Pew Research Center; 2013. URL: http://www.pewinternet.org/2013/01/15/health-online-2013/ [WebCite Cache ID 736f9FLiv]
45. Coker TR, Windon A, Moreno C, Schuster MA, Chung PJ. Well-child care clinical practice redesign for young children: a systematic review of strategies and tools. Pediatrics 2013 Mar;131(Suppl 1):S5-25 [FREE Full text] [doi: 10.1542/peds.2012-1427c] [Medline: 23457149]
46. Suziedelyte A. How does searching for health information on the internet affect individuals' demand for health care services? Soc Sci Med 2012 Nov;75(10):1828-1835. [doi: 10.1016/j.socscimed.2012.07.022] [Medline: 22884947]
47. Korenstein D, Falk R, Howell EA, Bishop T, Keyhani S. Overuse of health care services in the United States: an understudied problem. Arch Intern Med 2012 Jan 23;172(2):171-178. [doi: 10.1001/archinternmed.2011.772] [Medline: 22271125]
48. Naitre et grandir. URL: https://naitreetgrandir.com [accessed 2018-10-05] [WebCite Cache ID 72wohsIAW]
49. Pluye P, Granikov V, Bartlett G, Grad RM, Tang DL, Johnson-Lafleur J, et al. Development and content validation of the information assessment method for patients and consumers. JMIR Res Protoc 2014 Feb 18;3(1):e7 [FREE Full text] [doi: 10.2196/resprot.2908] [Medline: 24550180]
50. Pluye P, Sherif RE, Bartlett G, Granikov V, Grad RM, Doray G, et al. Perceived outcomes of online parenting information according to self-selected participants from a population of website users. Proc Assoc Info Sci Tech 2016 Feb 24;52(1):1-3. [doi: 10.1002/pra2.2015.145052010072]
51. Pluye P, El SR, Doray G. Santepop. 2015. [Evaluating the information of being born and growing up by parents] URL: https://www.santepop.qc.ca/fr/posts/rapport-devenement/levaluation-des-informations-de-naitre-et-grandir-par-les-parents [accessed 2018-10-12] [WebCite Cache ID 736fX6npn]
52. Sherif RE, Roy P, Tang D, Pluye P, Bush P, Doray G, et al. Toward an information management system for handling parenting information users' comments. In: Proc Assoc Info Sci Tech. 2016 Feb 24 Presented at: Annual Meeting of the Association for Information Science and Technology; November 6-10, 2015; St-Louis p. 1-3. [doi: 10.1002/pra2.2015.145052010076]
53. Bujold M, El SR, Bush P, Johnson-Lafleur J, Doray G, Pluye P. Ecological content validation of the Information Assessment Method for parents (IAM-parent): a mixed methods study. Eval Program Plann 2018 Dec;66:79-88 [FREE Full text] [doi: 10.1016/j.evalprogplan.2017.09.011] [Medline: 29053984]
54. Monitoring Knowledge Use and Evaluating Outcomes of Knowledge Use. Canadian Institute for Health Research (CIHR); 2018. URL: http://www.cihr-irsc.gc.ca/e/41945.html [WebCite Cache ID 72wrSxbMe]
55. van Dijk JA. Digital divide research, achievements and shortcomings. Poetics 2006 Aug;34(4-5):221-235. [doi: 10.1016/j.poetic.2006.05.004]
56. van Deursen AJ, van Dijk JA, ten Klooster PM. Increasing inequalities in what we do online: a longitudinal cross sectional analysis of Internet activities among the Dutch population (2010 to 2013) over gender, age, education, and income. Telemat Inform 2015 May;32(2):259-272. [doi: 10.1016/j.tele.2014.09.003]
57. Hargittai E. The digital reproduction of inequality. In: Grusky D, editor. Social stratification. Boulder, CO: Westview Press; 2008:936-944.
58. DiMaggio P, Hargittai E. From the 'Digital Divide' to 'Digital Inequality'. Princeton: Woodrow Wilson School, Princeton University; 2001. URL: https://culturalpolicy.princeton.edu/sites/culturalpolicy/files/wp15_dimaggio_hargittai.pdf [WebCite Cache ID 736gLD1iW]
59. Neter E, Brainin E. eHealth literacy: extending the digital divide to the realm of health information. J Med Internet Res 2012 Jan 27;14(1):e19 [FREE Full text] [doi: 10.2196/jmir.1619] [Medline: 22357448]
60. Chang BL, Bakken S, Brown SS, Houston TK, Kreps GL, Kukafka R, et al. Bridging the digital divide: reaching vulnerable populations. J Am Med Inform Assoc 2004;11(6):448-457 [FREE Full text] [doi: 10.1197/jamia.M1535] [Medline: 15299002]
61. Lavoie A, Fontaine C. [Getting to know parents better in Quebec: A portrait from the 2015 Survey of Parents of Children 0-5 Years of Age]. 2016. URL: http://www.stat.gouv.qc.ca/statistiques/conditions-vie-societe/environnement-familial/eqepe.pdf [WebCite Cache ID 736gbhQPC]

62. Knowledge Translation.: Canadian Institute for Health Research (CIHR); 2018. URL: http://www.cihr-irsc.gc.ca/e/29418.html [WebCite Cache ID 72ws2I6Ne]
63. Graham ID, Logan J, Harrison MB, Straus SE, Tetroe J, Caswell W, et al. Lost in knowledge translation: time for a map? J Contin Educ Health Prof 2006;26(1):13-24. [doi: 10.1002/chp.47] [Medline: 16557505]
64. Pluye P, Grad R, Repchinsky C, Dunikowski L, Frati F, Shohet L, et al. In primary health care, what are the outcomes associated with the use of online consumer health information? A participatory systematic mixed studies review protocol. 2014. URL: http://www.crd.york.ac.uk/PROSPERO/display_record.php?ID=CRD42014009738 [WebCite Cache ID 736gud9zE]
65. Granikov V, Sherif R, Pluye P. Patient information aid: promoting the right to know, evaluate, and share consumer health information found on the internet. J Consum Health Internet 2015 Nov 24;19(3-4):233-240. [doi: 10.1080/15398285.2015.1094302]
66. El Sherif R, Pluye P, Granikov V. What are the outcomes associated with the use of online consumer health information in primary health care? A systematic review with framework synthesis of quantitativequalitative evidence. 2016 Presented at: Mixed Methods International Research Association (MMIRA) Annual Conference; August 3-5, 2016; Durham, UK.
67. Granikov V, El Sherif R, Tang D. What are the outcomes associated with the use of online consumer health information in primary health care? A systematic review with framework synthesis of quantitative and qualitative evidence abstract. J Can Health Libr Assoc 2016;35(2):96-110.
68. Booth A, Carroll C. How to build up the actionable knowledge base: the role of 'best fit' framework synthesis for studies of improvement in healthcare. BMJ Qual Saf 2015 Nov;24(11):700-708 [FREE Full text] [doi: 10.1136/bmjqs-2014-003642] [Medline: 26306609]
69. Carroll C, Booth A, Leaviss J, Rick J. 'Best fit' framework synthesis: refining the method. BMC Med Res Methodol 2013 Mar 13;13:37 [FREE Full text] [doi: 10.1186/1471-2288-13-37] [Medline: 23497061]
70. Pluye P, Grad R, Repchinsky C, Jovaisas B, Johnson-Lafleur J, Carrier ME, et al. Four levels of outcomes of information-seeking: a mixed methods study in primary health care. J Am Soc Inf Sci Tec 2012 Dec 10;64(1):108-125. [doi: 10.1002/asi.22793]
71. Fisher K, Landry C, Naumer C. Social spaces, casual interactions and meaningful exchanges. Inf Res 2007 Jan;12(2) [FREE Full text]
72. Wilson TD. On user studies and information needs. J Doc 2006 Nov;62(6):658-670. [doi: 10.1108/00220410610714895]
73. Dervin B, Nilan M. Information needs and uses. Annu Rev Inf Sci Technol 1986;21:3-33 [FREE Full text]
74. Dervin B. Human studies and user studies: A call for methodological inter-disciplinarity. Inf Res 2003;9(1) [FREE Full text]
75. Courtright C. Context in information behavior research. Ann Rev Info Sci Tech 2008 Oct 24;41(1):273-306. [doi: 10.1002/aris.2007.1440410113]
76. Renahy E, Cadot E, Roustit C, Parizot I, Chauvin P. [Searching for health information on the Internet: A contextual analysis of SIRS data, a Parisian cohort]. 2010. URL: https://www.cairn.info/revue-sante-publique-2009-hs2-page-27.htm [WebCite Cache ID 736j4aw2S]
77. Savolainen R. Information behavior and information practice: reviewing the "Umbrella Concepts" of information‐seeking studies. Libr Q 2007 Apr;77(2):109-132. [doi: 10.1086/517840]
78. Saracevic T, Kantor P. Studying the value of library and information services. Part I. Establishing a theoretical framework. J Am Soc Inf Sci 1997 Jun;48(6):527-542. [doi: 10.1002/(SICI)1097-4571(199706)48:6<527::AID-ASI6>3.0.CO;2-W]
79. van Deursen AJ, van Dijk JA. Toward a multifaceted model of internet access for understanding digital divides: an empirical investigation. Inform Soc 2015 Sep 11;31(5):379-391. [doi: 10.1080/01972243.2015.1069770]
80. Zach L, Dalrymple PW, Rogers ML, Williver-Farr H. Assessing internet access and use in a medically underserved population: implications for providing enhanced health information services. Health Info Libr J 2012 Mar;29(1):61-71 [FREE Full text] [doi: 10.1111/j.1471-1842.2011.00971.x] [Medline: 22335290]
81. Yu L. Understanding information inequality: making sense of the literature of the information and digital divides. J Librarianship Inf Sci 2016 Jun 30;38(4):229-252. [doi: 10.1177/0961000606070600]
82. Luhmann N. What is communication? Commun Theory 1992 Aug;2(3):251-259. [doi: 10.1111/j.1468-2885.1992.tb00042.x]
83. Luhmann N, Bednarz J, Baecker D. Social Systems. Redwood City, California: Stanford University Press; 1996.
84. Luhmann N. [Politics and complexity: The contributions of the general theory of systems]. Paris: Les Éditions du Cerf; 1999.
85. Luhmann N. [Legitimation through the procedure]. Québec: Les Presses de l'Université Laval; 2001.
86. Anderson M, Perrin A. 13% of Americans don't use the internet: Who are they?. 2018 Mar 05. URL: http://www.pewresearch.org/fact-tank/2018/03/05/some-americans-dont-use-the-internet-who-are-they/ [WebCite Cache ID 72wt4rUwN]
87. Chalifoux E. Léger Recherche Stratégie Conseil. Les aspirations des Québécois en matière de politiques sociales. Montréal: Foundation Lucie et André Chagnon; 2015.
88. SOM Recherche & Sondages. Évaluation de l'impact du site et du magazine Naître et Grandir (personal communication). Montréal: Naître et grandir; 2015.

89. Organisation for Economic Co-operation and Development (OECD). Income Distribution Database. Paris: OECD; 2015. URL: http://www.oecd.org/social/income-distribution-database.htm [WebCite Cache ID 736kaPHiS]
90. Organisation for Economic Co-operation Development (OECD). The Survey of Adult Skills: Reader's Companion [PIAAC survey volume 2 on methodology and methods]. Paris: OECD Publishing; 2013.
91. Nahl D, Bilal D. Information and emotion: The emergent affective paradigm in information behavior research and theory. Medford: Information Today Inc; 2007.
92. Nahl D. Social–biological information technology: an integrated conceptual framework. J Am Soc Inf Sci 2007 Nov;58(13):2021-2046. [doi: 10.1002/asi.20690]
93. Anderson M, Perrin A. Pewresearch. 2018 Mar 05. 13% of Americans don't use the internet: Who are they? URL: http://www.pewresearch.org/fact-tank/2018/03/05/some-americans-dont-use-the-internet-who-are-they/ [accessed 2018-10-05] [WebCite Cache ID 72wt4rUwN]
94. AboutKidsHealth. URL: https://www.aboutkidshealth.ca/ [accessed 2018-10-05] [WebCite Cache ID 72wu5R7wO]
95. Burris B. Computerization of the workplace. Annu Rev Sociol 1998 Aug;24:141-157. [doi: 10.1146/annurev.soc.24.1.141]
96. DiMaggio P, Hargittai E, Neuman W, Robinson J. Social implications of the internet. Annu Rev Sociol 2001 Aug;27:307-336. [doi: 10.1146/annurev.soc.27.1.307]
97. Romanow R. Building on Values: The Future of Health Care in Canada. Saskatoon: Commission on the Future of Health Care in Canada; 2002.
98. Commission Clair, Commission d'étude sur les services de santé et les services sociaux. Les solutions émergentes: Rapport et recommandations. Québec: Ministère de la santé et des services sociaux; 2000.
99. World Summit on the Information Society (WSIS). tjsl.edu. Geneva: United Nations; 2005. Tunis agenda for the information society URL: https://www.tjsl.edu/slomansonb/5.2_TunisAgenda.pdf [accessed 2018-10-12] [WebCite Cache ID 736sX4t5Y]
100. Industry Canada. Canada at the World Summit on the Information Society (WSIS). Government of Canada 2009.
101. Centre francophone d'informatisation des organisations (CEFRIO). Génération A: Portrait de l'utilisation d'internet et de l'ordinateur par les aînés internautes du Québec. Montréal: CEFRIO; 2011.
102. Waterman H, Tillen D, Dickson R, de Koning K. Action research: a systematic review and guidance for assessment. Health Technol Assess 2001;5(23):iii-157 [FREE Full text] [Medline: 11785749]
103. Munn-Giddings C, McVicar A, Smith L. [Systematic review of the uptake and design of action research in published nursing research, 2000-2005]. Rech Soins Infirm 2010 Mar(100):124-133. [Medline: 20419948]
104. Munten G, van den Bogaard J, Cox K, Garretsen H, Bongers I. Implementation of evidence-based practice in nursing using action research: a review. Worldviews Evid Based Nurs 2010 Sep;7(3):135-157. [doi: 10.1111/j.1741-6787.2009.00168.x] [Medline: 19778316]
105. Soh K, Davidson P, Leslie G, Bin Abdul Rahman A. Action research studies in the intensive care setting: a systematic review. Int J Nurs Stud 2011 Feb;48(2):258-268. [doi: 10.1016/j.ijnurstu.2010.09.014] [Medline: 21030021]
106. Argyris C, Putnam R, Smith D. Action Science:Concepts, Methods, and Skills for Research and Intervention. San Francisco, CA: Jossey Bass; 1985.
107. Bush P, Pluye P, Loignon C. Improving health organization practices through participatory research - is it worth it? A participatory systematic mixed studies review poster presentation. 2014 Presented at: Annual Conference North American Primary Care Research Group; 2014; New York URL: https://www.mcgill.ca/familymed/files/familymed/rd_seminar_paula_bush_2014-10-16.pdf
108. Pluye P, Hong QN. Combining the power of stories and the power of numbers: mixed methods research and mixed studies reviews. Annu Rev Public Health 2014;35:29-45. [doi: 10.1146/annurev-publhealth-032013-182440] [Medline: 24188053]
109. Creswell J, Plano Clark V. Designing and conducting mixed methods research. Thousand Oaks: Sage; 2011.
110. Schwartz-Shea P, Yanow D. Interpretive Research Design: Concepts and Processes. New York: Routledge; 2013.
111. Patton M. Qualitative Research & Evaluation Methods. Thousand Oaks: Sage; 2005.
112. Abbott A. The causal devolution. Sociol Methods Res 1998 Jun 30;27:148-181. [doi: 10.1177/0049124198027002002]
113. Amirault M, Cobbett S, Doherty A. Consumer health information on the internet. J Can Health Libr Assoc 2005;26(2):41-46. [doi: 10.1093/her/16.6.671]
114. Fereday J, Muir-Cochrane E. Demonstrating rigor using thematic analysis: a hybrid approach of inductive and deductive coding and theme development. Int J Qual Methods 2006 Nov 29;5(1). [doi: 10.1177/160940690600500107]
115. Boyatzis R. Transforming Qualitative Information: Thematic Analysis and Code Development. Thousand Oaks: Sage; 1998.
116. Pavel S, Nolet D. Précis de terminologie / Handbook of Terminology. Ottawa: Minister of Public Works and Government Services Canada, Terminology and Standardization; 2001.
117. Clark D, Nicholas D, Jamali HR. Evaluating information seeking and use in the changing virtual world: the emerging role of Google Analytics. Learn Pub 2014 Jul 01;27(3):185-194. [doi: 10.1087/20140304]
118. Turner SJ. Website statistics 2.0: using Google Analytics to measure library website effectiveness. Tech Serv Q 2010 May 28;27(3):261-278. [doi: 10.1080/07317131003765910]

119. Crutzen R, Roosjen JL, Poelman J. Using Google Analytics as a process evaluation method for internet-delivered interventions: an example on sexual health. Health Promot Int 2013 Mar;28(1):36-42. [doi: 10.1093/heapro/das008] [Medline: 22377974]
120. McGuckin C, Crowley N. Using Google Analytics to evaluate the impact of the CyberTraining project. Cyberpsychol Behav Soc Netw 2012 Nov;15(11):625-629. [doi: 10.1089/cyber.2011.0460] [Medline: 23075266]
121. Pampalon R, Hamel D, Gamache P, Simpson A, Philibert M. Validation of a deprivation index for public health: a complex exercise illustrated by the Quebec index. Chronic Dis Inj Can 2014 Feb;34(1):12-22 [FREE Full text] [Medline: 24618377]
122. Pampalon R, Hamel D, Gamache P, Philibert MD, Raymond G, Simpson A. An area-based material and social deprivation index for public health in Québec and Canada. Can J Public Health 2012 Apr 30;103(8 Suppl 2):S17-S22. [Medline: 23618066]
123. François T. Louvain, Belgique: Centre de Traitement Automatique du Langage, Université Catholique de Louvain (UCL); 2011. Les apports du traitement automatique des langues à la lisibilité du français langue étrangère PhD thesis URL: http://old.atala.org/IMG/pdf/Francois-TAL54-1-2.pdf [accessed 2018-10-12] [WebCite Cache ID 736owyhMn]
124. Sandelowski M. What's in a name? Qualitative description revisited. Res Nurs Health 2010 Feb;33(1):77-84. [doi: 10.1002/nur.20362] [Medline: 20014004]
125. Campbell M, Fitzpatrick R, Haines A, Kinmonth AL, Sandercock P, Spiegelhalter D, et al. Framework for design and evaluation of complex interventions to improve health. Br Med J 2000 Sep 16;321(7262):694-696 [FREE Full text] [Medline: 10987780]
126. Eccles M, Grimshaw J, Campbell M, Ramsay C. Research designs for studies evaluating the effectiveness of change and improvement strategies. Qual Saf Health Care 2003 Feb;12(1):47-52 [FREE Full text] [Medline: 12571345]
127. Craig P, Dieppe P, Macintyre S, Michie S, Nazareth I, Petticrew M, Medical Research Council Guidance. Developing and evaluating complex interventions: the new Medical Research Council guidance. Br Med J 2008 Sep 29;337:a1655 [FREE Full text] [Medline: 18824488]
128. Curry LA, Nembhard IM, Bradley EH. Qualitative and mixed methods provide unique contributions to outcomes research. Circulation 2009 Mar 17;119(10):1442-1452. [doi: 10.1161/CIRCULATIONAHA.107.742775] [Medline: 19289649]
129. Lewin S, Glenton C, Oxman A. Use of qualitative methods alongside randomised controlled trials of complex healthcare interventions: methodological study. Br Med J 2009 Sep 10;339:b3496. [doi: 10.1136/bmj.b3496]
130. Malterud K. The art and science of clinical knowledge: evidence beyond measures and numbers. Lancet 2001 Aug 04;358(9279):397-400. [doi: 10.1016/S0140-6736(01)05548-9] [Medline: 11502338]
131. Shaw I. Qualitative research and outcomes in health, social work and education. Qual Res 2016 Aug 15;3(1):57-77. [doi: 10.1177/146879410300300103]
132. Miles M, Huberman M, Saldana J. Qualitative Data Analysis: A Methods Sourcebook. London: SAGE; Apr 2013.
133. Gallagher F. La recherche descriptive interprétative. In: Méthodes qualitatives, quantitatives et mixtes. Montreal: Presses de l'Université du Québec; 2014:5-28.
134. Creswell J. Qualitative inquiry and research design: Choosing among five approaches. Thousand oaks: Sage; 2007.
135. Morse JM. Critical Issues in Qualitative Research Methods. Thousand Oaks: Sage Publications; 1994.
136. Bamberg M. Stories: big or small. Narrat Inq 2006 Aug 29;16(1):139-147. [doi: 10.1075/ni.16.1.18bam]
137. Newman TB. The power of stories over statistics. Br Med J 2003 Dec 20;327(7429):1424-1427 [FREE Full text] [doi: 10.1136/bmj.327.7429.1424] [Medline: 14684635]
138. Sools A. Narrative health research: exploring big and small stories as analytical tools. Health (London) 2013 Jan;17(1):93-110. [doi: 10.1177/1363459312447259] [Medline: 22694917]
139. Nieuwboer CC, Fukkink RG, Hermanns JM. Online programs as tools to improve parenting: a meta-analytic review. Children Youth Serv Rev 2013 Nov;35(11):1823-1829. [doi: 10.1016/j.childyouth.2013.08.008]
140. Godin G. [Behaviors in the Field of Health]. Montréal: Presses de l'Université de Montréal; 2012.
141. Renaud L. [Internet and health promotion]. Montréal: Presses de l'Université du Québec; 2012:133-148.
142. Thoër C. Internet: un facteur de transformation de la relation médicin-patient. Communiquer 2013:1-24 [FREE Full text] [doi: 10.4000/communiquer.506]
143. Romeyer H. La santé en ligne [in French]. Communication 2012;30(1):1-22.
144. Masi CM, Suarez-Balcazar Y, Cassey MZ, Kinney L, Piotrowski ZH. Internet access and empowerment: a community-based health initiative. J Gen Intern Med 2003 Jul;18(7):525-530 [FREE Full text] [Medline: 12848835]
145. Fishbein M, Ajzen I. Predicting and Changing Behavior: The Reasoned Action Approach. London: Psychology Press; 2010.
146. Cihr-irsc. 2015. CIHR 2015-2018 Action Plan for Official Languages URL: http://www.cihr-irsc.gc.ca/e/47951.html [accessed 2018-10-05] [WebCite Cache ID 72wv4UuFN]
147. Commissioner of Official Languages. Officiallanguages.gc. Ottawa: Government of Canada, Minister of Public Services and Procurement Early childhood: Fostering the vitality of francophone minority communities URL: http://www.officiallanguages.gc.ca/en/publications/other/2016/early-childhood-report [accessed 2018-10-05] [WebCite Cache ID 72wv9hLDU]

148. Greenhalgh T, Robert G, Macfarlane F, Bate P, Kyriakidou O. Diffusion of innovations in service organizations: systematic review and recommendations. Milbank Q 2004;82(4):581-629 [FREE Full text] [doi: 10.1111/j.0887-378X.2004.00325.x] [Medline: 15595944]
149. Milat AJ, Newson R, King L, Rissel C, Wolfenden L, Bauman A, et al. A guide to scaling up population health interventions. Public Health Res Pract 2016 Jan 28;26(1):e2611604 [FREE Full text] [doi: 10.17061/phrp2541543] [Medline: 26863167]
150. Milat AJ, Bauman A, Redman S. Narrative review of models and success factors for scaling up public health interventions. Implement Sci 2015 Aug 12;10(17):113-141 [FREE Full text] [doi: 10.1186/s13012-015-0301-6] [Medline: 26264351]
151. Information Technology Primary Care Research Group. Mcgill. The Information Assessment Method (IAM) URL: https://www.mcgill.ca/familymed/research/projects/itpcrg [accessed 2018-10-05] [WebCite Cache ID 72wvH5qH8]
152. Unité de soutien SRAP Québec. URL: http://unitesoutiensrapqc.ca/ [accessed 2018-10-05] [WebCite Cache ID 72wvU9bHu]
153. Brillon K. L'usage et l'appropriation de l'Internet-santé: le cas des mères de famille thesis. Ottawa: Département de communication, Université d'Ottawa; 2015.
154. Thoër C, Lévy J. Internet et santé. Montréal: Presses de l'Université du Québec; 2012.
155. Dholakia UM. How customer self-determination influences relational marketing outcomes: evidence from longitudinal field studies. J Mark Res 2006;43(1):109-120. [doi: 10.1509/jmkr.43.1.109]
156. Dwyer F, Schurr P, Oh S. Developing buyer-seller relationships. J Mark 1987;51(2):11-27. [doi: 10.2307/1251126]
157. Leenheer J. The effectiveness of relational marketing instruments. Medium Econometrische Technieken 2006;14(1):20-24 [FREE Full text]
158. Palmatier R, Dant R, Grewal D, Evans K. Factors influencing the effectiveness of relationship marketing: a meta-analysis. J Mark 2006;70(4):136-153. [doi: 10.1509/jmkg.70.4.136]
159. Brownson RC, Diez RA, Swartz K. Commentary: generating rigorous evidence for public health: the need for new thinking to improve research and practice. Annu Rev Public Health 2014;35:1-7. [doi: 10.1146/annurev-publhealth-112613-011646] [Medline: 24328987]

Abbreviations

AKH: AboutKidsHealth
CDIAP: Canadian Deprivation Index Assignment Program
CIHR: Canadian Institutes of Health Research
IAM: Information Assessment Method
IRB: institutional review board
N&G: Naître et grandir
NPI: nominated principal investigator
OPR: organizational participatory research
SES: socioeconomic status

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Protocol

Evaluating the Use of Smart Home Technology by People With Brain Impairment: Protocol for a Single-Case Experimental Design

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Abstract

Background: Smart home technologies are emerging as a useful component of support delivery for people with brain impairment. To promote their successful uptake and sustained use, focus on technology support services, including training, is required.

Objective: The objective of this paper is to present a systematic smart home technology training approach for people with brain impairment. In addition, the paper outlines a multiple-baseline, single-case experimental design methodology to evaluate training effectiveness.

Methods: Adult participants experiencing acquired brain impairment who can provide consent to participate and who live in housing where smart home technology is available will be recruited. Target behaviors will be identified in consultation with each participant based on his or her personal goals for technology use. Target behaviors may include participant knowledge of the number and type of technology functions available, frequency of smart home technology use, and number of function types used. Usage data will be gathered via log-on smart home technology servers. A smart technology digital training package will also be developed and left on a nominated device (smartphone, tablet) with each participant to use during the trial and posttrial, as desired. Measures of the target behavior will be taken throughout the baseline, intervention, and postintervention phases to provide the evidence of impact of the training on the target behaviors and ascertain whether utilization rates are sustained over time. In addition, trial results will be analyzed using structured visual analysis, supplemented with statistical analysis appropriate to single-case methodology.

Results: While ascertaining the effectiveness of this training protocol, study results will offer new insights into technology-related training approaches for people with brain impairment. Preliminary data collection has been commenced at one supported housing site, with further scoping work continuing to recruit participants from additional sites.

Conclusions: Evaluation evidence will assist in planning for the smart technology set-up as well as training and support services necessary to accompany the provision of new devices and systems.

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KEYWORDS

assistive technology; clinical research protocol; disabled persons; housing; mobile phone

Introduction

There is growing recognition that electronic assistive technology (EAT) has the capacity to impact the way support is delivered to people with disability. Recent policy and research highlight that the end user should be empowered and supported to set goals for, choose, and implement the use of EAT, and this person-centered approach will benefit outcomes [1-4]. EAT encompasses mobile computing technologies in use by the wider population as well as specialized devices traditionally designed for and marketed to people with disability [5,6]. Mainstream devices such as smartphones and tablets are emerging as useful tools in developing the independence and participation of people with brain impairment-related disability in a range of life areas [6-9]. Apps that enable home automation and environmental control via these devices continue to emerge [10,11] and present exciting opportunities for this group to exercise environmental control and greater autonomy within the home.

In Australia, new models of supported housing for people with disability are beginning to integrate smart home technologies, including home automation and support staff communication systems, into their base design [12,13]. The use of EAT in these ways is of particular interest to funders of long-term care and support for people with disability, with potential cost benefit associated with reduced dependence on others within the home to complete daily tasks [14]. In Australia, the National Disability Insurance Agency has identified assistive technology, including home automation, environmental control systems, and tablet or smartphone apps, as offering the potential to reduce the lifetime care costs of people with severe disability and reduce the liability to the National Disability Insurance Scheme [2].

Recent research has demonstrated that the opportunities presented by EATs to people with disability living in supported housing have not yet been fully harnessed. A survey of 254 people with disability living in shared supported accommodation (SSA) in Victoria, Australia, demonstrated that only 43.7% had access to mainstream technology, and 10.6% had access to specialized technology [15]. Of 173 multifunction devices in use by surveyed SSA tenants, 42.8% were used for a single purpose and 7.4% had been abandoned (ie, were no longer used by a person) [16]. Qualitatively, interviews with people with acquired brain injury (N=22) living in SSA also indicated that many people were underutilizing the technologies they had access to while others were simply no longer using the devices they had previously purchased or had funded [5]. Participants were consistently more satisfied with the devices they used than they were with the support services they received in relation to the device use [5]. These services included procedures for obtaining the device, repairs or servicing, information and attention when using the device, and continuing support services [17].

Findings across these studies in SSA suggest that the underutilization and abandonment of devices may be attributed to gaps in "soft technology" support services. Soft technologies are defined as the "human factors" that lead to successful device or system uptake, such as any assessment, planning, training, and review involved in locating a suitable assistive technology [18]. Access to 24-hour shared support from disability support workers in SSA was not sufficient to promote and sustain the ongoing technology use for this group. Gaps were identified in support for device selection and set-up in the first instance, as well as ongoing support to modify, develop skills to use, or grade the use of specific devices over time [5]. Similarly, Sohlberg and Turkstra [19] pointed to limited systematic training received as a barrier to the effective use of cognitive aids, which can include EAT devices.

The findings of the above research, when coupled with other investigations, emphasize the need to develop structured approaches for the delivery of technology support services, including a person-centered approach to EAT use and training, for people with brain impairment. Powell et al [20] argued that systematic training delivers better skill maintenance and generalization than trial-and-error approaches. Following task analysis that defines the multiple steps that need to be trained, systematic training involves instructions on how to use the device as well as planning for the support that will promote use in the relevant environment [19]. Ponsford et al [21] similarly emphasized the importance of task analysis prior to multistep training and the importance of delivering interventions in real-life environments, tailored to the needs of an individual. Sohlberg and Turkstra [19] compared the training needs of two people with brain impairment to highlight the differences in training approach required between individuals. The comparison is made between a person with significant memory impairment that impacts his or her ability to learn new information and a person with a brain injury-related executive function impairment that impacts the initiation of device use. The authors suggested that persons with memory impairment may require highly structured, errorless learning approaches that incorporate practice with spaced retrieval. Meanwhile, persons with executive function impairment that impacts initiation may rather require external cues or prompting to use a device in context [19].

The new policy environment of a National Disability Insurance Scheme in Australia has further driven a positive change in consumer empowerment within a market-driven assistive technology environment [2,22]. This further directs the requirement for a person-centered, rather than technology-driven, approach to the uptake and use of EAT. With the need to deliver systematic approaches to technology support for people with brain impairment identified, as well as the opportunity for this group to now move into new models of supported housing with integrated smart home technology, this paper has two aims. First, it will document a systematic training intervention for use with people with brain impairment who have access to smart home technology in their housing. Following this, the paper will outline a multiple-baseline, single-case experimental design methodology that will be used to rigorously evaluate the effectiveness of the training program.

The single-case experimental design offers an intensive research method built on open systematic observation, repeated assessment, and data analysis [23-25]. This study design enables the evaluation of interventions tailored to suit an individual's needs and is, therefore, a valuable tool in collecting evidence on interventions that can be readily applied to clinical practice

[23]. Tate et al's [26] Model for Assessing Treatment Effect places single-case experimental design at the highest level (level 6) on a hierarchy for evaluating the viability of therapeutic interventions. The following training approach and evaluation protocol aims to positively influence the use of smart home technology, including smart phone- or tablet-controlled home automation or environmental control technology, by people with brain impairment living in technology-enabled housing. The training approach is designed to maximize technology uptake and multifunction use and minimize underutilization or abandonment risk for smart home technology devices and systems.

Methods

Research Questions

This project was designed to answer the following research questions:

1. Does smart home technology use increase over time with exposure to this training program, where technology use is defined as both frequency of use of smart home technology and the number of smart home technology functions used?
2. Does awareness or recall of the number and type of features of smart home technology available to an individual resident increase over time with exposure to this training program?

To examine generalization effects, this research will also seek to answer the following research questions:

1. Does exposure to the training program positively influence the psychosocial impact of the smart home technology for the person?
2. Does participants' satisfaction with their smart home technology increase with exposure to the training program?
3. If positive changes are noted following the training, are these changes sustained beyond the intervention period (to 4 weeks postintervention) and can these changes be attributed to specific phases of the intervention (eg, pre- or postneeds assessment phase, pre- or postsupported practice phase)?
4. Does participation in the training program lead participants to develop further goals for EAT uptake or usage?

The study design and associated participant recruitment as well as data collection procedures have been approved by Monash University's human research ethics committee.

Participants

Participants will be people aged >18 years with acquired brain impairment and associated memory impairment who reside in supported housing that offers integrated smart home technology and 24/7 staffing support available on-call, either onsite or remotely. Residents of these supported housing models who use the integrated technology will be invited to participate in this study. The key inclusion criteria of this study are that participants have identified goal(s) to increase their technology use. People identified through the initial "permission to contact" stage of a third-party recruitment strategy (see below) who do not wish to increase their technology use will not be recruited into the study.

In this study, a third-party recruitment strategy will be used. An invitation to participate (and contact details "permission to contact" slip) will be provided by the research group to a representative of the disability support provider at the housing model. This provider will pass the invitation on to eligible residents so they can consider whether they would like to release their contact details to the research group. This study will only include participants who can provide their own informed consent. The service provider handing on the invitation will know whether the person can provide his or her own consent to participate, as part of their service agreement with the resident. It is then the individual resident's decision as to whether he or she would like to fill out the permission slip and post or email a copy of it back to the research team so that the research group can contact him or her to provide more information about the study. This recruitment design ensures that the research group only accesses a person's contact details if the individual chooses to release them and that the service provider need not know who has, or has not, responded.

Intervention Setting

This training intervention will be carried out in the homes of consenting participants.

Target Behavior

The following are the target behaviors of this intervention:

1. Frequency of smart home technology use each day
2. Number of smart home technology function types used, which may include the following functions: lights on or off, blinds up or down, door open or close, heater or cooler on or off
3. Participants' knowledge of the number and type of smart home technology functions they can access

Data on frequency and number of functions in use will be gathered daily via actual logged data stored on the smart home technology server at the chosen housing site. Measures will be taken throughout the baseline, intervention, and postintervention phases to provide evidence of the impact of the training on the target behaviors and to ascertain whether utilization rates of the integrated technology are sustained over time. In addition, emphasis will be placed on developing an integrated digital training package that can be left with the persons with disability (or where appropriate, a family member or other carer) so that they can be referred back to if required in future.

Baseline Measurement

The frequency of use and the type of smart home technology function used is logged by the server controlling the smart home system every time a function is used (including the time and date it is used). Data can be extracted from the server with the consent of the resident via a system-generated log report provided by the technology company that installed the system. In addition, baseline data on participants' frequency and type of technology use will be gathered daily over 7 days via review of these system-generated logs, thus, providing 7 baseline data points. In this way, the research team will be provided with a thorough understanding of participants' preintervention frequency and type of technology use. Furthermore, a review

of data logs will take place prior to each intervention session to monitor participants' progress.

A short questionnaire will be used to gather baseline data on the participants' knowledge of the number and type of smart home technology functions they can access at their home. The questionnaire will commence using a free recall format, asking participants to name each function that can be controlled using the installed smart home technology (eg, "Can you please tell me all of the functions that you are able to control using your smart home technology?"). Following this, participants will be presented with a list of functions that may be controlled by the smart home technology; this list will also contain distractor items or functions that are not controlled by the smart home technology installed in participants' home. In addition, participants will be asked to select the functions that their smart home technology can control (eg, "What functions are available on your device? Please tick all that apply"). Data on the number of functions named correctly or incorrectly via free recall will be collected along with data on the number of functions selected correctly or incorrectly via the prepared list. Furthermore, the questionnaire will be customized to the housing site within which the research takes place to ensure that all smart home technology functions available are captured and appropriate distractor items are included.

Once these baseline data have been collected, participants will be oriented to the range of functions that their smart home technology can be used for via a prepared list that participants will keep. Participants will be supported to post this list on a prominent place (eg, a noticeboard or fridge) to refer to between sessions. Use of this short questionnaire will continue throughout the intervention to explore whether participants' knowledge and awareness of the number of functions available increases from baseline.

In this study, we will use a concurrent multiple-baseline design across 3 participants. According to Kazdin [25], typically ≥3 baselines are used in multiple-baseline design research to demonstrate the impact of the intervention applied. As per this method, baseline data will be collected continuously and concurrently for 3 participants, and the intervention will be introduced in a staggered or time-lagged fashion across participants at different time-points. Specifically, the training package will be implemented with the first participant while baseline data gathering continues with the remaining participants. The training package will be implemented with a second participant once the first participant shows that the intervention is impacting his or her technology use. This process will be repeated before a third participant is added to the intervention phase. As described by Kazdin [25], staggering the start of an intervention is undertaken to ensure that it is the intervention that is responsible for the change, rather than other external factors. The design effectively minimizes threats to internal validity, such as history and maturation.

Equipment

Smart Home Technology

Participants may access the smart home technology features integrated within the design of their supported housing via a number of smart technologies that include iOS smartphone, Android smartphone, and iOS or Android tablet.

These devices may be used by participants for other reasons beyond smart home technology functionality (eg, electronic social networking). Each device is smart home technology-enabled via a software app, and participants may use multiple devices to access this functionality (eg, a combination of smartphone and tablet). This app is loaded on to the smartphone or tablet to be used and provides a software-user interface for residents to access and control their smart home technology. A brief software operating guide, detailed operating guide, and step-by-step flowchart guide will be developed by the research team, specific to the software app in use at the housing site. Note that in the absence of smart devices, the smart home technology features can be operated by residents or support staff manually via wall-mounted switches or standard remote controls (eg, air conditioner remote control).

Video Training Tool

A video training tool will be developed in consultation with each research participant; it will target priorities for smart home technology use identified by the individual participant. The video training tool will consist of text, audio, and video components, providing a step-by-step demonstration to participants for using each prioritized technology function. Furthermore, video footage will be captured by the research team and edited using a Web-based video production tool to include step-by-step audio and text. This training tool will be saved to the smartphone or tablet that the person uses so that he or she can refer to it between sessions, show it to informal or paid support persons, or continue to view or share it with others once the intervention is complete, if desired.

Intervention Phases

Figure 1 shows the 3 intervention phases of the study.

Phase One

Meeting One—Recruitment

We will follow project explanation and informed consent process using human research ethics committee-approved forms. Once consent is provided, the World Health Organization Disability Assessment Schedule 2.0 [27] will be administered to document the functional status of participants. Then, baseline data recording will commence. Data logs will be downloaded from the server via the technology provider for 7 days.

Phase Two

Meeting Two—Needs Assessment

Meeting two will be conducted with one participant at a time and only once baseline usage data have been collected.

1. Two published measures examining the experience of technology use will be used to collect preintervention data: the Psychosocial Impact of Assistive Devices Scale (Question 3) [28] and the Quebec User Evaluation of Satisfaction with assistive Technology (Question 4) [17].
2. A short questionnaire to ascertain participants' preintervention understanding of the functions available on their assistive technology will be administered. Specifically,

this questionnaire will ask participants to use free recall to name all of the functions available and, then, ask participants to select all of the functions available from a prepared list that contains distractor items.

3. Participants will be oriented to the number of functions available on their smart home technology, verbally and with a numbered list, which will be left with the person on a prominent place that they can view between sessions. Any barriers to technology use will be identified and ameliorated if possible.

If there is a major barrier to participants' technology use, for example, ineffective mounting of the device to participants' motorized wheelchair, an occupational therapist will assess and recommend a solution prior to the start of the intervention.

Meeting Three—Goal Setting

The events below will take place during meeting three. Goal setting will be undertaken, which will involve the following:

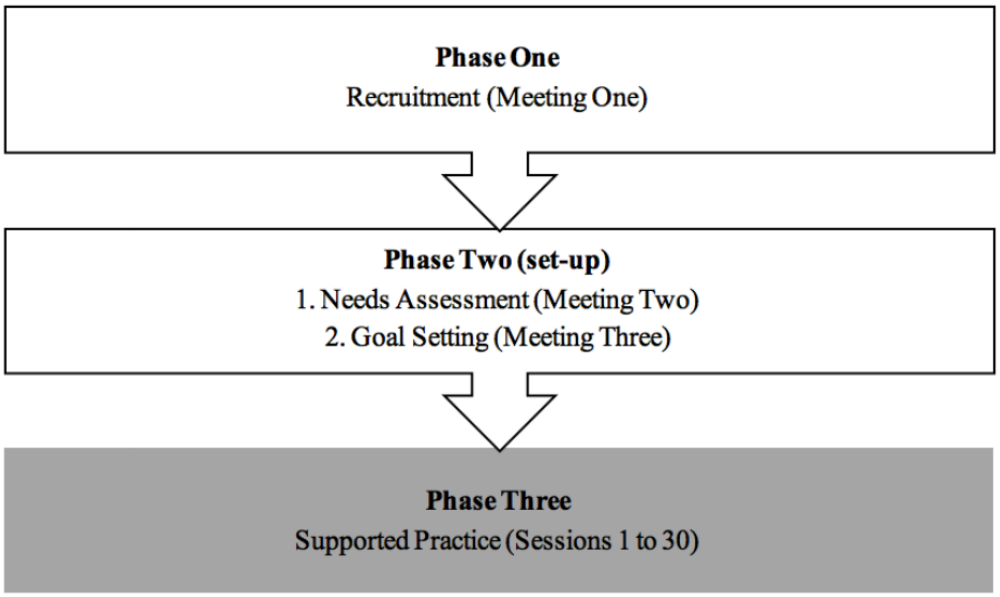
1. Reviewing the number of functions available on the device with participants—verbally and with a numbered list
2. Comparing the baseline data that show the frequency and type of current smart home technology function use against all the functions available on the smart home technology system to determine whether there are any functions that are not in use, or that are utilized infrequently, that participants may be interested in using. Alternative control methods in use (ie, wall-mounted switch or standard remote controls) will be discussed with participants, and the preferred method of control will be confirmed.
3. If more than one function is identified, the functions that the person would like to increase their use of via their participation in this intervention program will be prioritized (to a maximum of 3 functions). A visual reminder of the prioritized functions will be prepared and left with participants on a prominent location for them to review between sessions. This visual reminder of prioritized functions will be incorporated within the list of all 12 functions previously prepared.
4. Preparation of video training tools to act as a step-by-step guide to using the prioritized technology function(s)
5. Preparation of a low-technology (paper-based) flowchart that will be used to prompt participants on the steps to navigate to the function(s) if they are unsuccessful in navigating the user interface to locate and activate the nominated smart home technology function(s) after viewing the video twice

Phase 3—Supported Practice

According to Sohlberg and Mateer [29], "consistent practice and support for evaluating one's performance can result in improved error recognition and correction" [pg 255] following acquired brain injury. Short, frequent sessions will, therefore, be utilized within this phase to provide participants with multiple opportunities to practice their technology use in the presence of a disability support worker who can provide feedback. A trained disability support worker having experience working with people with brain injury and related cognitive impairment will be employed to deliver these practice sessions. Sessions length will range between 20 and 30 minutes every second day (including one weekend day).

The duration of the training program will be guided by participants' achievement of the mastery criterion, that is, when a participant demonstrates an increased usage of the smart home technology functions (target behaviors) he or she prioritized for the intervention. The duration of the training program will not extend past 10 weeks.

Figure 1. Intervention phases; gray cell denotes the active intervention phase.



Treatment Adherence

Training sessions will be video- and audiotaped to allow an assessor (an independent member of the project team) to rate whether the disability support worker administered all components of the training program as outlined in the intervention protocol.

Session Guide

Session One

At the beginning of the first intervention session, participants will be asked, in free recall format, to name all the functions that can be controlled by the smart home technology installed in their home. Participants will then be provided with a list containing each of the smart home technology functions available, as well as distractor items. Next, participants will be asked to select the items that their smart home technology can control. Responses will be recorded and counted to compare against the number of functions available and the number of functions identified by participants in Meeting Two at baseline. In addition, participants will be provided with feedback on their responses to this question and, if required, reoriented to the number of functions their technology can be used for. These data will be compared with data gathered during the intervention period, providing evidence as to whether the intervention has expanded participants' awareness or recall of the number of smart home technology functions available to them. Furthermore, these data will be compared against actual technology use to determine whether there are any differences between the knowledge of what technology can be used for and the actual use.

The disability support worker will then ask participants to identify which function it was that they had prioritized to focus on within the training intervention. The disability support worker will prompt participants to check the visual reminder developed in the previous session if they are unable to recall this. The disability support worker will demonstrate how to access the link to the video training tool, saved in a "memo" on the person's smart device. Participants will then be prompted by the disability support worker to view the video of the first smart home technology function they prioritized in the goal setting interview. They will then practice using it once while the disability support worker is present. The disability support worker will make a record of the steps completed successfully using a progress monitoring form (Multimedia Appendix 1), providing immediate feedback to participants on their performance once they have completed their first attempt. If a participant makes an error in navigating through the user interface, locating the desired function on the device or activating the function, and does not initiate self-correction, the disability support worker will immediately provide feedback and prompt the participant to review the video for a second time. If the participant is unable to navigate the user interface, locate, and activate the desired smart home technology function after viewing the video for a second time, the disability support worker will provide the person with the paper-based step-by-step guide for navigating, locating, and activating the desired function and use this in conjunction with verbal prompting to guide the participant through each step of using the nominated smart home technology function.

Instances in which a participant requires subsequent review of the video or the paper-based written and verbal prompting will be noted on the progress monitoring form. This procedure of prompting incorporates components of errorless learning, modeling the skill before participants attempt it (via video tool), and providing immediate feedback if participants make an error. These strategies have been included in this study to ensure a high rate of accuracy during the acquisition phase of learning. Given the goal of the acquisition phase of learning is to improve the accuracy of skill performance, this training program has been developed to support participants to experience correct use of the function and to avoid participants internalizing memory of incorrect use [29]. The flowchart will be designed so that it can be kept on the inside cover of the iPad, or at another accessible place, depending on the needs of participants.

Subsequent Intervention Sessions

At the beginning of subsequent intervention sessions, participants will be asked, in free recall format, to name the functions that they can control using their smart home technology. Then, participants will be provided with the list used in intervention session one and asked to select the functions that their smart home technology can control. Data will be recorded and counted to compare against the number of functions available and the number of functions identified by participants at baseline. Participants will be provided with feedback on their responses to this question and, if required, reoriented to the number of functions the technology can operate (using the existing list).

The reflection-prediction technique, a metacognitive strategy, will be utilized within each remaining session to allow participants to compare their predictions of performance with actual performance. According to Sohlberg and Mateer [29], "this process gives the client information about his or her real-world functioning in such a way that the client can learn more about what is working and not working" [pg 289]. Use of the reflection-prediction technique in this study will involve the review of performance since the previous session, at the start of the next session that immediately follows. This process will assist to identify behaviors that have been targeted successfully and highlight areas that require further practice. The disability support worker will utilize the following script to facilitate the reflection-prediction technique:

- Do you think your technology use has changed since we last met?
- I have some data here on your technology use since we last met. It looks like the frequency of your technology use has (increased or decreased or stayed the same), and it looks like you are using (more or less or the same) types of functions within your smart home technology. Since our last session you are using X, Y, and Z. Why do you think your technology use has changed or stayed the same or decreased since the last session?
- Have you been using the video outside of the intervention? The video has had (x) views. Were any or all of those views by you?

Cumulative review, defined as a regular review of previously learned skills [30], will then be used to review the content covered in the last session using probes including the following:

- What function did you focus on in the last session?
- Can you show me the steps to using [the function focused on last session]?

The disability support worker will prompt participants to review the part of the video training tool that demonstrates this function if they are unable to demonstrate the correct use of the function during this review phase of the session.

If participants have increased the frequency of use of their first prioritized technology function and can successfully demonstrate its use in the review phase, they will be prompted by the disability support worker to address the second prioritized function. As in session one, the disability support worker will provide feedback within the session on participants' performance, aligned with the principles of errorless learning. If a participant makes an error, the disability support worker will prompt the participant to review the video for a second time. If the participant is unable to use the smart home technology function after viewing the video for a second time, the disability support worker will provide the resident with the printed step-by-step flowchart to assist with navigating, locating, and activating the desired function and use this in conjunction with verbal prompting to guide the participant through each step of using the smart home technology function. Steps completed successfully and instances in which a participant requires a second review of the video, or written and verbal prompting, will be noted on the progress monitoring form.

The procedure explained above will be repeated session after session until each of the participant's technology use priorities have been addressed.

Postintervention Follow-Up (4 Weeks Postintervention)

Four weeks following the cessation of the intervention, system-generated data logs will be reviewed to check whether the person has maintained the frequency and type of technology use that was logged at the end of the intervention. A final meeting will be arranged with participants to discuss the data log and their perspective on the effectiveness of the training intervention and any changes to their technology use over that time since the end of the intervention, including whether participants wish to further increase their use of the smart home technology system or explore other EAT device uptake options. Questions regarding whether the training tool has been used since the intervention and, if so, by whom and how often will also be asked. Furthermore, video "view" data will be recorded. The Psychosocial Impact of Assistive Devices Scale and Quebec User Evaluation of Satisfaction with assistive Technology will be administered for the final time to detect any changes in psychosocial impact and satisfaction since the cessation of the intervention.

Results

This project has received funding from the Transport Accident Commission, through the Institute for Safety, Compensation and Recovery Research. The Institute for Safety, Compensation and Recovery Research is a joint initiative of the Transport Accident Commission, WorkSafe Victoria, and Monash University. An initial 2 participants underwent written explanatory and consent processes and provided signed consent to participate in the study. These participants were from a single apartment development that offers tenants access to home automation and communication technologies. After the collection of demographic data, initial testing of the home automation technology server indicated that data were not being reliably recorded. The technology supplier was contacted to rectify this issue. The consenting participants were advised that data collection would be placed on hold. Further participant recruitment and data collection will be resumed when this server issue is rectified at the specified site. In the meantime, scoping work for recruitment of additional participants at alternate sites offering the necessary server data collection is being undertaken.

Discussion

The availability of smart home technology, and recognition of the utility of such technologies for people with disability, continues to grow. There is a need to ensure that people with access to such technology are able to maximize device usage, as desired, so that the opportunities presented by these devices and systems are not lost. The above training intervention was designed to be implemented collaboratively with people with brain impairment who wish to maximize the use of the smart home technology made available to them in supported housing and, thus, ensure that the underutilization and abandonment of these technologies can be avoided. The design of this single-case experiment protocol meets the requirements of level 6 on the Model for Assessing Treatment Effect hierarchy [26]. Target behavior measurements are to be taken frequently and repeatedly in both the baseline and intervention phases, and treatment delivery can be staggered using a multiple-baseline approach. In this way, any cause-effect relationships between the intervention and target behaviors can be demonstrated [31]. The existing literature in the area of smart home technology includes descriptions of the types of technology available [6,7] and research that has evaluated residents' experience of integrated technology in housing [12]. However, the existing literature does not report on specific interventions that may support smart home technology uptake and use. To the best of the authors' knowledge, this is the first systematic training program targeting smart home technology uptake and use by people with brain impairment to have been documented, which also presents a single-case experimental design methodology for its evaluation.

The training activities proposed for use in this trial were designed to be as clinically accessible as possible while still grounded in learning theory derived from practice and research on people with acquired brain impairment [19-21,29]. A Web-based video production tool was selected as an easily accessible and low-cost platform that would enable the packaging of audio, video, and text into a single training resource that can then be viewed and shared by the end user—residents using smart home technology in housing. Furthermore, the use of such a platform means that individualized, video-based training resources can be developed

to meet the unique needs of each participant in a cost-effective manner. All other resources to be developed as part of the intervention are low tech in nature (eg, paper-based flowchart) and can be easily adapted to the needs and smart home technology goals of each participant. The theoretical background of this training approach, incorporating the use of evidence-based metacognitive strategies and errorless learning principles [19,29,30], supports its potential effectiveness. Data will be collected on participants' actual usage, their awareness of functionality availability, their satisfaction with the smart home technology, and psychosocial impact of use, providing a wide-ranging examination of the impact of this training program.

This single-case experimental design protocol clearly defines the behaviors to be targeted via the training intervention and the ways in which these behaviors will be repeatedly measured. According to Tate et al [32], the reliability of the target behavior measures used is an important consideration. The opportunity to use a computer server to objectively log or record data on participants' smart home technology use may overcome potential challenges presented by the use of human raters, who may not be able to record actual use data as accurately. The analysis of this "big data," automatically recorded by many smart home devices and systems [33], enables researchers to quantify actual use and monitor any changes that occur as a result of the intervention. While conducting ethical human research, it is paramount that participant consent is obtained prior to the collection and analysis of this private data. Furthermore, so that the reliability of this data can be assured, data recorded via the computer servers at housing sites will need to be reviewed for accuracy, prior to participant recruitment and intervention commencement in this study.

Findings garnered from the future trial of this training approach will present important considerations for therapists who prescribe EAT to people with brain impairment. The findings of this research should guide therapists in planning for technology support services that must accompany the provision of any assistive device to clients, including smart home technology. In doing so, therapists can contribute to the longevity and utility of assistive technology solutions for their clients. Furthermore, documenting this intensive training approach offers the potential to provide the evidence of EAT usage and capacity building to the funders of EAT, including state-based insurers and the National Disability Insurance Agency. This evidence includes the amount and type of support services required to ensure the effective uptake and sustained use of EATs beyond the investment that needs to be made in the device or system itself.

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Conflicts of Interest

None declared.

Multimedia Appendix 1

Progress monitoring sheet.

[PDF File (Adobe PDF File), 28KB - resprot_v7i11e10451_app1.pdf]

References

1. Steel EJ, Buchanan R, Layton N, Wilson E. Currency and Competence of Occupational Therapists and Consumers with Rapidly Changing Technology. Occup Ther Int 2017:1-5 [FREE Full text] [doi: 10.1155/2017/5612843] [Medline: 29097973]
2. National Disability Insurance Agency. Assistive Technology Strategy. 2015 Oct. URL: https://www.ndis.gov.au/html/sites/default/files/AT-Paper_0.pdf [accessed 2016-02-01] [WebCite Cache ID 6xgVvMcAh]
3. Mirza M, Hammel J. Consumer-Directed Goal Planning in the Delivery of Assistive Technology Services for People who are Ageing with Intellectual Disabilities. Journal of Applied Research in Intellectual Disabilities 2009;22:445-457. [doi: 10.1111/j.1468-3148.2009.00495.x]
4. Rehabilitation Engineering and Assistive Technology Society of North America. RESNA Policy Position Statement. 2015 Dec. URL: https://www.resna.org/knowledge-center/government-relations/resna-policy-position-statement [accessed 2017-10-24] [WebCite Cache ID 70gO1jLFM]
5. Jamwal R, Callaway L, Ackerl J, Farnworth L, Winkler D. Electronic assistive technology used by people with acquired brain injury in shared supported accommodation: Implications for occupational therapy. British Journal of Occupational Therapy 2017 Feb 01;80(2):89-98. [doi: 10.1177/0308022616678634]
6. Gentry T. Smart homes for people with neurological disability: state of the art. NeuroRehabilitation 2009;25(3):209-217. [doi: 10.3233/NRE-2009-0517] [Medline: 19893189]

7. Dewsbury G, Linskell J. Smart home technology for safety and functional independence: the UK experience. NeuroRehabilitation 2011;28(3):249-260. [doi: 10.3233/NRE-2011-0653] [Medline: 21558630]
8. Wong D, Sinclair K, Seabrook E, McKay A, Ponsford J. Smartphones as assistive technology following traumatic brain injury: a preliminary study of what helps and what hinders. Disabil Rehabil 2017 Nov;39(23):2387-2394. [doi: 10.1080/09638288.2016.1226434] [Medline: 27748145]
9. Wild MR. Assistive Technology for Cognition Following Brain Injury: Guidelines for Device and App Selection. Perspect Neurophysiol Neurogenic Speech Lang Disord 2013 Jun 01;23(2):49. [doi: 10.1044/nnsld23.2.49]
10. Dickey N, Banks D, Sukittanon S. Home automation using Cloud Network and mobile devices. In: 2012 Proceedings of IEEE Southeastcon. USA: IEEE; 2012 Mar Presented at: Southeastcon; 15-18 March 2012; Orlando, FL URL: https://ieeexplore.ieee.org/document/6197003/ [doi: 10.1109/SECon.2012.6197003]
11. Piyare R. Internet of Things: Ubiquitous Home Control and Monitoring System using Android based Smart Phone. International Journal of Internet of Things 2013;2(1):5-11. [doi: 10.5923/j.ijit.20130201.02]
12. Callaway L, Tregloan K, Williams G, Clark R. Evaluating Access and Mobility within a New Model of Supported Housing for People with Neurotrauma: A Pilot Study. Brain Impairment 2016 Apr 7;17(01):64-76. [doi: 10.1017/BrImp.2016.7]
13. Ryan S, Reynolds A. New housing options for people with significant disability - Design Insights. Melbourne: Summer Foundation Ltd; 2015. URL: https://www.summerfoundation.org.au/resources/design-report/ [accessed 2018-09-19] [WebCite Cache ID 72YyCGLe2]
14. Oddy M, da Silva Ramos S. Cost effective ways of facilitating home based rehabilitation and support. NeuroRehabilitation 2013;32(4):781-790. [doi: 10.3233/NRE-130902] [Medline: 23867404]
15. Wood R, Farnworth L, Winkler D, Ackerl J, Callaway L. Using technology in supported accommodation to improve outcomes following acquired brain disorders. 2015 Presented at: 5th INS/ASSBI Pacific Rim Conference; 3 July; Sydney, Australia.
16. Jamwal R, Callaway L, Farnworth L, Winkler D. Electronic assistive technology use in Australian shared supported accommodation: rates and user characteristics. Disabil Rehabil Assist Technol 2018 Oct;13(7):634-640. [doi: 10.1080/17483107.2017.1360948] [Medline: 28774211]
17. Demers L, Weiss-Lambrou R, Ska B. The Quebec User Evaluation of Satisfaction with assistive Technology (QUEST 2.0) An overview and recent progress. Technology & Disability 2002;14(3):101-105. [doi: 10.13072/midss.298]
18. Australian Rehabilitation & Assistive Technology Association. ARATA: Participation through technology. 2012 URL: http://www.arata.org.au/download/arata_flyermay2012.pdf [accessed 2016-02-01] [WebCite Cache ID 6xgNH07cj]
19. Sohlberg M, Turkstra L. Optimizing Cognitive Rehabilitation: Effective Instructional Methods. New York: Guilford Publications; May 17, 2011.
20. Powell LE, Glang A, Ettel D, Todis B, Sohlberg MM, Albin R. Systematic instruction for individuals with acquired brain injury: results of a randomised controlled trial. Neuropsychol Rehabil 2012;22(1):85-112 [FREE Full text] [doi: 10.1080/09602011.2011.640466] [Medline: 22264146]
21. Ponsford J, Sloan S, Snow P. Traumatic brain injury: Rehabilitation for everyday adaptive living. 2nd ed. Hove, East Sussex: Psychology Press; 2013.
22. National Disability Insurance Agency. Planning to facilitate opportunities enabled under the NDIS. 2016. URL: https://www.ndis.gov.au/about-us/governance/IAC/iac-advice-opportunities [accessed 2018-07-05] [WebCite Cache ID 70gOcSthj]
23. Tate RL, McDonald S, Perdices M, Togher L, Schultz R, Savage S. Rating the methodological quality of single-subject designs and n-of-1 trials: introducing the Single-Case Experimental Design (SCED) Scale. Neuropsychol Rehabil 2008 Aug;18(4):385-401. [doi: 10.1080/09602010802009201] [Medline: 18576270]
24. Tate R, Perdices M. Single-case experimental designs for clinical research and neurorehabilitation settings: Planning, conduct, analysis and reporting. Abingdon, UK: Routledge; 2018.
25. Kazdin A. Single-case research designs: methods for clinical and applied settings. 2nd ed. New York, New York: Oxford University Press; 2011.
26. Tate RL, Taylor C, Aird V. Applying empirical methods in clinical practice: introducing the model for assessing treatment effect. J Head Trauma Rehabil 2013;28(2):77-88. [doi: 10.1097/HTR.0b013e31824e103e] [Medline: 22647962]
27. World Health Organization. WHO Disability Assessment Schedule 2.0 (WHODAS 2.0). URL: http://www.who.int/classifications/icf/whodasii/en/ [accessed 2018-07-06] [WebCite Cache ID 70h91Ykya]
28. Jutai J, Day H. Psychosocial Impact of Assistive Devices Scale (PIADS). Technology and Disability 2002;14(3):107-111. [doi: 10.1037/t45599-000]
29. Sohlberg M, Mateer C. Cognitive Rehabilitation: An Integrative Neuropsychological Approach. New York: Guilford Publications; 2001.
30. Ehlhardt LA, Sohlberg MM, Glang A, Albin R. TEACH-M: A pilot study evaluating an instructional sequence for persons with impaired memory and executive functions. Brain Inj 2005 Aug 10;19(8):569-583. [Medline: 16175811]
31. Tate RL, Aird V, Taylor C. Bringing Single-case Methodology into the Clinic to Enhance Evidence-based Practices. Brain Impairment 2013 Jan 17;13(03):347-359. [doi: 10.1017/BrImp.2012.32]

32. Tate RL, Perdices M, Rosenkoetter U, Wakim D, Godbee K, Togher L, et al. Revision of a method quality rating scale for single-case experimental designs and n-of-1 trials: the 15-item Risk of Bias in N-of-1 Trials (RoBiNT) Scale. Neuropsychol Rehabil 2013;23(5):619-638. [doi: 10.1080/09602011.2013.824383] [Medline: 24050810]
33. Vimarlund V, Wass S. Big data, smart homes and ambient assisted living. Yearb Med Inform 2014;9(1):143-149 [FREE Full text] [doi: 10.15265/IY-2014-0011] [Medline: 25123734]

Abbreviations

EAT: electronic assistive technology
SSA: shared supported accommodation

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Protocol

Issues in Child and Adolescent Inpatient Assessment and Evaluation After Discharge: Protocol for App Development and a Randomized Controlled Trial

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Abstract

Background: New methods are needed for collecting data of in- and outpatients and for improving outpatient compliance after discharge. Mobile technologies, such as smartphone apps, have shown promising results, (eg, helping unwell people by offering support and resources). Screening for the condition, including comorbidities, is a vital part of psychiatric care. Comorbid conditions, especially in emergency evaluation, are often missed, leading to inaccurate diagnosis and treatment. One way of improving diagnostic accuracy is to use a structured diagnostic process. Digitalized screening and follow-up have the advantage of making administration and scoring easier and less time consuming, thereby increasing response rate. To address these problems, we decided to create a smartphone app called The Blue App. The Blue App was developed through 6 steps, described in the manuscript.

Objective: The aim of this paper is to describe (1) the development of The Blue App and (2) 2 planned research studies to evaluate the app.

Methods: Two studies will be performed. Study 1 has a descriptive design, mapping comorbidities before and after the introduction of The Blue App. Study 2 has a randomized controlled design, measuring compliance with outpatient treatments as well as depressive symptoms, rated as changes in Montgomery-Åsberg Depression Scale scores during a 1-year follow-up.

Results: We have described app development. Data collection for Study 1 started in autumn 2017. Study 2 will start in autumn 2018. We expect to have enrolled the 150 patients in Study 2 by December 2019. Final results will be published in a scientific journal.

Conclusions: A technically advanced and easy-to-use Web-based mobile phone app corresponding to the unit's needs was developed, and 2 studies are planned to evaluate its usefulness.

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KEYWORDS

app; data collection; mobile phone; research protocol; screening

Introduction

Emergency units with 24/7 evaluation and admission facilities are important services for stabilizing adolescents with mental health crisis [1,2]. On admission to a unit, patients often need extensive mental health resources [3]. Demand for health production is high in emergency units when inpatient stays are short [4].

The largest intervention effect is reached during the first week of admission [5]. Short inpatient stays for acute stabilization are a challenge when it comes to structured diagnostic screening. Despite the availability of validated diagnostic screening instruments, pen-and-paper versions lead to poor response rates and consume resources, making their use less attractive [6]. The current toolbox is outdated for use in our population of adolescents, and new methods are needed for inpatient data collection and for improving outpatient compliance. Mobile technologies, such as smartphone apps, have shown promising results in terms of data collection and as an intervention for behavioral change, but little empirical evidence has been found to date [7,8].

Literature in the field of child and adolescent psychiatric inpatient emergency care is scarce, and studies are limited to characteristics of admitted patients [3]. Therefore, little is known about the course of illness after discharge. In Sweden, there has been no comprehensive evaluation and follow-up of children and adolescents admitted and discharged from psychiatric emergency units.

Diagnosing the condition and screening for comorbidity using validated instruments is a vital part of psychiatric care. Moreover, a structured screening procedure is also perceived as positive and valid by patients and their parents [9].

In psychiatric care, diagnostic interrater reliability among clinicians is weak [10]. Comorbid conditions are commonly missed during psychiatric evaluations, leading to inaccurate diagnosis and treatment. One way of increasing diagnostic accuracy is to use a structured diagnostic process, involving diagnostic screening instruments [11].

Digitalized screening and follow-up make administration and scoring easier and less time consuming for patients, parents, and staff. This helps increase the frequency of completed systematic psychiatric screenings. It also has the advantage of availability, as questionnaires can be sent to and answered on patients' smartphones, increasing response rates [6]. This structured data collection would enable studies of child and adolescent psychiatric emergency inpatients in further research.

Apps have proved effective in helping unwell people, by offering support, resources, and information [7]. In recent years, several new smartphone-based solutions have been developed for mental health in general and specifically for child and adolescent psychiatry [12-16]. However, apps developed by health care professionals for adolescents must be innovative, useful, and fun to compete with apps not encouraging healthy behaviors [7].

To address these problems, we decided to create a smartphone app: The Blue App (referring to blue as the color of hope, as well as expressing moodiness). The Blue App is a Web-based tool made to resemble and function as a mobile app.

The aim of this paper is to describe the development of The Blue App and to present 2 research protocols aimed at evaluating the app.

Methods

Development of The Blue App

The process of developing The Blue App, from concept to working product, was divided into 6 steps.

Step 1. Identifying the Need for Quick and Easy Information Gathering

Since 2010, members of our group have introduced and developed interactive voice response (IVR) into Swedish child and adolescent psychiatry. This is a technology in which a server is programmed to use scripts in interaction with the user on their cell phone [9,14]. Johansson et al [17] have shown that emergency patients had their own cell phones and that the response rate among participating patients (N=60) was promising as each individual responded on average 91% (365/402) of their calls. An answering frequency of 100% was shown by 71% (30/42).

Our work with IVR inspired us to further develop technology to meet the unit's needs regarding improved methods for the diagnostic and follow-up processes. In 2013, we published our first IVR paper [17]. Simultaneously, we were discussing the shortcomings at the unit regarding the identification of comorbidities. We were also discussing the development of a more sophisticated follow-up tool that would provide feedback using a visual presentation of changes in symptoms over time. At the same time, smartphones were becoming more common among adolescents. This enabled us to integrate our previous work with our efforts to widen the use of screening questionnaires in a better package than the older cell phones could offer.

To address the issues related to short inpatient stays and need for improved diagnostic screening, we decided to create a smartphone app based on our previous work.

Step 2. Identifying Desired Information and Choosing Adequate Screening Questionnaires

In addition to clinical evaluations, we wanted to screen for and describe the psychiatric conditions that were most frequently presented at emergency units. The most common reasons for admission to the unit were suicidal ideation, severely depressed mood, and acute crises. Our experience corresponds well with literature on child and adolescent psychiatry with regard to frequent comorbid states [2]. We also wanted to map changes in symptom severity before and after admission.

The validated screening questionnaires were chosen in collaboration with national key opinion leaders and with regard to frequent comorbid states in child and adolescent psychiatry [18-20].

The following 10 questionnaires were chosen:

1. Montgomery-Åsberg Depression Scale (MADRS-S): a 9-item diagnostic self-rating questionnaire measuring depressive symptoms during the previous 3 days [21]
2. Mini International Neuropsychiatric Interview for Children and Adolescents (MINI-KID): a semi structured diagnostic interview concerning the core psychiatric disorders among children and adolescents [22]
3. Alcohol Use Disorders Identification Test-Consumption: a 3-item screening questionnaire regarding alcohol use [23]
4. Drug Use Disorders Identification Test: an 11-item screening questionnaire regarding drug use [24]
5. Hopkins Symptom Checklist-10: a symptom inventory that measures signs of anxiety and depression [25]
6. Sheehan Disability Scale: a scale assessing functional impairment in domains of work or school, social, and family life [26]
7. Autism Spectrum Screening Questionnaire: a 27-item checklist that assesses symptoms characteristics of high-functioning autism spectrum disorder [27]
8. Swanson Nolan and Pelham Questionnaire: a 30-item questionnaire assessing attention-deficit/hyperactivity disorder symptoms and behavioral problems [28]
9. Deliberate Self-Harm Inventory-9: a scale showing the frequency of different ways of self-harming [29]
10. Treatment Satisfaction Scale 2: a 6-item measure of treatment effectiveness [30] (included to evaluate the satisfaction of treatment but not a part of the research protocols)

Step 3. Examining the Feasibility in an Emergency Psychiatric Unit: Pilot Study

To evaluate the feasibility of the screening procedure, a pilot study was performed with adolescents admitted to the psychiatric emergency unit. The first aim was to assess the feasibility of administration of 10 questionnaires in a small consecutive population. The second aim was to learn more about the clinical relevance of the systematic screening, that is, would the results indicate more comorbidities than found in the medical records? Patients admitted to the unit between February 11, 2014, and March 14, 2014, were invited to participate and complete the 10 questionnaires regarding psychiatric morbidity and comorbidity to be included in The Blue App. All screening questionnaires involved using pen and paper.

We included 16 patients (12 girls and 4 boys; age: mean 15.6 (SD 1.31) years). Of these, 12 completed all the pen-and-paper screening questionnaires, whereas 4 patients could not complete their screening procedures due to early discharge. Of 10, 9 diagnoses at discharge were confirmed using MINI-KID. MINI-KID also identified, on average, 5 diagnostic areas of potential psychiatric interest, including the hazardous use of alcohol or substance abuse, none of which had been clearly addressed during the inpatient stay or mentioned in the psychiatric records.

Step 4. Getting Organizational Acceptance: Feasibility Study

The next step was to secure a way forward for The Blue App. As our aim was to use the tool in daily clinical practice, we decided to apply for funding from the funding body for all public psychiatric health care in Scania, South Sweden. All potential new procedures in Swedish public health care require a thorough assessment procedure to clarify the cost-benefit ratio, safety, and potential risks (feasibility study). The aim of this feasibility study was to clarify the requirements of The Blue App and to elucidate the cost-benefit and safety aspects so as to generate a basis for decision making for the funding body. Another part of the feasibility study was to collect knowledge about alternative solutions allowing the same functionality by investigating if comparable products were available on the market.

The feasibility study included about 15 meetings with the IT and finance departments. Clinicians' needs were highlighted, which resulted in a thorough description of the technical requirements for 90 user cases, including mock-ups, flowcharts, and wireframes. The study concluded that no existing solution was available on the market. The final document was presented to the funding board with the working title "The Blue App." The board approved funding in May 2015.

Step 5. App Construction

After approval, the next step was to call for public procurement using the feasibility study documents. In total, 3 tenders were considered, and representatives from each company were interviewed. The clinicians working on The Blue App were involved in decision making. Work with the company chosen, Stretch Öresund, proceeded with workshop sessions, creating a shared language and translating clinicians' needs to the mindset of app architects. The work continued with meetings being held every 2nd week for a 6-month period, during which mutual feedback on the progress of The Blue App was given. The company's CEO met with the unit staff to demonstrate the app and collect feedback to increase the chance of successful implementation.

The work resulted in an app corresponding with the unit's needs. The structure of the development process, with frequent and regular meetings, was necessary to avoid misunderstandings. The development process allowed the app architects to gain a profound understanding of psychiatric care and to adapt solutions to the unit's requirements.

Step 6. Workshop With Adolescents: What Do the Patients Think?

During the development of The Blue App, feedback was obtained through a workshop with adolescent end users. The main aim was to assess the user-friendliness of the app. We arranged the workshop in spring 2016, during which 10 adolescents, 5 boys and 5 girls aged 14-17 years, participated. Of these, 2 adolescents were undergoing psychiatric outpatient treatment. The participating adolescents were introduced to the app and then navigated through The Blue App follow-up user interface. The participants found the app easy to navigate and

suggested some minor improvements, such as the integration of graphic design.

Planned Research Studies to Evaluate The Blue App: Research Studies 1 and 2

The objective was to design several studies to evaluate The Blue App. In the first study (Study 1), we aim to assess whether additional comorbid conditions could be identified using The Blue App. In the second study (Study 2), we want to evaluate whether the use of The Blue App can improve outpatient compliance and treatment outcome through feedback of psychiatric symptoms.

Design

Study 1

In Study 1, we want to map the prevalence of psychiatric comorbidity found in the medical records before and after the introduction of The Blue App. The hypothesis is that more diagnoses will be found in the records after the introduction of The Blue App.

Study 2

At discharge, eligible patients will be offered participation in a 1-year follow-up study using a randomized controlled design (Figure 1). After receiving informed consent, patients will be randomized into 3 groups and asked to answer questions regarding depressive symptoms (MADRS-S) at different time intervals over a period of 1 year after discharge. The time intervals were chosen to minimize dropout while being long enough to detect effects in the patient. We undertook a power calculation, as we found no comparable studies. Based on estimated scores on the depression rating scale (MADRS-S) at discharge, we expect scores at discharge to be around 30, with SD 7.1.

The null hypothesis for Study 2 is that no significant difference is found in the randomized controlled trial; that is, the feedback given through The Blue App would not improve the outcome or compliance. In the alternative hypothesis, we expect all patients to reduce their MARS-S scores during the study period and expect a difference of about 4 points on MADRS-S between intervention and control groups. With a power of .8, we will therefore need 3 groups of 50 patients each in order to detect differences at a 5% level.

Setting and Participants: Studies 1 and 2

Scania in southern Sweden has a population of over 1 million, of which 280,000 are children and adolescents. The university hospital in Malmö, the major city in the area, provides the only psychiatric emergency unit for children and adolescents, with 11 hospital beds. The hospital admits 350 unique patients annually together with a parent for acute stabilization. The most common reasons for admission are suicidal ideations, severely depressed moods, and acute crises. A majority of the patients are aged 13-17 years, with an even gender distribution.

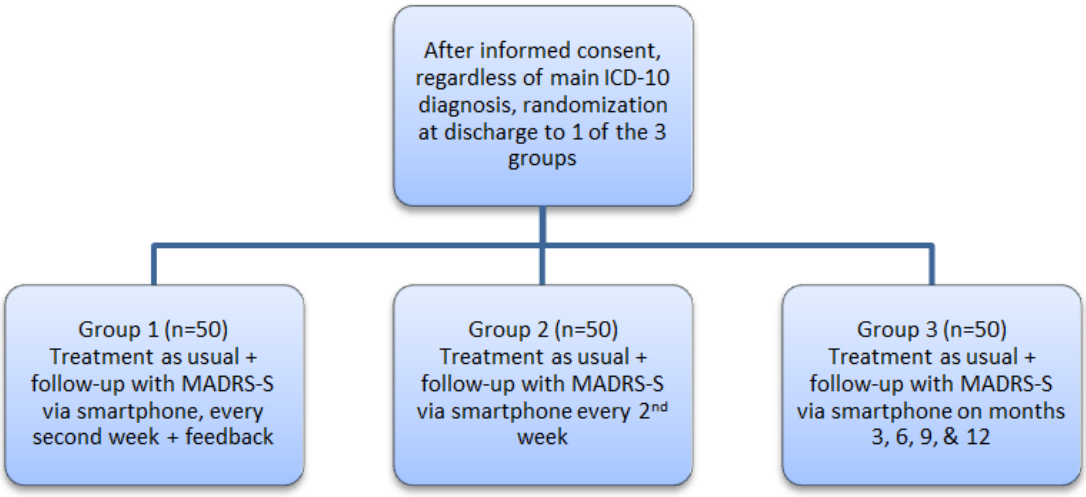
A treatment plan is drawn up by the unit physician together with patients and parents. Nearly 15% of the patients are treated according to the Swedish Compulsory Mental Care Act. The unit team consists of physicians, psychologists, social workers, nurses, and treatment staff, often in collaboration with open-care units, schools, and social authorities. Before discharge, a rescue plan is drawn up together with patients and parents in the event of a recurrent emergency situation. Nearly 95% of the patients are discharged within a week of admission.

Procedure

Study 1

All eligible patients will be offered participation in Study 1 and will be invited to complete the questionnaire (exclusion criteria: language other than Swedish, admission for <24 hours, severely ill, age <12 years old). We expect about 190 of the 350 patients admitted per year to be eligible for inclusion. The feasibility study indicated little attrition, but we anticipate that about 30% might not want to participate, leaving us with about 130 per year for possible inclusion.

Figure 1. Study design with 3 randomization groups for the follow-up study at the Child and Adolescent Psychiatric Emergency unit, Malmö, Sweden. ICD-10: International Classification of Diseases, 10th revision; MADRS-S: Montgomery-Åsberg Depression Scale.



Patients and parents will be asked to complete questionnaires on psychiatric symptoms, treatment satisfaction, and quality of life. Included patients will be registered on The Blue App, allowing them to log in via their smartphone using a personal identity number at the log-in page (Figure 2).

The patients will then receive a short message service text message with a one-time password, enabling them to enter The Blue App and answer the questionnaires. It is also possible to generate one-time passwords and complete the questionnaires via The Blue App staff administration view. Parents can use their child's log-in when answering the parental questionnaires.

The screening process at the unit will be divided into 3 stages (Figure 3). The first stage is defined as the first 24 hours at the unit. The second stage, during treatment, is defined as the time between intake and discharge. The discharge stage is defined as the last 24 hours at the unit. Patients and their parents will be given access to the questionnaires at each stage, which they will complete with the help of staff. At the unit, the questionnaires will be administered mainly on tablets, but can also be filled in via the patients' own devices.

Study 2

At discharge, participation in study 2 will be offered to all patients who complete the questionnaires for Study 1 (Figure 3).

All patients in the study will receive treatment as usual at their outpatient units. Patients will use the same log-in procedure as in Study 1. With app-assisted technology, a link to the MADRS-S questionnaire (Figure 4) will be sent to all participants at predefined intervals depending on randomization.

Figure 2. Screenshot of The Blue App login screen. Source: Region Skåne.

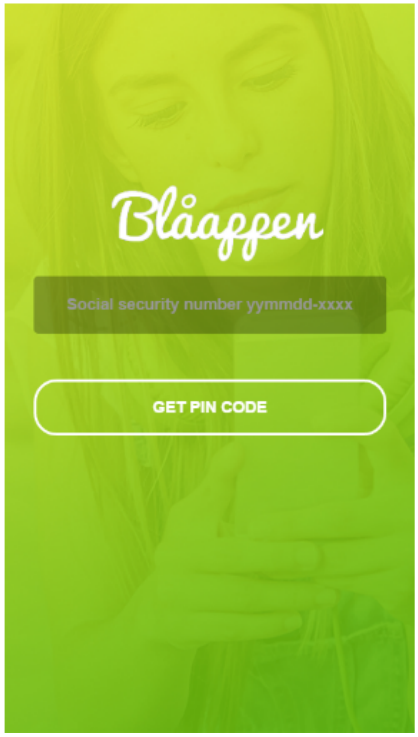


Figure 3. Questionnaires used at the different stages during the inpatient stay at the Child and Adolescent Psychiatric Emergency Unit, Malmö, Sweden. ASSQ: Autism Spectrum Screening Questionnaire; AUDIT-C: Alcohol Use Disorders Identification Test-Consumption; DSHI-9: Deliberate Self-Harm Inventory-9; DUDIT: Drug Use Disorders Identification Test; HSCL-10: Hopkins Symptom Checklist-10; MADRS-S: Montgomery-Åsberg Depression Scale; MINI-KID: Mini International Neuropsychiatric Interview for Children and Adolescents; SDS: Sheehan Disability Scale; SNAP-IV: Swanson Nolan and Pelham Questionnaire; TSS-2: Treatment Satisfaction Scale 2.

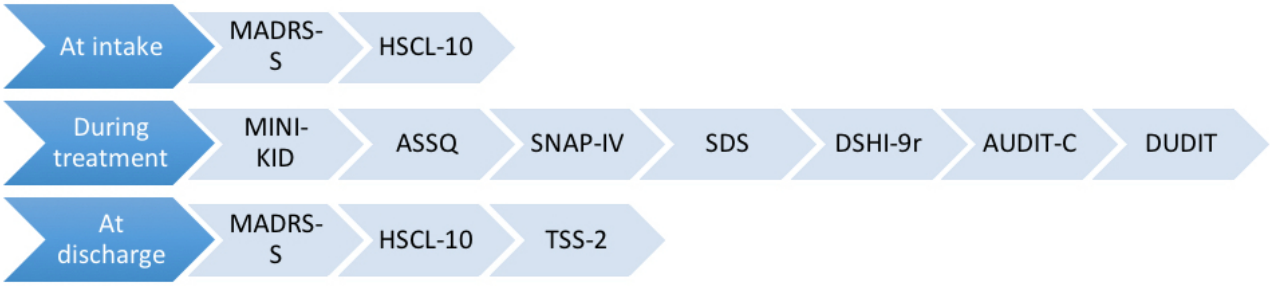
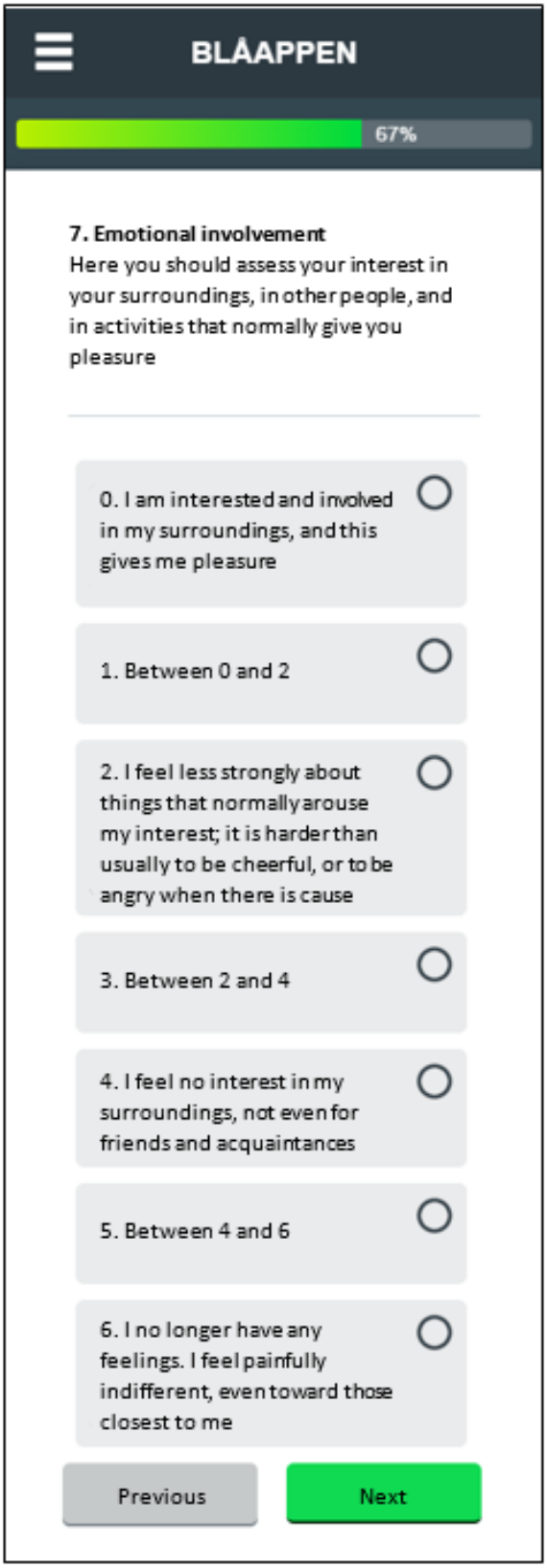


Figure 4. Screenshot of the MADRS-S (Montgomery-Åsberg Depression Scale) questionnaire item 7. Source: Region Skåne.



After discharge, researchers and staff will not be able to trace the group to which a patient is assigned. Patients readmitted to the ward during follow-up will remain in the study.

In group 1, feedback on depressive symptoms will be presented in a graph, together with a brief recommendation [31] on each follow-up occasion (Figure 5). A text below the graph will describe how patients can contact the emergency unit if they experience very severe symptoms or danger, with a button to make a direct call to the 24/7 emergency facilities.

Figure 5. Screenshot of the MADRS-S (Montgomery-Åsberg Depression Scale) feedback screen for group 1. Source: Region Skåne.

Dropout analysis will examine for any group differences in terms of gender, age, and main International Classification of Diseases, 10th revision diagnoses. Information regarding reasons for missed appointments and dropouts will be taken from the medical records. Outcome measures are changes in MADRS-S scores and treatment compliance, as measured by attended outpatient appointments during the study period.

Ethical Approval

No compensation will be offered. Subjects in the study will be protected by the informed consent process. The Regional Ethical Board in Lund has approved the study (2013-06-19; Nr 423/2013).

Statistical Analysis

The two studies will be analyzed separately, and baseline variables will be analyzed with descriptive statistics. Pearson's chi-square tests will be used to determine differences between the groups in terms of gender distribution and proportion of participants scoring above cut-off in the questionnaires used.

In Study 1, we will use descriptive statistics (mean, SD, median, interquartile range, continued variables, frequency and counts, categorical variations, and exact CIs for proportions) to describe the cohort and analyze differences in the number of psychiatric diagnoses before and after the introduction (*t* test) of The Blue App [32].

In Study 2, we will analyze differences between the 3 groups in terms of changes in MADRS-S scores and treatment compliance. Outcome measures (MADRS-S scores and dropout from outpatient care) will be analyzed according to intention to treat. Linear mixed model analyses will be used to identify changes over time in depressive symptoms and to examine compliance with outpatient treatments. In these analyses, group, time, and the intercept between the groups and time will be used as fixed effects and subjects as random intercepts.

Results

The app development is described. Data collection for Study 1 started in autumn 2017. Study 2 will be initiated in autumn 2018. We expect to have enrolled 150 patients for Study 2 by December 2019. Funding for both Study 1 and Study 2 have have been granted by Region Skåne, the regional council for health care in south of Sweden. Final results will be published in a scientific journal.

Discussion

Principal Findings

This study is a process description of a child and adolescent emergency inpatient unit, where an app was developed with the aim of identifying comorbidity and improving outpatient compliance and treatment outcomes.

Strengths

The Blue App is a dynamic tool capable of adjustment to new demands, with variable settings, and to other units with potential to improve the transition between inpatient and outpatient care. The Blue App will help us collect data to make it easier to evaluate the work at the inpatient unit and will lay a foundation for future research in the field.

One important factor behind the development process was the support given to the project group from all levels in the organization, from stakeholders to staff [33]. Other crucial factors were related to the project group's acceptance in the organization and to the committed team members whose perseverance has extended over several years. The organization benefits from the shared visions and team learning [33]. Finally, we want to highlight the importance of being offered enough time to work on this project.

Limitations

The Blue App has been developed in a Swedish context, which limits its generalizability. Questionnaires are in Swedish, thereby excluding non-Swedish speaking patients. In the next version of The Blue App, the questionnaires will be available in the 4 most common languages at the unit (English, Dhari, Arabic, and French).

The design chosen for Study 2, in which selection is based on participation in Study 1, might affect inclusion and, therefore, could be regarded as a weakness. However, participation in Study 1 gives a thorough assessment of comorbidities at baseline, which is the strength of the design.

Conclusions

A technically advanced and easy-to-use Web-based mobile phone app corresponding to the unit's needs was developed, and 2 studies to evaluate its usefulness are planned.

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The authors want to acknowledge Peter Höglund for valuable statistical input, and Jakob Täljemark for language improvements. We thank Stiftelsen Lindhaga and Region Skåne, the regional council for health care in south of Sweden, for grants.

Authors' Contributions

SE, KH, and BAJ initiated the study. CA and MR made substantial contributions to the concept and design. KH, SE, and BAJ were involved in drafting the paper, and MR and CA made significant contributions when reviewing the manuscript. All 5 authors have approved the final version.

Conflicts of Interest

None declared.

References

1. Stewart C, Spicer M, Babl FE. Caring for adolescents with mental health problems: challenges in the emergency department. J Paediatr Child Health 2006 Nov;42(11):726-730. [doi: 10.1111/j.1440-1754.2006.00959.x] [Medline: 17044902]
2. Hanssen-Bauer K, Heyerdahl S, Hatling T, Jensen G, Olstad PM, Stangeland T, et al. Admissions to acute adolescent psychiatric units: a prospective study of clinical severity and outcome. Int J Ment Health Syst 2011 Jan 06;5(1):1 [FREE Full text] [doi: 10.1186/1752-4458-5-1] [Medline: 21211046]
3. Bettmann JE, Jasperson RA. Adolescents in Residential and Inpatient Treatment: A Review of the Outcome Literature. Child Youth Care Forum 2009 Apr 28;38(4):161-183. [doi: 10.1007/s10566-009-9073-y]
4. Case BG, Olfson M, Marcus SC, Siegel C. Trends in the inpatient mental health treatment of children and adolescents in US community hospitals between 1990 and 2000. Arch Gen Psychiatry 2007 Jan;64(1):89-96. [doi: 10.1001/archpsyc.64.1.89] [Medline: 17199058]
5. Green J. Provision of Intensive Treatment: In-patient Units, Day Units and Intensive Outreach. In: Rutter M, editor. Rutter's Child and Adolescent Psychiatry. Oxford, UK: Blackwell Publishing Ltd; 2008:1126-1142.
6. Andersson C, Danielsson S, Silfverberg-Dymling G, Löndahl G, Johansson BA. Evaluation of Interactive Voice Response (IVR) and postal survey in follow-up of children and adolescents discharged from psychiatric outpatient treatment: a randomized controlled trial. Springerplus 2014;3:77 [FREE Full text] [doi: 10.1186/2193-1801-3-77] [Medline: 24567883]
7. Weaver ER, Horyniak DR, Jenkinson R, Dietze P, Lim MS. "Let's get Wasted!" and Other Apps: Characteristics, Acceptability, and Use of Alcohol-Related Smartphone Applications. JMIR Mhealth Uhealth 2013 Jun 25;1(1):e9 [FREE Full text] [doi: 10.2196/mhealth.2709] [Medline: 25100681]
8. Cohn AM, Hunter-Reel D, Hagman BT, Mitchell J. Promoting behavior change from alcohol use through mobile technology: the future of ecological momentary assessment. Alcohol Clin Exp Res 2011 Dec;35(12):2209-2215 [FREE Full text] [doi: 10.1111/j.1530-0277.2011.01571.x] [Medline: 21689119]
9. Thienemann M. Introducing a structured interview into a clinical setting. J Am Acad Child Adolesc Psychiatry 2004 Aug;43(8):1057-1060. [Medline: 15266202]
10. Miller PR. Inpatient diagnostic assessments: 2. Interrater reliability and outcomes of structured vs. unstructured interviews. Psychiatry Research 2001 Dec;105(3):265-271. [doi: 10.1016/S0165-1781(01)00318-3]
11. Rettew DC, Lynch AD, Achenbach TM, Dumenci L, Ivanova MY. Meta-analyses of agreement between diagnoses made from clinical evaluations and standardized diagnostic interviews. Int J Methods Psychiatr Res 2009 Sep;18(3):169-184. [doi: 10.1002/mpr.289] [Medline: 19701924]
12. Gregory JM, Sukhera J, Taylor-Gates M. Integrating Smartphone Technology at the Time of Discharge from a Child and Adolescent Inpatient Psychiatry Unit. J Can Acad Child Adolesc Psychiatry 2017;26(1):45-50 [FREE Full text] [Medline: 28331503]
13. Dahne J, Lejuez CW. Smartphone and Mobile Application Utilization Prior to and Following Treatment Among Individuals Enrolled in Residential Substance Use Treatment. J Subst Abuse Treat 2015 Nov;58:95-99 [FREE Full text] [doi: 10.1016/j.jsat.2015.06.017] [Medline: 26231698]
14. Liss DT, Serrano E, Wakeman J, Nowicki C, Buchanan DR, Cesan A, et al. "The Doctor Needs to Know": Acceptability of Smartphone Location Tracking for Care Coordination. JMIR Mhealth Uhealth 2018 May 04;6(5):e112 [FREE Full text] [doi: 10.2196/mhealth.9726] [Medline: 29728349]
15. Torous J, Chan SR, Yee-Marie TS, Behrens J, Mathew I, Conrad EJ, et al. Patient Smartphone Ownership and Interest in Mobile Apps to Monitor Symptoms of Mental Health Conditions: A Survey in Four Geographically Distinct Psychiatric Clinics. JMIR Ment Health 2014 Dec;1(1):e5 [FREE Full text] [doi: 10.2196/mental.4004] [Medline: 26543905]
16. Benarous X, Edel Y, Consoli A, Brunelle J, Etter J, Cohen D, et al. Ecological Momentary Assessment and Smartphone Application Intervention in Adolescents with Substance Use and Comorbid Severe Psychiatric Disorders: Study Protocol. Front Psychiatry 2016 Sep;7:157 [FREE Full text] [doi: 10.3389/fpsyt.2016.00157] [Medline: 27703435]
17. Johansson BA, Remvall S, Malgerud R, Lindgren A, Andersson C. Interactive voice response - an automated follow-up technique for adolescents discharged from acute psychiatric inpatient care: a randomised controlled trial. Springerplus 2013 Dec;2(1):146 [FREE Full text] [doi: 10.1186/2193-1801-2-146] [Medline: 23641319]
18. Thapar A, Collishaw S, Pine DS, Thapar AK. Depression in adolescence. The Lancet 2012 Mar;379(9820):1056-1067. [doi: 10.1016/S0140-6736(11)60871-4]
19. Marangoni C, De Chiara CL, Faedda GL. Bipolar disorder and ADHD: comorbidity and diagnostic distinctions. Curr Psychiatry Rep 2015 Aug;17(8):604. [doi: 10.1007/s11920-015-0604-y] [Medline: 26084666]
20. Mason MJ, Aplasca A, Morales-Theodore R, Zaharakis N, Linker J. Psychiatric Comorbidity and Complications. Child Adolesc Psychiatr Clin N Am 2016 Jul;25(3):521-532. [doi: 10.1016/j.chc.2016.02.007] [Medline: 27338972]
21. Svanborg P, Åsberg M. A new self-rating scale for depression and anxiety states based on the Comprehensive Psychopathological Rating Scale. Acta Psychiatr Scand 1994 Jan;89(1):21-28. [doi: 10.1111/j.1600-0447.1994.tb01480.x]

22. Sheehan DV, Sheehan KH, Shytle RD, Janavs J, Bannon Y, Rogers JE, et al. Reliability and validity of the Mini International Neuropsychiatric Interview for Children and Adolescents (MINI-KID). J Clin Psychiatry 2010 Mar;71(3):313-326. [doi: 10.4088/JCP.09m05305whi] [Medline: 20331933]
23. Bush K. The AUDIT Alcohol Consumption Questions (AUDIT-C): An Effective Brief Screening Test for Problem Drinking. Arch Intern Med 1998 Sep 14;158(16):1789. [doi: 10.1001/archinte.158.16.1789]
24. Berman AH, Bergman H, Palmstierna T, Schlyter F. Evaluation of the Drug Use Disorders Identification Test (DUDIT) in criminal justice and detoxification settings and in a Swedish population sample. Eur Addict Res 2005 Dec;11(1):22-31. [doi: 10.1159/000081413] [Medline: 15608468]
25. Strand BH, Dalgard OS, Tambs K, Rognerud M. Measuring the mental health status of the Norwegian population: a comparison of the instruments SCL-25, SCL-10, SCL-5 and MHI-5 (SF-36). Nord J Psychiatry 2003 Jul;57(2):113-118. [doi: 10.1080/08039480310000932] [Medline: 12745773]
26. Sheehan DV. The Anxiety Disease. New York: Charles Scribner and Sons; 1983:151.
27. Ehlers S, Gillberg C, Wing L. A screening questionnaire for Asperger syndrome and other high-functioning autism spectrum disorders in school age children. Journal of Autism and Developmental Disorders 1999;29(2):129-141. [doi: 10.1023/A:1023040610384]
28. Bussing R, Fernandez M, Harwood M, Wei H, Garvan CW, Eyberg SM, et al. Parent and teacher SNAP-IV ratings of attention deficit hyperactivity disorder symptoms: psychometric properties and normative ratings from a school district sample. Assessment 2008 Sep;15(3):317-328 [FREE Full text] [doi: 10.1177/1073191107313888] [Medline: 18310593]
29. Lundh L, Karim J, Quilisch E. Deliberate self-harm in 15-year-old adolescents: a pilot study with a modified version of the Deliberate Self-Harm Inventory. Scand J Psychol 2007 Feb;48(1):33-41. [doi: 10.1111/j.1467-9450.2007.00567.x] [Medline: 17257367]
30. Clinton D, Björck C, Sohlberg S, Norring C. Patient satisfaction with treatment in eating disorders: cause for complacency or concern? Eur Eat Disorders Rev 2004 Jun 24;12(4):240-246. [doi: 10.1002/erv.582]
31. Sarris J, O'Neil A, Coulson CE, Schweitzer I, Berk M. Lifestyle medicine for depression. BMC Psychiatry 2014 Apr 10;14:107 [FREE Full text] [doi: 10.1186/1471-244X-14-107] [Medline: 24721040]
32. Altman D. Practical Statistics for Medical Research. Boca Raton: CRC Press; 1990.
33. Drucker PF. Practice of Management. Oxford: Butterworth-Heinemann (Elsevier); 2007.

Abbreviations

IVR: interactive voice response
MADRS-S: Montgomery-Åsberg Depression Scale
MINI-KID: Mini International Neuropsychiatric Interview for Children and Adolescents

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Protocol

A Smartphone Attention Bias Intervention for Individuals With Addictive Disorders: Protocol for a Feasibility Study

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Abstract

Background: Substance use disorders are highly prevalent globally. Relapse rates following conventional psychological interventions for substance use disorders remain high. Recent reviews have highlighted attentional and approach or avoidance biases to be responsible for multiple relapses. Other studies have reported the efficacy of interventions to modify biases. With advances in technologies, there are now mobile versions of conventional bias modification interventions. However, to date, no study has evaluated bias modification in a substance-using, non-Western sample. Existing evaluations of mobile technologies for the delivery of bias interventions are also limited to alcohol or tobacco use disorders.

Objective: This study aims to examine the feasibility of mobile-based attention bias modification intervention among treatment-seeking individuals with substance use and alcohol use disorders.

Methods: This is a feasibility study, in which inpatients who are in their rehabilitation phase of clinical management will be recruited. On each day that they are in the study, they will be required to complete a craving visual analogue scale and undertake both a visual probe-based assessment and and modification task in a smartphone app . Reaction time data will be collated for the computation of baseline attentional biases and to determine whether there is a reduction of attentional bias across the interventions. Feasibility will be determined by the number of participants recruited and participants' adherence to the planned interventions up until the completion of their rehabilitation program and by the ability of the app in detecting baseline biases and changes in biases. Acceptability of the intervention will be assessed by a short questionnaire of users' perceptions of the intervention. Statistical analyses will be performed using SPSS version 22.0, while qualitative analysis of the perspectives will be performed using NVivo version 10.0.

Results: This study was approved by the National Healthcare Group Domain Specific Research Board, with approval number (2018/00316). Results will be disseminated by means of conferences and publications.Currently, we are in the process of recruitment for this study.

Conclusions: To the best of our knowledge, this is the first study to evaluate the feasibility and acceptability of a mobile attention bias modification intervention for individuals with substance use disorders. The data pertaining to the feasibility and acceptability are undoubtedly crucial because they imply the potential use of mobile technologies in retraining attentional biases among inpatients admitted for medical-assisted detoxification and rehabilitation. Participants' feedback pertaining to the ease of use, interactivity, and motivation to continue using the app is crucial because it will determine whether a codesign approach might be warranted to design an app that is acceptable for participants and that participants themselves would be motivated to use.

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KEYWORDS

addiction; approach bias; attention bias; bias modification; feasibility; pilot; psychiatry; mobile phone; mHealth; eHealth

Introduction

Background

Illicit drug and alcohol use are highly prevalent globally. The United Nations Office on Drugs and Crime reported that in 2015, a quarter of a billion individuals experimented with substances, and 29.5 million individuals were diagnosed with substance disorders [1]. Cannabis, opioids, and stimulants such as amphetamines are most commonly abused [1]. Substance use is associated with other comorbidities like retroviral diseases and hepatitis C infection. In addition, substance use is associated with significant mortality, and in 2015, an estimated 190,000 deaths were attributed to drug use [1]. Globally, alcohol use is a major problem too [2]. Reportedly, alcohol disorders tend to be more prevalent in developed countries and higher-income status countries [2]. In the most recent report released by the World Health Organization, it was reported that the harmful use of alcohol resulted in an overall mortality of 3 million individuals in 2016 [3]. In Singapore, in a prior study conducted by the World Health Organization in 2004, the prevalence of alcohol use disorders among females and males was estimated to be 0.19% and 1.40%, respectively, and the prevalence of drug use disorders among females and males to be 0.07% and 0.28%, respectively [4]. While there are no large-scale prevalence studies in Singapore, the Central Narcotics Bureau has reported that in 2017, 40% of those apprehended were new abusers, and >64% of these new abusers were under the age of 30 years [5]. Of 3091 abusers arrested in 2017, 1991 were abusing methamphetamine, and the remaining 848 and 204 were abusing heroin and cannabis, respectively. Of importance, 2570 abusers were polysubstance abusers. Thus, substance use disorders are of growing concern as indicated by the increasing numbers of offenders and their changing demographics. Taking into consideration the prevalence, there is a growing need for efficacious interventions.

The treatment options for substance use are both pharmacological and nonpharmacological. Pharmacological options are varied; for opioid use disorders, opiate substitution therapy such as that with methadone or buprenorphine could be considered. In Singapore, opiate substitution therapy is only prescribed for elderly individuals and pregnant women [6] as legislation restricts its administration for other patient groups. The prescription of opiate substitution medications such as buprenorphine is limited due to the risk of diversion [7] and medical comorbidities like infective endocarditis and other cutaneous complications [8,9]. For cannabis and amphetamine disorders, pharmacological options are limited, and symptomatic medications such as hypnotics or antipsychotics are considered in the acute treatment phase. Given the limited pharmacological therapeutic options, especially with the absence of medications to help with abstinence, psychological options are integral. Therapies like cognitive behavioral therapy are effective, with an effect size of 0.45 (Cohen *d*) [10]. Nonetheless, despite this effectiveness, 40%-50% of individuals relapse within a year of successful treatment and another 70% relapse within 3 years [11]. Such high relapse rates following a moderately effective intervention demonstrate that conventional psychological therapies may not be adequately addressing the factors leading individuals to a lapse or relapse.

Recent advances in experimental psychology have reported how automatic attentional biases could predispose individuals toward a relapse. Field et al [12] and Cox et al [13] have highlighted the presence of these automatic attentional processes in individuals with substance use disorders and recommended the use of interventions to modify these automatic processes. Attentional biases refer to the preferential allocation of attention toward substance-related stimuli [14,15], while approach biases refer to automatic tendencies to reach out and approach substance-related cues [16]. The underlying theoretical basis is that of the dual-process model, which suggests that the repeated use of a substance would lead to increased automatic processing of the substance-related cue and, hence, increased automatic tendencies to approach substance-specific cues and corresponding inhibition of normal cognitive control processes. Tasks such as the visual probe task have been used for bias assessment and modification. In the conventional visual probe task, a pair of images is presented, in which one is substance related and the other is a neutral image. Following the presentation of the images, a small probe (or stimulus such as an arrow) would replace one of these images. Participants are required to indicate the position of the stimulus or the direction of the arrow as quickly as they could. When the visual probe task is used for bias modification, the task is as described, but the frequencies at which the probe or stimulus replace the drug or neutral image is altered [14].

There has been an extensive evaluation of bias modification for substance use disorders, and a recent meta-analysis study synthesized the overall effectiveness of bias modification [14]. Cristea et al [14] were only able to identify trials relating to alcohol or tobacco use disorders (25 trials). They reported that bias modification for both attentional and approach biases was moderately effective with an effect size of 0.60 (Hedge 0.60) [14]. However, a prior review found no association between the reduction in biases and other outcomes such as cravings, and the authors posited that this might be because more time is needed for a change in biases to be reflected regarding a change in symptomatology [14]. Nevertheless, a prior review demonstrated that bias modification could potentially reduce biases. Since the publication of Cristea et al's [14] meta-analyses, there have been other publications [17] highlighting the problems with the evidence synthesized, given that the evidence synthesis included both experimental laboratory studies and clinical studies. Wiers et al [17] reviewed the evidence by the nature of studies and reported small and robust effects of bias modification on treatment outcome when biases were retrained in a clinical setting for individuals with

alcohol use disorders. Since Cristea et al's meta-analysis [14], Zhang et al [18] conducted a systematic review and reported that attentional biases were present in opioid use and stimulant use disorders. Other studies have evaluated attention bias modification among substance-using individuals. Ziaee et al [19] recruited a sample of opioid users who were on methadone maintenance and found that attentional bias modification led to a reduction in attentional biases, as well as cravings to use, dosing of medications, and relapses. Wolf et al [20] recruited a sample of moderate and heavy cannabis-using students and found an attentional bias only for heavy users of cannabis and not moderate users; the authors did not find bias retraining to be effective. Mayer et al [21] undertook the first study evaluating the efficacy of bias modification for treatment-seeking individuals with cocaine use disorders. Like Wolf et al [20], Mayer et al [21] also reported that bias modification was not effective. Not all studies have examined treatment-seeking individuals in a clinical setting. Schoenmakers et al [22] administered attentional bias modification to 43 individuals with alcohol dependence and reported that bias modification was effective in increasing individuals' ability to disengage from alcohol cues. Manning et al [23] stressed the importance of evaluating a clinical sample that was in a detoxification and rehabilitation program because intervening during this period could capitalize on neural recovery. To date, Wiers et al [24], Eberl et al [25], and Manning et al [23] have examined bias modification among individuals admitted for medical-assisted detoxification and rehabilitation. While these studies have provided evidence for the effectiveness of bias modification during this critical period, the biases targeted were approach or avoidance biases and the evaluation was limited to individuals with alcohol disorders. To date, no study has evaluated attention bias modiifcation in a non-Western sample among a group of substance-using individuals who are in treatment (medical-assisted detoxification or rehabilitation).

Advances in technologies in the last decade have transformed how bias modification interventions are delivered. An increase in the number of remote Web-based therapies has been attributed to the advances in electronic health (eHealth). eHealth technologies facilitate the delivery of low-cost psychotherapy, which is highly accessible and enables anonymity of use [26]. This has led to increasing research examining the effectiveness of Web-based interventions. Further advances in technologies coupled with increased ownership of mobile devices have resulted in a growing number of interventions that tap on mobile technologies. Mobile health (mHealth) technologies are increasingly being harnessed for the delivery of bias modification as mobile technologies allow for training to be conducted in diverse locations, thus, helping in the generalization of clinical benefits [27]. The use of mobile technologies enables the frequency of training to be increased, which may improve outcomes [27]. mHealth technologies have an advantage over existing Web-based version as they do not require individuals to be consistently connected to the internet to undertake the bias modification task. Zhang et al [28] in their review managed to identify 8 studies that have evaluated the potential and effectiveness of mHealth bias modification. Seven studies [29-35] reported that mHealth bias modification was effective; these studies were conducted among participants with insomnia, alcohol, tobacco use, or social anxiety disorders. Only a single study reported mobile bias modification to be ineffective. Despite the evidence for effectiveness being inconclusive, Zhang et al's [28] prior review reported bias modification to be effective for addictive disorders such as alcohol and tobacco use disorders.

Rationale for This Study

To date, no study has evaluated bias modification in a substance-using, non-Western, treatment-seeking sample. In addition, while technologies like eHealth and mHealth have been widely utilized for the delivery of bias modification interventions, our prior review [28] of the published literature demonstrated that mobile technologies have only been evaluated among individuals with alcohol or tobacco use disorders. Hence, this proposed study aims to examine the feasibility of a mobile-based attention bias modification intervention among treatment-seeking individuals with alcohol or substance use disorders. If deemed feasible, this will guide further evaluative research investigating the efficacy of such a complex intervention.

Objectives

The primary aim of this study is to determine the feasibility of an attention bias modification mobile app for the reduction of attention biases to substance-related cures among individuals with addictive disorders. Feasibility is determined by the number of participants recruited, participants' adherence to the planned interventions up until the day of discharge, and the ability of the app to detect baseline biases and changes in biases. The secondary aim is to determine the acceptability of the intervention, which will be assessed through a questionnaire of users' perceptions.

Research Questions

1. Will the mobile attention bias modification intervention be feasible and acceptable among individuals with addictive disorders?
2. Is the developed mHealth app capable of detecting the changes in biases?

Methods

Study Setting and Study Design

This study will be conducted among individuals who are admitted for inpatient medication-assisted detoxification and rehabilitation at the National Addictions Management Service (NAMS), Institute of Mental Health Singapore. Notably, at NAMS, all patients are admitted voluntarily for treatment, which implies that patients are free to discharge should they be not willing to complete the detoxification or rehabilitation phase of the program. At any one time, a maximum of 30 patients could be accommodated in the ward environment. Patients are managed by an attending psychiatrist with a multidisciplinary team comprising addiction-trained counselors, nurses, and social workers. In the first week of the treatment program, patients would undergo medication-assisted detoxification. In the second week of their treatment program, patients would attend community meetings and group-based counseling. Individual

counseling will also be provided to patients. Only participants who have completed their detoxification phase (first week of their stay) will be recruited for this study as participants would be free from withdrawal symptoms. This is a feasibility study, where participants' attention biases will be assessed following the bias modification intervention. The study protocol has been approved by the National Healthcare Group's Domain Specific Research Board (May 2, 2018; Ethics Approval Reference Number: 2018/00316).

Recruitment

All participants will be recruited from the inpatient unit at the NAMS, Institute of Mental Health, Singapore. Participants will be informed of the study by their attending health care professionals on admission and will be approached by the study team on the first day of their rehabilitation phase. The study team will provide participants with further information about the study, and if participants agree to participate, they will complete the informed consent form.

Sample Size

Power computation has not been undertaken for this study as study design is that of a feasibility study. Considering the diversity of the addictive disorders included, the proposed sample size is 30 participants.

Eligibility Criteria

Inclusion and Exclusion Criteria

Participants will be eligible for the feasibility study if they meet the inclusion criteria presented in Textbox 1.

Participants will not be eligible if they meet any of the exclusion criteria presented in Textbox 2.

Participants with moderate to severe symptoms of comorbid psychiatric disorders are excluded from this feasibility study as there is a high likelihood that their comorbid psychiatric disorder will affect their attentional bias scores. Moreover, patients with other psychiatric disorders will usually be on other psychotropic medications. Zhang et al have highlighted that several pharmacological agents, such as those targeting dopaminergic, noradrenaline, glutaminergic, and serotonergic neurotransmissions, have an acute effect on attentional biases [36].

Intervention

Patients will be invited to participate in this study only upon the completion of their medical detoxification treatment. If they consent to participate, they will complete a set of baseline questionnaires including a demographic and clinical information questionnaire, the Addiction Severity Index (ASI)-Lite questionnaire, the Severity of Substance Dependence (SDS) questionnaire, and the Short-Form 12 (SF-12) questionnaire. In addition, participants are required to complete a visual analogue scale for craving before and after the completion of each session. Table 1 provides an overview of the outcome measures that participants need to complete for each session. Participants will receive a 15-minute briefing on the use of the mobile app (by members of the study team who are familiar with the app) before the commencement of the assessment and intervention. Participants will be provided with tablets by the study team to use the mobile attention bias modification intervention.

Textbox 1. Inclusion criteria.

- Participants aged 21-65 years
- Participants diagnosed with a primary psychiatric disorder of alcohol dependence, opioid dependence, cannabis dependence, stimulant dependence, or polysubstance use disorder
- For participants diagnosed with polysubstance use disorder, the main substance of use must be alcohol, opioid, cannabis, or a stimulant
- Participants need to be able to read and write in English
- Participants need to be able to use a smartphone or a tablet device

Textbox 2.

Exclusion criteria

- Having a known history of cognitive impairment or dementia
- Having a history of seizures (apart from febrile seizures) or a prior history of withdrawal seizures
- Having a medical history of migraines (triggered by flashing lights)
- Having moderate to severe symptoms of comorbid psychiatric disorders (affective disorders, anxiety disorders, and psychotic disorders) based on clinical assessment

Table 1. An overview of the outcome measures that participants need to complete for each session.

Instrument	Aim	Day of rehabilitation				
		1	2	3	4	5[a]
Baseline demographic and clinical information questionnaire	Baseline characteristic of participants	✓				
Addiction Severity Index questionnaire	Details about substance use	✓				
Severity of Substance Dependence questionnaire	Assessment of severity of psychological dependence	✓				
Short-Form 12	Baseline health status	✓				
Attention bias modification assessment task	Measurement of attentional biases	✓[b]	✓	✓	✓	✓
Attention bias modification intervention task	Retraining of attentional biases	✓	✓	✓	✓	✓
Visual analogue scale for craving	Assessment of cravings	✓[c]	✓[c]	✓[c]	✓[c]	✓[c]
Perspective questionnaire	Acceptability of intervention			✓		

[a]Participants will undertake a maximum of 5 sessions considering that the study will not be conducted on weekends.

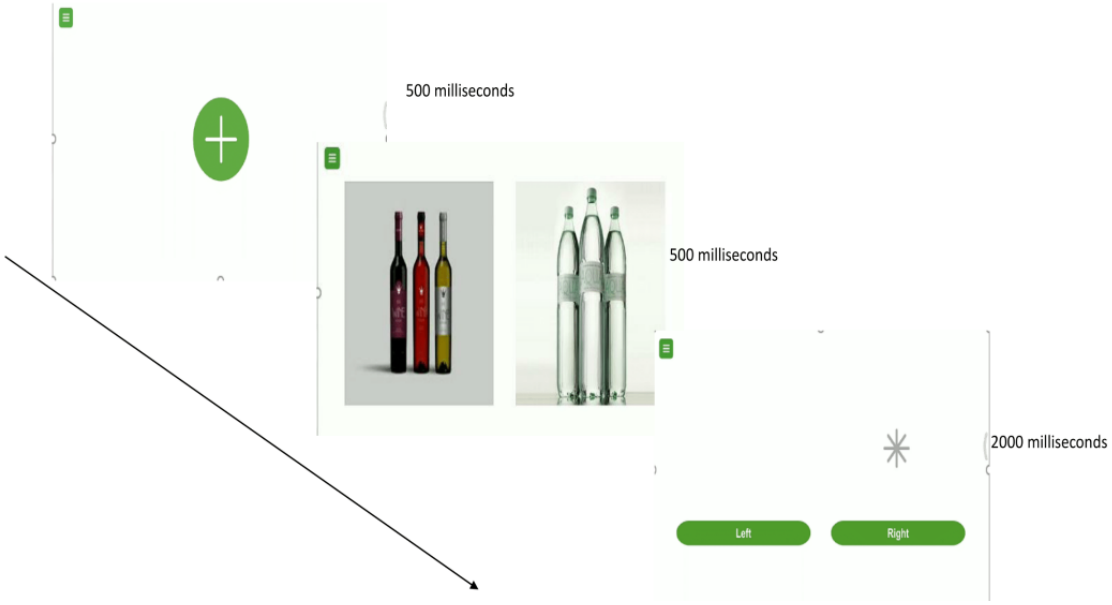
[b]The attention bias modification assessment task will be completed twice on the first day: first assessment will provide information pertaining to the baseline attentional biases; second assessment will assess for the change in attentional biases following the first intervention.

[c]Start and end of each session.

On the first day of their rehabilitation, participants will be required to complete a baseline attention bias assessment task and an attention bias modification task. They will be allowed to rest for 15 minutes before they complete a reassessment of their attention bias. Participants can rest for slightly longer on the first day, given that they are required to complete two tasks—an assessment and a modification task. On the subsequent days of their rehabilitation, they will complete the attention bias modification task and will be allowed 10 minutes of rest before retaking an attention bias assessment task. Participants will be required to complete the visual analogue scale for craving before and after the completion of each of the bias modification task. Participants who have completed 3 sessions will be asked to complete the app perception questionnaire. Participants are expected to undertake the intervention throughout their rehabilitation stay on the ward, except for weekends and public holidays. The intervention is not administered on these days due to the possibility of image-triggered cravings and the absence of a counselor to address the heightened cravings.

The mobile version of the visual probe task that participants will use adheres to the protocol of the original visual probe task [37]. In the attention bias assessment task, participants will be required to complete a total of 200 trials (with 10 set of images being repeated 20 times). In each trial, participants will be presented with a fixation cross in the center of the screen for 500 ms. Subsequently, they will be presented with a set of two images for another 500 ms. In each set of images, one of the images will be a neutral image, which is closely related to that of the alcohol or drug image (eg, an image of a man drinking from a can of beer, which will be paired with tan image of a man drinking from a soft drink can). Following the disappearance of the images, an asterisk will replace the position of one of the images (either on the right or on the left). Participants will be required to indicate a response by selecting the physical onscreen buttons as fast as they could. The next set of images will be presented once participants have indicated a response (by pressing the left or right button depending on where the probe is) or if the time of 2000 ms has lapsed (Figure 1). In the assessment phase, 50% of the time, the asterisk will replace the neutral image, and the rest 50% of the time, it will replace the alcohol or substance image. For the intervention or bias modification task, participants will be required to take the same task as that described. However, the asterisk will replace the position of the neutral image 100% of the time for the attentional bias to be retrained. Figure 1 provides an overview of the task that participants undertake on the smartphone or tablet device.

Figure 1. Overview of the task that participants undertake on the smartphone or tablet device.



Outcomes

The primary outcome feasibility is defined by the number of participants recruited and participants' adherence to the intervention. In our protocol, we have proposed a total recruitment sample size of 30 participants, and the study is considered feasible if we manage to recruit 25% of the invited number of participants (8 participants). We have proposed a 25% recruitment target for feasibility as we anticipate that there will be challenges to recruitment as the inpatient treatment program is a voluntary program (ie, patients could be discharged voluntarily from the program at any time) and that some patients would leave following the completion of their medical-assisted detoxification. In addition, 25% has been proposed as the target, due also, in part, to our strict inclusion and exclusion criteria. We have specifically mentioned that we will exclude participants with medical comorbidities such as seizures and migraines. To a large extent, most individuals with alcohol disorders often have a history of withdrawal seizures and, hence, they are not eligible for the study, thus, potentially affecting the overall recruitment. Furthermore, we have specifically mentioned that individuals with moderate to severe psychiatric comorbidities are not included. As other psychiatric conditions like depression or anxiety disorders are often comorbidities of substance use disorder, a large group of individuals cannot be recruited. The other criterion for feasibility is patients' adherence to the planned interventions, and we will consider the study to be feasible if all participants complete at least 60% of the planned interventions.

Attention bias will be computed using the mean reaction time that participants take to react to asterisks or probes that replace the neutral and alcohol or substance images in the assessment task. Attention bias is present if the mean reaction time taken by participants to react to probes that replace the neutral image is longer in comparison to that of alcohol or substance images. The underlying rationale is that an alcohol or substance image would preferentially draw one's attention, and the reaction time taken to react to asterisk or probes replacing the image is naturally much faster. Attention bias, as measured by the assessment tasks, will be compared to determine if the interventions result in a reduction in overall biases (by comparing the final attention bias score with the baseline score). Cravings will be assessed using the single-item measure, the visual analogue scale [38], with scores ranging from 0 (no cravings) to 100 (extreme levels of cravings). The visual analogue scale is often used for the assessment of current cravings and urges mainly in terms of craving frequency and intensity [30]. There are inherent advantages to the use of the single-item visual analogue scale given that it is easy to administer [30], and in our case, it would also help reduce respondents' burden and risk of refusal, given the need for repeated measures. The scores on the visual analogue scales will be compared before and after the sessions and between sessions. If participants report increased cravings, they will be referred for counseling.

The secondary outcome acceptability will be assessed through a perception questionnaire, which consists of the following questions:

1. Prior to using the app, how confident are you in managing your addiction problems? (rated on a 5-point Likert scale)
2. How easy was it to use the app? (rated on a 5-point Likert scale and participants are asked to provide verbatim comments)
3. How interactive was the app? (rated on a 5-point Likert scale and participants are asked to provide verbatim comments)
4. Do you feel motivated to continue using the app? (rated on a 5-point Likert scale and participants are asked to provide verbatim comments)
5. Do the images in the app remind you of your substance use? (rated on a 5-point Likert scale)
6. After using the app, how confident are you in managing your addiction problem? (rated on a 5-point Likert scale).

The study is deemed acceptable if participants are willing to use the app daily; if at least 30% of participants rate ease of use,

interactivity, motivation, and reality (questions 2-5) positively (either very or extremely on the 5-point Likert scale); and if at least 30% of participants perceive a change in their confidence level after having received 3 sessions of the intervention task (questions 1 and 6). The app is also deemed acceptable by the absence of any severe adverse events (such as intense cravings leading to a premature discharge from the inpatient program).

Baseline demographic and clinical information will be collected from participants. This includes information about nationality, gender, martial status, race, religion, highest level of employment, housing conditions, current substance use, method of consumption of substance, quantity of substance consumed each time, frequency of use, previous treatment history, chronic diseases, (psychiatric or physical disorders), and current psychiatric medications. Furthermore, participants are required to complete a modified ASI-Lite, SDS, and SF-12 questionnaires.

The ASI-Lite collates information for the following domains: drug and alcohol use, medical, employment or school, legal, family, and social and psychiatric [39]. In our modified version, we have retained the drug and alcohol use questions. Participants will be asked about their alcohol and substance use in the last 30 days, last month, and their lifetime use. The SDS comprises 5 items, all of which are explicitly concerned with the psychological components of dependence [40]. The scale has been used to measure the degree of dependence among individuals using different types of substances [40]. The SF-12has been widely used in the assessment of self-reported quality of life. It covers the 8 health domains as the original SF-36 [41].

Data Management and Monitoring

All participants will be allocated a subject number upon recruitment. No participant-related identifiers will be captured on the hard copy forms. The completed hard copy forms and questionnaires will be stored in secure, locked cabinets in a restricted area. The electronic data from the smartphone app will be automatically synchronized onto a secured, password-protected cloud database. The main investigator will back-up a copy of the electronic data records onto a local secured computer. The principal investigator and the research assistants will take the responsibility for coding the data from the hard copy forms. An independent coinvestigator will routinely check the data entry for reliability and quality. All records will be kept securely for at least 6 years after the completion of the study.

Planned Statistical Analyses

Data collated with be analyzed using SPSS version 22 (SPSS Inc, IL, USA). Baseline demographic information of subjects will be summarized using descriptive statistics, including means and SDs. Chi-square tests or Fisher's test will be considered to examine any differences in the baseline demographic characteristics among the different substance disorders. The presence of attentional biases will be determined based on the mean reaction times taken to respond to the position of the probes that replace drug or neutral stimuli. In addition, statistical tests (analysis of variance) will be performed to determine whether there are statistically significant differences in the attentional bias scores across the sessions for participants. $P<.05$ will be considered statistically significant. Participants' perspectives and feedback will be analyzed qualitatively using a thematic analysis approach using NVivo version 10.0.

Adverse Events

Any adverse events that occur during the conduct of the feasibility study will be reported to the Domain Specific Research Board in accordance with the local institutional policy.

Dissemination Policies

We will publish our research in peer-reviewed journals and will also present the findings at regional and international conferences.

Patient and Public Involvement

Patients and public were not involved in planning for this protocol.

Results

This study was approved by the National Healthcare Group Domain Specific Research Board, with approval number (2018/00316). Results will be disseminated by means of conferences and publications. Currently, we are in the process of recruitment for this study.

Discussion

To the best of our knowledge, this is the first study to evaluate the feasibility and acceptability of a mobile attention bias modification intervention for individuals with substance use disorders such as cannabis opioid, stimulant, and alcohol disorders. The data pertaining to the feasibility and acceptability are undoubtedly crucial because they imply the potential use of mobile technologies in retraining attentional biases among inpatients who are admitted for medical-assisted detoxification and rehabilitation. Participants' feedback pertaining to the ease of use, interactivity, and motivation to continue using the app is crucial because it will determine whether a codesign approach might be warranted to design an app that is acceptable for participants and that participants themselves would be motivated to use. Apart from substance use disorders, increasing research has demonstrated the presence of attentional biases in behavioral disorders such as gambling and internet gaming disorders [42,43]. If deemed feasible, attention bias modification could potentially be applicable to behavioral disorders, and the use of mobile technologies would be most appropriate for low-resource settings [44]. Moreover, prior meta-analysis research has demonstrated that behavioral forms of addiction, such as internet addiction, are positively associated with alcohol abuse [45]. Hence, attentional biases appear to be a common therapeutic target in both these conditions.

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Authors' Contributions

MZ, JY, GS, DSSF, and HS conceived the study and were involved in study design and protocol development. MZ wrote the initial draft of the manuscript, which was revised by JY, GS, DSSF and HS.

Conflicts of Interest

None declared.

References

1. European Monitoring Centre for Drugs. Perspectives on Drugs: The role of psychosocial interventions in drug treatment. 2018. URL: http://www.emcdda.europa.eu/publications/topics/pods/psychosocial-interventions_en [WebCite Cache ID 73i7LQqf1]
2. World Health Organization. Prevalence of Alcohol Use Disorders. URL: http://www.who.int/gho/substance_abuse/burden/alcohol_prevalence/en/ [accessed 2018-05-08]
3. World Health Organization. Alcohol Use Disorders. URL: http://www.who.int/substance_abuse/publications/global_alcohol_report/en/ [accessed 2018-09-28]
4. World Health Organization. ATLAS of Substance Use Disorders. URL: http://www.who.int/substance_abuse/publications/atlas_report/profiles/singapore.pdf [accessed 2018-05-08]
5. Central Narcotics Bureau, Singapore. Drug Situation Report. URL: https://www.cnb.gov.sg/newsandevents/reports-(overview)/drug-report [accessed 2018-05-08]
6. Ministry of Health Singapore. URL: https://elis.moh.gov.sg/elis/publishInfo.do?task=download&pkId=268 [accessed 2018-05-24]
7. Ho R, Chen K, Broekman B. Buprenorphine: aspects of prescription, misuse and service provision from a global perspective. Advances in Psychiatric Treatment 2009;15:354-363.
8. Ho RCM, Ho ECL, Tan CH, Mak A. Pulmonary hypertension in first episode infective endocarditis among intravenous buprenorphine users: case report. Am J Drug Alcohol Abuse 2009;35(3):199-202. [doi: 10.1080/00952990902939719] [Medline: 19462305]
9. Ho RCM, Ho ECL, Mak A. Cutaneous complications among i.v. buprenorphine users. J Dermatol 2009 Jan;36(1):22-29. [doi: 10.1111/j.1346-8138.2008.00581.x] [Medline: 19207433]
10. McHugh RK, Hearon BA, Otto MW. Cognitive behavioral therapy for substance use disorders. Psychiatr Clin North Am 2010 Sep;33(3):511-525 [FREE Full text] [doi: 10.1016/j.psc.2010.04.012] [Medline: 20599130]
11. Cutler RB, Fishbain DA. Are alcoholism treatments effective? The Project MATCH data. BMC Public Health 2005 Jul 14;5:75 [FREE Full text] [doi: 10.1186/1471-2458-5-75] [Medline: 16018798]
12. Field M, Marhe R, Franken IHA. The clinical relevance of attentional bias in substance use disorders. CNS Spectr 2014 Jun;19(3):225-230. [doi: 10.1017/S1092852913000321] [Medline: 23663386]
13. Cox WM, Fadardi JS, Intriligator JM, Klinger E. Attentional bias modification for addictive behaviors: clinical implications. CNS Spectr 2014 Jun;19(3):215-224. [doi: 10.1017/S1092852914000091] [Medline: 24642267]
14. Cristea I, Kok R, Cuijpers P. The Effectiveness of Cognitive Bias Modification Interventions for Substance Addictions: A Meta-Analysis. PLoS One 2016;11(9):e0162226 [FREE Full text] [doi: 10.1371/journal.pone.0162226] [Medline: 27611692]
15. Wiers R, Rinck M, Dictus M, van den Wildenberg E. Relatively strong automatic appetitive action-tendencies in male carriers of the OPRM1 G-allele. Genes Brain Behav 2009 Feb;8(1):101-106 [FREE Full text] [doi: 10.1111/j.1601-183X.2008.00454.x] [Medline: 19016889]
16. Wiers R, Rinck M, Kordts R, Houben K, Strack F. Retraining automatic action-tendencies to approach alcohol in hazardous drinkers. Addiction 2010 Feb;105(2):279-287. [doi: 10.1111/j.1360-0443.2009.02775.x] [Medline: 20078486]
17. Wiers R, Boffo M, Field M. What's in a Trial? On the Importance of Distinguishing Between Experimental Lab Studies and Randomized Controlled Trials: The Case of Cognitive Bias Modification and Alcohol Use Disorders. J Stud Alcohol Drugs 2018 May;79(3):333-343. [Medline: 29885138]
18. Zhang M, Ying J, Wing T, Song G, Fung DSS, Smith H. A Systematic Review of Attention Biases in Opioid, Cannabis, Stimulant Use Disorders. Int J Environ Res Public Health 2018 Jun 01;15(6) [FREE Full text] [doi: 10.3390/ijerph15061138] [Medline: 29857586]
19. Ziaee SS, Fadardi JS, Cox WM, Yazdi SAA. Effects of attention control training on drug abusers' attentional bias and treatment outcome. J Consult Clin Psychol 2016 Oct;84(10):861-873. [doi: 10.1037/a0040290] [Medline: 27281374]
20. Wolf P, Salemink E, Wiers RW. Attentional retraining and cognitive biases in a regular cannabis smoking student population. SUCHT 2017;62:355-365 [FREE Full text]

21. Mayer AR, Wilcox CE, Dodd AB, Klimaj SD, Dekonenko CJ, Claus ED, et al. The efficacy of attention bias modification therapy in cocaine use disorders. Am J Drug Alcohol Abuse 2016 Dec;42(4):459-468 [FREE Full text] [doi: 10.3109/00952990.2016.1151523] [Medline: 27184297]
22. Schoenmakers TM, de Bruin M, Lux IFM, Goertz AG, Van Kerkhof DHAT, Wiers RW. Clinical effectiveness of attentional bias modification training in abstinent alcoholic patients. Drug Alcohol Depend 2010 Jun 01;109(1-3):30-36. [doi: 10.1016/j.drugalcdep.2009.11.022] [Medline: 20064698]
23. Manning V, Staiger P, Hall K, Garfield J, Flaks G, Leung D. Cognitive Bias Modification Training During Inpatient Alcohol Detoxification Reduces Early Relapse: A Randomized Controlled Trial. Alcohol Clin Exp Res 2016;40(9):A.
24. Wiers RW, Eberl C, Rinck M, Becker ES, Lindenmeyer J. Retraining automatic action tendencies changes alcoholic patients' approach bias for alcohol and improves treatment outcome. Psychol Sci 2011 Apr;22(4):490-497. [doi: 10.1177/0956797611400615] [Medline: 21389338]
25. Eberl C, Wiers RW, Pawelczack S, Rinck M, Becker ES, Lindenmeyer J. Approach bias modification in alcohol dependence: do clinical effects replicate and for whom does it work best? Dev Cogn Neurosci 2013 Apr;4:38-51 [FREE Full text] [doi: 10.1016/j.dcn.2012.11.002] [Medline: 23218805]
26. Mucic D, Hilty DM, editors. E-Mental Health. Switerland: Springer International Publishing; 2016.
27. Yang R, Cui L, Li F, Xiao J, Zhang Q, Oei TPS. Effects of Cognitive Bias Modification Training via Smartphones. Front Psychol 2017;8:1370 [FREE Full text] [doi: 10.3389/fpsyg.2017.01370] [Medline: 28855880]
28. Zhang M, Ying J, Song G, Fung DS, Smith H. Attention and Cognitive Bias Modification Apps: Review of the Literature and of Commercially Available Apps. JMIR Mhealth Uhealth 2018 May 24;6(5):e10034 [FREE Full text] [doi: 10.2196/10034] [Medline: 29793899]
29. Clarke PJF, Bedford K, Notebaert L, Bucks RS, Rudaizky D, Milkins BC, et al. Assessing the Therapeutic Potential of Targeted Attentional Bias Modification for Insomnia Using Smartphone Delivery. Psychother Psychosom 2016;85(3):187-189. [doi: 10.1159/000442025] [Medline: 27043732]
30. Dennis-Tiwary TA, Denefrio S, Gelber S. Salutary effects of an attention bias modification mobile application on biobehavioral measures of stress and anxiety during pregnancy. Biol Psychol 2017 Dec;127:148-156 [FREE Full text] [doi: 10.1016/j.biopsycho.2017.05.003] [Medline: 28478138]
31. Dennis-Tiwary TA, Egan LJ, Babkirk S, Denefrio S. For whom the bell tolls: Neurocognitive individual differences in the acute stress-reduction effects of an attention bias modification game for anxiety. Behav Res Ther 2016 Feb;77:105-117 [FREE Full text] [doi: 10.1016/j.brat.2015.12.008] [Medline: 26745621]
32. Kerst WF, Waters AJ. Attentional retraining administered in the field reduces smokers' attentional bias and craving. Health Psychol 2014 Oct;33(10):1232-1240. [doi: 10.1037/a0035708] [Medline: 24818609]
33. Dennis T, O'Toole L. Mental Health on the Goffects of a Gamified Attention Bias Modification Mobile Application in Trait Anxious Adults. Clin Psychol Sci 2014;2(5):576-590.
34. Cox M, Intrilligator J, Hillier C. Chimpshop and alcohol reduction - using technology to change behaviour. Perspect Public Health 2015 May;135(3):126-127. [doi: 10.1177/1757913915580926] [Medline: 25925306]
35. Robinson CD, Muench C, Brede E, Endrighi R, Szeto EH, Sells JR, et al. Effect of attentional retraining on cognition, craving, and smoking in African American smokers. Psychol Addict Behav 2017 Dec;31(5):636-646 [FREE Full text] [doi: 10.1037/adb0000286] [Medline: 28627913]
36. Zhang MW, Ying JB, Song G, Fung DSS, Smith HE. Recent Advances in Attention Bias Modification for Substance Addictions. Int J Environ Res Public Health 2018 Dec 04;15(4) [FREE Full text] [doi: 10.3390/ijerph15040676] [Medline: 29617325]
37. MacLeod C, Mathews A, Tata P. Attentional bias in emotional disorders. J Abnorm Psychol 1986 Feb;95(1):15-20. [Medline: 3700842]
38. Kavanagh DJ, Statham DJ, Feeney GFX, Young RM, May J, Andrade J, et al. Measurement of alcohol craving. Addict Behav 2013 Feb;38(2):1572-1584. [doi: 10.1016/j.addbeh.2012.08.004] [Medline: 23142210]
39. McLellan AT, Luborsky L, Woody GE, O'Brien CP. An improved diagnostic evaluation instrument for substance abuse patients. The Addiction Severity Index. Journal of Nervous and Mental Disorders 1980;168(1):26-33.
40. Gossop M, Darke S, Griffiths P, Hando J, Powis B, Hall W, et al. The Severity of Dependence Scale (SDS): psychometric properties of the SDS in English and Australian samples of heroin, cocaine and amphetamine users. Addiction 1995 May;90(5):607-614. [Medline: 7795497]
41. Huo T, Guo Y, Shenkman E, Muller K. Assessing the reliability of the short form 12 (SF-12) health survey in adults with mental health conditions: a report from the wellness incentive and navigation (WIN) study. Health Qual Life Outcomes 2018 Feb 13;16(1):34 [FREE Full text] [doi: 10.1186/s12955-018-0858-2] [Medline: 29439718]
42. McGrath D, Meitner A, Sears C. The specificity of attentional biases by type of gambling: An eye-tracking study. PLoS One 2018;13(1):e0190614 [FREE Full text] [doi: 10.1371/journal.pone.0190614] [Medline: 29385164]
43. Jeromin F, Nyenhuis N, Barke A. Attentional bias in excessive Internet gamers: Experimental investigations using an addiction Stroop and a visual probe. J Behav Addict 2016 Mar;5(1):32-40 [FREE Full text] [doi: 10.1556/2006.5.2016.012] [Medline: 28092198]

44. Tran BX, Huong LT, Hinh ND, Nguyen LH, Le BN, Nong VM, et al. A study on the influence of internet addiction and online interpersonal influences on health-related quality of life in young Vietnamese. BMC Public Health 2017 Dec 31;17(1):138 [FREE Full text] [doi: 10.1186/s12889-016-3983-z] [Medline: 28143462]
45. Ho RC, Zhang MW, Tsang TY, Toh AH, Pan F, Lu Y, et al. The association between internet addiction and psychiatric co-morbidity: a meta-analysis. BMC Psychiatry 2014 Jun 20;14(1). [doi: 10.1186/1471-244x-14-183]

Abbreviations

ASI: Addiction Severity Index
eHealth: electronic health
mHealth: mobile health
NAMS: National Addictions Management Service
SDS: Severity of Substance Dependence
SF-12: Short Form-12

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Protocol

User Perspectives of a Web-Based Data-Sharing Platform (Open Humans) on Ethical Oversight in Participant-Led Research: Protocol for a Quantitative Study

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Abstract

Background: Advances in medicine rely to a great extent on people's willingness to share their data with researchers. With increasingly widespread use of digital technologies, several Web-based communities have emerged aiming to enable their users to share large amounts of data, some of which can possibly be employed for research purposes by scientists, or to conduct participant-led research (PLR). Scholarship has recently addressed the necessity of interrogating how existing ethical standards can and should be applied and adapted in view of the specificities of such Web-based activities. So far, no study has explored participants' beliefs about and attitudes toward ethical oversight when it comes to platforms that involve medical data sharing.

Objective: This paper presents the protocol for a survey study aimed at understanding users' beliefs about Web-based data-sharing platforms regarding how research ethics principles should be applied in such a setting. Furthermore, the study aims at quantitatively assessing the relationship between participants' perspectives on ethical oversight and other variables such as previous participation in research, beliefs about data sharing, and attitudes toward self-experimentation.

Methods: We are conducting a Web-based survey with users of a popular Web-based data-sharing platform, Open Humans. The survey has been sent to approximately 4640 users registered for the Open Humans newsletter. To fill out the survey, participants need to have an account on Open Humans. We expect a 5%-10% response rate (between 200 and 400 completed surveys out of approximately 4000 survey invitations sent). Independent variables include past data-sharing behavior and intention, beliefs about data sharing, past participation in research, attitudes toward self-experimentation, perceived knowledge of the platform's guidelines and terms, perceived importance of having transparent guidelines, and governance-related beliefs. The main dependent variable is participants' expectations regarding who should ensure that ethical requirements are met within research projects conducted on open data-sharing platforms, based on Emanuel et al's ethical framework. We will use chi-square tests to assess the relationship between participants' expectations regarding ethical oversight and their past behavior, future intentions, beliefs, attitudes, and knowledge.

Results: Data collection started on June 13, 2018. A reminder to fill out the survey was sent to participants in mid-July. We expect to gain insights on users' perspectives on the ethical oversight of Web-based data-sharing platforms and on the associated experiences, beliefs, and sociodemographic characteristics.

Conclusions: When digital tools allow people to engage in PLR including medical data, understanding how people interpret and envision the ethical oversight of their data-sharing practices is crucial. This will be the first study to explore users' perspectives on ethical oversight of Web-based data-sharing platforms. The results will help inform the development of a framework that can be employed for platforms hosting various kinds of research projects to accommodate participants' ethical oversight needs.

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KEYWORDS

ethics; data sharing; patient participation; patient-generated health data; survey; questionnaire; mobile phone

Introduction

Toward Participatory Medicine

Medicine is undergoing a great revolution that is radically transforming health care by not only improving diagnostics and therapeutics but also providing new understandings of disease prevention [1,2]. Contributing to such transformation are some intimately intertwined factors such as the introduction of systems medicine (application of systems biology approaches to disease); big data (availability of large quantities of data); new technologies (that allow study of new magnitudes of individuals' data); and patients' increasing participation, engagement, and involvement in health care [1-6]. Large amounts of data are necessary to make sense of systems medicine, and, in turn, sophisticated technologies are crucial for big data to be adequately analyzed and interpreted. Similarly, individuals' participation, engagement, and involvement in health care are crucial for a constant supply of big data because, by sharing their data with research, individuals can contribute to the accumulation of a vast amount of information [7]. The convergence of these elements is typically referred to as "4P medicine," a term initially coined by systems biologist Leroy Hood to indicate a type of medicine that is predictive, preventive, personalized, and participatory at the same time [2,4,8-11]. However, 4P faces both technical and societal challenges [2]. While there appear to be rapid technical developments in the capacity to process people's data, the transition from a reactive to a proactive, empowered approach to medicine seems to pose greater difficulties [1-3]. The key concept of 4P medicine that "the individual is at the center of action-taking related to health and health care" [12] raises the question of not only how to best educate patients, physicians, and public about the opportunities offered by 4P medicine but also how to acquire the amount and type of data necessary for predictive and personalized medicine to be realized [2,12-14]. Reaching out to larger communities of individuals may require looking beyond the traditional researcher-led enrollment system conducted in university hospitals and research centers. Patient-activated networks and patient-initiated research activities may help address this challenge [2,3]. According to many, it is exactly these patient-initiated phenomena that will be the most powerful tools in the strive to push forward the 4P agenda because they may increasingly provide data while fostering individuals' empowerment and boosting transparency and accountability in science at the same time [3,12,15-18]. We set out to analyze the opportunities and challenges these activities offer and focus on the ethical oversight requirements of such phenomenon.

Participant-Led Research

The major strategies adopted to promote a participatory approach to medicine involve increasing individuals' participation, engagement, and involvement in their health and in health research [5,19]. According to Woolley, participation in medical research encompasses activities that involve not only an active, intentional role but also more passive forms of inclusion [5]. The concept of public engagement in scientific studies, on the other hand, does not depend on individuals' participation in research, that is, individuals can feel engaged even if they do not actively participate in the research. Engagement can be higher or lower according to scientists' effort to communicate their intentions and request public's collaboration in collecting data through so-called participant-centric initiatives [5,20]. Finally, involvement characterizes activities where members of public can play an active role in initiating research, selecting the scientific questions to address, and designing a study and implementing it [5,21]. This latter type of initiatives is commonly referred to as participant-led research (PLR), participant-driven research, or participatory research, and it includes a wide spectrum of approaches such as self-experimentation, self-surveillance, analyses of genetic information, and genome-wide associated studies [22,23]. In this study, we decided to adopt the label "PLR" over others because we believe it better emphasizes the main characteristic of this activity, which is not only initiated but also conducted by those who participate in it.

PLR has been facilitated by the integration of a wide range of increasingly affordable technologies into everyday life like computers, smartphones, tablets, and wearable gadgets and by the emergence of social media platforms where people can nowadays share (health-related) information about themselves to be used for a variety of research purposes [23]. For example, platforms like PatientsLikeMe and the Quantified Self offer people the opportunity to design, conduct, and analyze their own studies by uploading different types of data about themselves [12,18,24]. An example of a successful PLR initiative, the results of which were eventually published in an international scientific journal, is the lithium study, in which a group of patients suffering from amyotrophic lateral sclerosis and belonging to the PatientsLikeMe community initiated and conducted a study on the effects of lithium on their condition [25]. The study findings were later confirmed by a standard clinical trial [26]. While the lithium study involved testing a substance on one's own body, most PLR activities involve uploading one's data to Web-based platforms (often genetic data derived from direct-to-consumer genetic testing) with the scope of starting or contributing to a research project [15,27,28]. Users may want to publicly share their data on Web-based platforms for a variety of reasons. For example, studies have found that users may want to learn about themselves or contribute to the advancement of medical research and, in the case of genetic and genomic data, want to improve the predictability of genetic testing because they find it fun to explore genotypic and phenotypic data [29,30-34].

PLR activities have some clear limitations, such as an evident self-selection bias due to the fact that its participants usually come from a selected, hyperactivated, and highly educated subset of the general population, leading to little variance in the sociodemographic characteristics of those who join it [35]. However, there is much consensus on the opportunities offered by this novel approach to science [19,22]. First, PLR promotes individuals' empowerment, one of the pillars of the patient-centered health care model, by allowing people to make more informed and autonomous decisions on their own health [22]. From a patient or participant perspective, taking part in PLR could fulfill individuals' need for involvement and self-determination that can otherwise be lacking in investigator-led research and that is currently urged in patient care [36]. It can also create opportunities for social support among individuals sharing the same condition or health concerns [21]. PLR supports the democratization of research, a system where anyone has a human right to contribute to science and actively participate in the research process, and significantly helps cut research-related recruitment and logistic costs [18,37,38]. Furthermore, such activities can provide great support to large-scale and longitudinal research studies, accelerate the pace of their execution, and explore areas that standard medical research often overlooks or cannot reach [13,22,39]. Just as in other forms of crowdsourcing, the underlying belief that fuels PLR activities is that the more people are allowed to participate, the more accurate and complete the generated information will be [40]. However, due to the general lack of qualified supervision that distinguishes standard research practice, these bottom-up initiatives challenge existing ethical paradigms and raise questions that scholars have only recently started to address [13,40].

Ethical Oversight of Participant-Led Research

Just like investigator-led research, PLR poses evident questions related to its ethical, legal, and social implications, potentially resulting in barriers to the optimal integration of its outcomes into scientific evidence and, ultimately, into health care [3]. Beyond issues of accountability, the main concerns are whether PLR can be conducted (1) in a scientifically thorough fashion and (2) in an ethically appropriate manner [14,37]. The first concern follows the consideration that being self-reported, self-collected, and mostly generated without an experienced researcher's supervision, data produced by PLR may not meet the highest scientific standards characterizing investigator-led research and contain major biases that may lead to questioning data's reliability and validity [22,26]. In response to this worry, recent scholarship has proposed that PLR can, at least in principle, reach the same level of scientific accuracy of standard research, provided that participants are adequately trained on how to collect and report their data [16,41]. Furthermore, with the widespread use of these approaches, PLR holds the promise of introducing increasingly novel methods for validating its results to secure their publication in international journals and their integration into health care practice [19]. The second concern builds on the assumption that PLR activities bear potential risk of harm for those taking part in them [15,23]. For example, testing off-label drugs without a researcher's supervision might lead to serious health consequences as much as sharing one's identifiable genetic data on Web-based platforms may lead to privacy issues that can result in discrimination by employers or insurance companies [7].

Following these considerations, some scholars have argued that PLR should be ethically regulated, and a debate is currently taking place regarding what forms of ethical oversight mechanisms should be adopted in such contexts [16]. While some scholars believe that we should try to capture such research within existing regulatory frameworks (requiring, for example, ethical review by an Institutional Review Board; IRB) [42], Vayena et al have proposed that existing ethical standards should be applied to the specificities of participant-led health research with alternative mechanisms [16]. They have proposed a distinction into 3 categories representing different levels of similarity between a given PLR project and standard research, the level of risk involved, and the type of agent conducting the research; they suggest crowdsourcing review as an alternative method of ethical oversight [12,16,21,23,42]. In particular, a given PLR activity will fall into the first category (and, thus, it will be subject to the standard form of ethics review) if it is performed by state or for-profit institutions; if the activity does not meet the "institution-plus" criterion, it will fall either into the second category (if it involves more than minimal risk to participants) or in the third category (if it involves no more than minimal risk to participants) [16]. While the second category will demand a form of ethics review equivalent to an expedited review (eg, a faster review conducted by the IRB chair and one or more experienced reviewers), no formal ethics review is morally required for the third category [16].

The need to adapt ethical standards to PLR also finds justification in the great amount of evidence showing that participants are more willing to donate their data when an ethical review body has approved the study protocol [43]. But establishing the appropriate ethical oversight mechanism in PLR is not without challenges. In fact, these activities represent a revolutionary movement in contrast to mainstream research, and, as such, they often position themselves as opposed to the traditional elitism of standard research practice [38,44]. Furthermore, applying the same mechanisms of ethical oversight that are also employed to review standard research is likely to impose a burden on PLR in terms of finances, time, and logistics, with the possible consequence of discouraging participation [13,21]. Thus, we can expect some forms of resistance by this novel approach to science against any top-down attempts to regulate it.

Objective of the Study

The literature suggests a substantial lack of information on individuals' perspectives regarding ethical oversight in participant-led health research [13,16,38,42]. Previous research has explored the reasons why users decide to publicly share their data on Web-based platforms for research purposes and what prevents them from doing so [29], but no study has so far investigated participants' perspectives on what ethical oversight methods should be in place in such settings. Even scholarship from other disciplines that has investigated users' attitudes toward Web-based platform policies has so far addressed issues such as privacy [45] and copyright [46], but overlooked medical

research ethics. Considering that most participant-led health research activities take place on Web-based platforms and involve publicly sharing individuals' data in anonymized, coded, or identifiable forms, the goal of this study is to investigate whether the users and visitors of a Web-based data-sharing platform apply the same ethical principles of standard research to Web-based data sharing and, in particular, to Web-based participant-led health research projects. Furthermore, we aim to investigate the mechanisms of ethical oversight that users think should be adopted in such a context.

Methods

Study Design

We will adopt survey methodology in this study. We target the users of the Web-based data-sharing platform Open Humans who have subscribed to the Open Humans newsletter [47]. Initially, we developed a conceptual model that seeks to explain individuals' ethical oversight expectations of data-sharing platforms with their past data-sharing behavior, their previous participation in research, their perceived importance of having transparent guidelines on Web-based data-sharing platforms and perceived knowledge of them, their attitudes toward data sharing and self-experimentation, and their future data-sharing intention (see Multimedia Appendix 1). Subsequently, we developed a Web-based questionnaire using the survey platform SurveyMonkey [48] on the basis of the literature discussing the main ethical principles applying to standard research and, in particular, Emanuel et al's ethical framework for clinical research [49]. We developed items to measure the variables that potentially have a relationship with users' opinions on ethical oversight, such as past data-sharing behavior [29], previous participation in research [50], attitudes toward self-experimentation [51,52] and data sharing [30-34], perceived importance of having transparent guidelines, and knowledge about the platform's guidelines [30,31]. To content and face validate the questionnaire, we conducted a pretest with a convenience subsample of 6 participants. We contacted potential pretest participants through the Open Humans platform and asked them to fill out the Web-based survey by providing specific feedback on the clarity and appropriateness of each survey item. Data collection continued until data saturation was achieved.

Once the pretest had been conducted and the survey questions refined, we created a research project on a dedicated page of the Open Humans platform where we described the scope of the study and provided a link to the Web-based survey. Open Humans research projects are meant to ask an engaged audience of participants to join and contribute to research. Past and current research projects include the Genevieve Genome Report (matching participants' genome against public variant data), the Twitter Archive Analyzer (to explore social media usage), and the Keeping Pace project (seeking to study data about how participants move around and to understand how seasons and local environments influence their movement patterns). Altogether, Open Humans research projects have so far involved more than 3000 users.

An invitation to visit the research project Web page and fill out the Web-based survey was sent through the Open Humans regular newsletter to all subscribers (approximately 4640 users) on June 13, 2018. Those who do not have an account on Open Humans are requested to create one to be able to fill out the survey. We expect a response rate of 5%-10% (between 200 and 400 completed surveys out of approximately 4000 survey invitations sent), in line with previous research [53]. To increase the response rate, a second newsletter including a reminder about our research project and the upcoming deadline was sent to potential participants in mid-July 2018.

Survey Administration

By clicking on the link to the survey, participants are directed to a dedicated page of the Open Humans platform describing the project's goal ("Data sharing and ethical oversight") and its academic and nonprofit nature, providing the name and contact details of the principal investigator, and providing the informed consent form as well as a downloadable version of it. Users can only be redirected to the actual survey if they consent to participate in the study by clicking on the corresponding button. If they agree, the participants are directed to the survey on surveymonkey.com, where a short introduction reminds them about the study's scope and guarantees that no data are extracted from participants' accounts. An anonymized unique identifier is attributed to each Open Humans platform account to detect multiple entries from the same individual. If such multiple entries are found from the same individual, we will keep the first entry for analysis. To start the survey, participants are asked to confirm that they "have joined the project on openhumans.org, read the description, and accepted the corresponding consent form." The survey displays 1-3 questions on each page according to the questions' length, and participants can review and change their answers through a "back" button. We ensured that survey questions are appropriately displayed on mobile phones. Completion of the survey is estimated to take approximately 15-18 minutes. To avoid missing data, answers to the questions are mandatory, except for sociodemographic variables. We offer no remuneration for participation in this study. However, we ask participants whether they would like to receive their responses to the survey and the aggregated answers from all respondents for comparison.

Analysis

Once the survey has been closed, we will import the data into SPSS (IBM Corp, version 24.0). We will compute frequencies and correlations and use chi-square tests to assess the relationships between participants' ethical oversight expectations and their past behavior, future intentions, beliefs, attitudes, and knowledge. A priori power analysis suggests that a sample size of 142 respondents would be adequate to detect a moderate effect with alpha=.05 and power=.8 [54]. Thus, our proposed minimum sample size of N=200 will be more than adequate for the main objective of this study. Data missing at random will be handled using multiple imputation [55]. Depending on the nature of the comments provided in the open-ended questions, we might also be able to gather important qualitative insights. In this case, two researchers will code the comments and label

them. Similar labels will then be merged into broader themes to provide a comprehensive description of the findings [56].

Institutional Review Board Approval

The study protocol, including survey questions, has been approved by the Ethics Commission of the Federal Institute of Technology, Zurich on May 7, 2018, with the title "Ethical oversight in online data-sharing platforms" (Ref.: EK 2018-N-36). We expect there will be no risks to participants in this study.

Measures

This is the first study to explore individuals' ethical oversight expectations regarding research projects on open data-sharing platforms. For this reason, we developed our own conceptual model in an effort to explain participants' ethical oversight expectations through their past data-sharing behavior, their previous participation in research, their perceived importance of having transparent guidelines on Web-based data-sharing platforms and perceived knowledge of them, their attitudes toward data sharing and self-experimentation, and their future data-sharing intention (see Multimedia Appendix 1). To build measures for our variables of interest, we relied on the literature on the ethical principles of standard research [49,57-59], on what characterizes PLR [12,16,19,37,60-62], and on barriers to and facilitators of data sharing in varous contexts (eg, biobanking) [30-32]. Below we have described how survey questions were created on the basis of the literature across all variables. The survey questions can be found in Multimedia Appendix 2.

Independent Variables

Past Data-Sharing Behavior

The level of users' engagement with data sharing represents a key variable for comparison between the ethical oversight expectations of more or less engaged users. We speculate that the amount of data users have publicly shared in the past will be significantly linked to the type of ethical oversight mechanism preferred. We will measure past data-sharing behavior with 4 questions. A filter question will ask participants whether they have ever tracked, collected, or been in possession of different types of data (such as vital signs, stress levels, and mood). The next 2 questions will target specific types of data selected by participants and will ask participants whether they have ever shared that data on the Open Humans platform and on any Web-based platforms other than Open Humans. We extracted the list of types of data from the 2014 Report of the Health Data Exploration Project and adapted it to the digital context [63]. The fourth question will focus on genetic data and will ask participants whether they have ever shared this type of data in any of the most popular genetic data-sharing platforms (eg, OpenSNP, SNPedia, and DNAland). A multiple answer option will be provided for all questions (see Multimedia Appendix 2).

Intention to Share Data in the Future

Intention is a well-known antecedent of actual behavior [64]. We will measure participants' intention to share their data with a matrix question asking to what extent participants would agree to share their data for research purposes if they were asked to do so in the future. The list of types of data will be the same employed to measure past data-sharing behavior extracted from the 2014 Report of the Health Data Exploration Project and adapted to the digital context [63], and we will collect answers on a 5-point Likert scale measuring agreement and anchoring at "strongly disagree" and "strongly agree."

Beliefs About Data Sharing

Data-sharing beliefs have been found to be linked to intention to share and interest in sharing [30-33]. To measure participants' beliefs regarding data sharing, we will employ 5 items adapted from a previous survey study involving users publicly sharing their data, for instance, "sharing my data makes me feel part of scientific research," "I want to contribute to the advancement of medical research," and "I want to compare my data to that of other people" [29]. Answers will be collected on a 5-point Likert scale measuring agreement and anchoring at "strongly disagree" and "strongly agree."

Past Participation in Research

Previous research has found that 15.57% of surveyed individuals who had publicly shared their data were or had been research participants [29]. To measure participants' previous participation in research, we will ask them whether they have ever taken part in a clinical trial, a survey or questionnaire study, a qualitative study (eg, interview or focus group), a nonclinical trial, or another type of research study they might want to specify. Answer options will include (1) "no, never"; (2) "yes, in the past week"; (3) "yes in the past month"; (4) "yes, in the past 6 months"; (5) "yes, in the past year"; and (6) "yes, more than 1 year ago."

Attitude Toward Self-Experimentation

Self-experimentation is one of the forms that PLR activities can take [52,65]. However, self-experimentation can, in turn, take different shapes, according to the level of risk involved in the experimental activity [51,52]. Due to the lack of studies on people's attitudes toward self-experimentation, we speculate that individuals with a positive attitude toward the most extreme forms will be significantly more likely to expect less institutional ethical oversight mechanisms. To measure participants' attitudes toward self-experimentation, we will provide 3 brief scenarios describing different examples of self-experimentation, from low-risk to high-risk behaviors [52,65]. Answers will be collected on a 5-point Likert scale measuring approval and anchoring at "strongly disapprove" and "strongly approve"; Multimedia Appendix 2 provides a full description of the scenarios.

Perceived Knowledge of the Guidelines and Terms of Open Humans

Perceived knowledge about what is involved in an action or a decision is a known predictor of individuals' self-determination in many behavioral and decisional contexts [66]. Individuals' self-determination might, in turn, regulate the expectation of a more or less rigorous institutional review for a given PLR project. We speculate that participants with higher levels of perceived knowledge regarding the platform's guidelines will be significantly more likely to indicate less institutional ethical

oversight mechanisms for public data-sharing activities because they feel more autonomous in their decision making. This variable will measure the perceived knowledge of the main guidelines and terms of use of the Open Humans platform, such as privacy, projects, and community guidelines. Participants will be asked to indicate how familiar they are with each guideline. We purposely decided not to include objective questions (such as a quiz) because we do not want our participants to feel they are being tested. However, to detect automatic replies and those conforming to social desirability, we have added control questions about hypothetical guidelines that do not actually exist, and we will, thus, be able to filter answers of the individuals who state they are "(extremely) familiar" with these. Answers will be measured on a 5-point Likert scale anchoring at "not familiar at all" and "extremely familiar." This question is meant to measure, in general, the extent to which participants perceive themselves knowledgeable about the platform's guidelines. We employed broad, recognizable labels so that participants can more easily assess whether they are in possession of that information regarding the platform's guidelines. Perhaps then, our labels do not exactly reflect the names appearing on the website. We will calculate a summative score for this set of questions, excluding the control questions.

Perceived Importance of Having Transparent Guidelines and Other Governance-Related Variables

Barazzetti et al have addressed the expectations of people in regulatory governance of biobank research. Although their study was not about a Web-based platform, their results underline the need to inquire further into the alignment between perception, regulation, and actual communication [67]. Additionally, Earp et al looked closely at users' expectations of information regarding privacy and compared them with both actual regulation and the existing policy statements, finding important divergences [68]. Fiesler et al focused on users' expectations compared with actual legislation regarding copyright aspects, but their article also gives a useful overview of previous work related to the perception of Terms of Services more generally [69]. In an effort to assess users' governance-related expectations, we decided to measure the extent to which participants believe it important to have transparent guidelines on both the Open Humans platform and other open data-sharing platforms. Main guidelines will include areas such as privacy, projects, and community. Answers will be measured on a 5-point Likert scale measuring importance and anchoring at "not important at all" and "extremely important." The survey will also include a variety of questions aimed at measuring participants' perceptions of other aspects of governance of the Open Humans platform such as (1) the perceived influence of the nonprofit status of Open Humans on the decision to sign up or navigate the platform (measured on a 5-point Likert scale anchoring at "not influential at all" and "extremely influential"); (2) beliefs regarding who should make decisions about the Open Humans platform (eg, users taking part in research projects, any users of the platform, and independent nonqualified ethical committee); (3) participants' desire to be involved in decisions about the governance of the Open Humans platform (measured on a 5-point Likert scale anchoring at "strongly disagree" and "strongly agree"); and (4) amount of time participants are willing to invest into governing the Open Humans platform (measured on a 5-point Likert scale anchoring at "none at all" and "a great deal").

Dependent Variable

Expectations Regarding Ethical Oversight

Participants' expectations regarding ethical oversight mechanisms on Web-based data-sharing platforms will be measured with 11 question asking them who they think should ensure that 6 ethical requirements for clinical research [49] are met within the research projects conducted on Web-based data-sharing platforms. The ethical framework that guided the creation of these questions is Emanuel et al's "7 ethical requirements" framework [49]. Each ethical requirement will be covered by one or more questions. We decided to not include 1 of the 7 ethical requirements, that is, "value," because it has to do with the dissemination of the research results and the potential of the research to increase knowledge [49]. This requirement dictates whether the study will receive funding and, thus, represents a preliminary evaluation of the research project that does not match the core characteristic of PLR activities, the peculiarity of which is a noninstitutional, bottom-up approach [16]. The ethical requirements selected by us are (1) scientific validity ("Who should ensure that the research is conducted in a methodologically rigorous manner?"); (2) fair subject selection ("Who should ensure that recruitment is fair and balanced and not restricted to certain populations on the basis of convenience or efficiency or by exploiting vulnerable individuals or communities?"); (3) favorable risk-benefit ratio (eg, "Who should ensure that potential risks to individual subjects are minimized?"); (4) independent review (eg, "Who should ensure a research project's compliance with ethical requirements?"); (5) informed consent (eg, "Who should ensure that individuals are accurately informed about the purpose, methods, risks, benefits, and alternatives to the research?"); and (6) respect for potential or enrolled subjects ("Who should ensure that individuals' privacy is respected by managing the information in accordance with confidentiality rules?"). Participants will be asked to choose among 9 answer options, namely (1) "No one in particular, because it does not apply"; (2) "No one in particular, for another reason (please specify)"; (3) "Users participating in the project"; (4) "Any registered users of the platform"; (5) "The creators or directors of the project"; (6) "The creators or owners or directors of the platform"; (7) "An independent, nonspecialized committee (eg, a group of citizen volunteers)"; (8) "An independent ethics committee (eg, a university IRB)"; and (9) "Other" (with the possibility of entering text).

Sociodemographic Variables

We will also ask participants a number of questions pertaining to their sociodemographic status, such as perceived health status, presence of a chronic condition (both referring to the participant and to the participant's family members), gender, age, ethnicity, country of residence, education, marital status, number of children, employment status, health and life insurance coverage, and past experience in the health field.

Results

We initially conducted a pretest with a convenience sample of 6 users of the Open Humans platform; subsequently, we refined the survey questions and started data collection on June 13, 2018. Results will provide information on not only which mechanisms of ethical oversight participants expect to be implemented within research projects conducted on the Open Humans platform but also the behavioral and psychosocial features of the Open Humans users participating in the study. Although we expect mainly US participants to join the study (as Open Humans is based in the United States), users from other countries can also participate. In case we detect important differences based on national contexts, we will take into account the main US and European laws and regulations on privacy that are important for ethical considerations for the analysis and interpretation of responses.

We speculate that participants will envision stronger ethical oversight mechanisms for principles like autonomy, while they will perceive other principles such as privacy and confidentiality as less applicable to this context. This is because open data sharing is a voluntary activity that involves participants' affirmation of their autonomy, conducted without any privacy protection (data can be accessed by anyone) [16]. Furthermore, we hypothesize that previous participation in research, past data-sharing behavior, perceived importance and knowledge of Open Humans guidelines and terms, attitudes toward self-experimentation and data sharing, and future data-sharing intention will have significant relationships with their expectations regarding ethical oversight. In particular, we formulated the following hypotheses:

> *H_1: Participants will highly value certain principles such as respect for autonomy, while they will deem other principles such as privacy and confidentiality less important in this setting. Due to the public nature of open data sharing (no privacy protection is offered), participants might assume that they have relinquished their privacy, accepting that it cannot be protected. On the other hand, those publicly sharing their own data are likely to expect that their self-determination is respected and enhanced.*
>
> *H_2: Participants with previous participation in research will be significantly more likely to indicate that an independent ethics committee should be in charge of applying the main ethical principles on Web-based data-sharing platforms compared with those with no previous participation in research. Because of their previous exposure to the investigator-led research model, they might overgeneralize and assume that standard ethical review should also apply to PLR [43].*
>
> *H_3: Participants with more positive attitudes toward self-experimentation will be significantly more likely to indicate that users participating in the project should themselves be in charge of applying the main ethical principles on Web-based data-sharing platforms. Self-experimentation represents an expression of self-determination or autonomy that can regulate the expectation regarding the type of ethical oversight applying to PLR [51,52,65].*
>
> *H_4: Participants with lower perceived knowledge of the platform's guidelines will be more likely to indicate that an external review board should be in charge of applying the main ethical principles on Web-based data-sharing platforms. Multiple studies based on self-determination theory have found perceived knowledge to be significantly and positively correlated with self-determination [66], which might regulate one's ethical oversight expectation (more or less institutional).*

Discussion

Study Rationale

Research is likely to benefit from fostering more engaged research participation [3]. The integration of digital tools into everyday life is facilitating people's active involvement in research, and PLR activities are becoming an increasingly popular phenomenon [70]. PLR initiatives hold great promise for science, not only because they are a tangible expression of a response to the push for a more participatory medicine but also because they offer significant opportunities for advances in a variety of fields by offering novel solutions to complicated challenges [22]. Yet, if not duly overcome, some challenges are likely to become burdensome bottlenecks to the successful realization of these activities. In particular, ethical oversight mechanisms need to be adapted to PLR to ensure that the same ethical standards of investigator-led research are fulfilled while PLR values are, at the same time, respected and promoted [16,21,23]. Some alternative solutions to standard ethics review (such as crowdsourcing ethics review) have been proposed [16], but evidence is currently missing on the perspectives of individuals who are directly involved in PLR activities. Our study represents the first attempt to explore what ethical oversight mechanisms users and visitors of a Web-based platform hosting research projects think should be in place. The results will also inform a broader debate on PLR and its potential impact outside the medical realm. In fact, the potential significance of PLR is much broader than medical research and also invests health or wellness research and nonmedical human research (this reflection was contributed by an anonymous reviewer). On the basis of the type of data that our participants report to be engaged with, we will be able to establish which fields of application are suitable for the preferred PLR ethical oversight mechanisms.

Limitations

A number of limitations to this study are worth mentioning. First, we will recruit our participants from a relatively small, US-based data-sharing platform; therefore, the results—while representative of the Open Humans population—might not be generalizable to other platforms. The decision to restrict our inquiry to the Open Humans community has been dictated by the availability of the platform to join this study. Furthermore, because this is the first study of this kind, we aim to collect an initial set of information from a single, circumscribed group of

people. A second limitation is that while the users of Open Humans can share their data for research purposes by contributing to dedicated research projects, other platforms such as PatientLikeMe represent more common venues to start leading PLR activities. However, Open Humans represents a fast-growing platform for initiating and conducting research projects with a diverse and highly involved community. Third, we will ask our participants what potential ethical oversight mechanisms they think should be in place within research projects on the Open Humans platform, thus, introducing a hypothetical bias [71]. Soliciting their opinions solely on already established oversight mechanisms might have provided a more valid and reliable account, but in the current state, it remains unclear what these would have entailed. Finally, we will compare engaged and nonengaged users on the basis of their answers to the past data-sharing behavior questions. Having access to their account activity data would have represented a more reliable and objective measure of engagement. However, we purposely decided not to include this type of data to ensure that participants feel comfortable in sharing their opinions and experiences with the research team.

Future Research

This study is the first attempt to elicit individuals' perspectives on the ethical oversight of Web-based PLR activities and to compare such views with their experiences, beliefs, knowledge, and sociodemographic characteristics. Future research should replicate our effort in novel methodological and contextual ways. First, because our study will follow a quantitative approach, qualitative research might be a valuable approach to further investigate people's expectations regarding which forms of ethical oversight should be applied to PLR. Second, as we restricted our enquiry to a single platform, exploring and comparing different geographical settings will certainly provide more insights on users' expectations and allow for a better refinement of any policy recommendations. Furthermore, it would be interesting to study whether practitioners' beliefs about ethical oversight can differ on the basis of research type (including medical research, wellness research, or scientific research involving human data).

To maximize the extent to which it can benefit from research, society has a legitimate priority and concern about protecting research participants and ensuring that a high-quality research is conducted in an ethical manner [23]. As PLR is capable of producing generalizable scientific knowledge, just as standard research, it is crucial to understand what criteria are important to PLR participants to determine who should be in charge of ensuring that standard ethical principles are satisfied [23].

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Conflicts of Interest

MPB and BGT are executive director and director of research at the Open Humans Foundation, respectively. Other authors have nothing to declare.

Multimedia Appendix 1

Conceptual model.

[PDF File (Adobe PDF File), 10KB - resprot_v7i11e10939_app1.pdf]

Multimedia Appendix 2

Survey.

[PDF File (Adobe PDF File), 135KB - resprot_v7i11e10939_app2.pdf]

References

1. Auffray C, Hood L. Editorial: Systems biology and personalized medicine - the future is now. Biotechnol J 2012 Aug;7(8):938-939. [doi: 10.1002/biot.201200242] [Medline: 22887882]
2. Hood L, Friend SH. Predictive, personalized, preventive, participatory (P4) cancer medicine. Nat Rev Clin Oncol 2011 Mar;8(3):184-187. [doi: 10.1038/nrclinonc.2010.227] [Medline: 21364692]
3. Hood L, Auffray C. Participatory medicine: a driving force for revolutionizing healthcare. Genome Med 2013;5(12):110 [FREE Full text] [doi: 10.1186/gm514] [Medline: 24360023]
4. Hood L, Flores M. A personal view on systems medicine and the emergence of proactive P4 medicine: predictive, preventive, personalized and participatory. N Biotechnol 2012 Sep 15;29(6):613-624. [doi: 10.1016/j.nbt.2012.03.004] [Medline: 22450380]
5. Woolley JP, McGowan ML, Teare HJA, Coathup V, Fishman JR, Settersten RA, et al. Citizen science or scientific citizenship? Disentangling the uses of public engagement rhetoric in national research initiatives. BMC Med Ethics 2016 Dec 04;17(1):33 [FREE Full text] [doi: 10.1186/s12910-016-0117-1] [Medline: 27260081]

6. Auffray C, Chen Z, Hood L. Systems medicine: the future of medical genomics and healthcare. Genome Med 2009 Jan 20;1(1):2 [FREE Full text] [doi: 10.1186/gm2] [Medline: 19348689]
7. Francis LP. Genomic knowledge sharing: A review of the ethical and legal issues. Appl Transl Genom 2014 Dec 01;3(4):111-115 [FREE Full text] [doi: 10.1016/j.atg.2014.09.003] [Medline: 27294025]
8. Hood L. A doctor's vision of the future of medicine. URL: https://www.newsweek.com/doctors-vision-future-medicine-80793 [accessed 2018-11-12] [WebCite Cache ID 73sUbuJZJ]
9. Hood L. Lee Hood. Nat Biotechnol 2011 Mar;29(3):191. [doi: 10.1038/nbt.1809] [Medline: 21390010]
10. Tian Q, Price ND, Hood L. Systems cancer medicine: towards realization of predictive, preventive, personalized and participatory (P4) medicine. J Intern Med 2012 Feb;271(2):111-121 [FREE Full text] [doi: 10.1111/j.1365-2796.2011.02498.x] [Medline: 22142401]
11. Weston AD, Hood L. Systems biology, proteomics, and the future of health care: toward predictive, preventative, and personalized medicine. J Proteome Res 2004;3(2):179-196. [Medline: 15113093]
12. Swan M. Health 2050: The Realization of Personalized Medicine through Crowdsourcing, the Quantified Self, and the Participatory Biocitizen. J Pers Med 2012;2(3):93-118 [FREE Full text] [doi: 10.3390/jpm2030093] [Medline: 25562203]
13. Blasimme A, Vayena E. "Tailored-to-You": Public Engagement and the Political Legitimation of Precision Medicine. Perspectives in Biology and Medicine 2016;59(2):172-188. [doi: 10.1353/pbm.2017.0002]
14. Blasimme A, Vayena E. Becoming partners, retaining autonomy: ethical considerations on the development of precision medicine. BMC Med Ethics 2016 Dec 04;17(1):67 [FREE Full text] [doi: 10.1186/s12910-016-0149-6] [Medline: 27809825]
15. Vayena E, Tasioulas J. The ethics of participant-led biomedical research. Nat Biotechnol 2013 Sep;31(9):786-787. [doi: 10.1038/nbt.2692] [Medline: 24022150]
16. Vayena E, Tasioulas J. Adapting standards: ethical oversight of participant-led health research. PLoS Med 2013;10(3):e1001402 [FREE Full text] [doi: 10.1371/journal.pmed.1001402] [Medline: 23554580]
17. Swan M. Crowdsourced health research studies: an important emerging complement to clinical trials in the public health research ecosystem. J Med Internet Res 2012;14(2):e46 [FREE Full text] [doi: 10.2196/jmir.1988] [Medline: 22397809]
18. Vayena E, Tasioulas J. "We the Scientists": a Human Right to Citizen Science. Philos. Technol 2015 Jun 20;28(3):479-485. [doi: 10.1007/s13347-015-0204-0]
19. Anderson N, Bragg C, Hartzler A, Edwards K. Participant-Centric Initiatives: Tools to Facilitate Engagement In Research. Appl Transl Genom 2012 Dec 1;1:25-29 [FREE Full text] [doi: 10.1016/j.atg.2012.07.001] [Medline: 24772384]
20. Kaye J, Curren L, Anderson N, Edwards K, Fullerton SM, Kanellopoulou N, et al. From patients to partners: participant-centric initiatives in biomedical research. Nat Rev Genet 2012 May;13(5):371-376 [FREE Full text] [doi: 10.1038/nrg3218] [Medline: 22473380]
21. Vayena E, Brownsword R, Edwards SJ, Greshake B, Kahn JP, Ladher N, et al. Research led by participants: a new social contract for a new kind of research. J Med Ethics 2016 Apr;42(4):216-219 [FREE Full text] [doi: 10.1136/medethics-2015-102663] [Medline: 25825527]
22. Streuli JC, Vayena E. The promising revolution of participant-led research in rare neurological diseases; potential benefits and pitfalls. Epileptologie 2015;32:177-182 [FREE Full text] [doi: 10.5167/uzh-123041]
23. Vayena E, Mastroianni A, Kahn J. Ethical issues in health research with novel online sources. Am J Public Health 2012 Dec;102(12):2225-2230. [doi: 10.2105/AJPH.2012.300813] [Medline: 23078484]
24. Dolgin E. Personalized investigation. Nat Med 2010 Sep;16(9):953-955. [doi: 10.1038/nm0910-953] [Medline: 20823867]
25. Frost JH, Massagli MP, Wicks P, Heywood J. How the Social Web Supports patient experimentation with a new therapy: The demand for patient-controlled and patient-centered informatics. AMIA Annu Symp Proc 2008 Nov 06:217-221 [FREE Full text] [Medline: 18999176]
26. Wicks P, Vaughan TE, Massagli MP, Heywood J. Accelerated clinical discovery using self-reported patient data collected online and a patient-matching algorithm. Nat Biotechnol 2011 May;29(5):411-414. [doi: 10.1038/nbt.1837] [Medline: 21516084]
27. Greshake B, Bayer PE, Rausch H, Reda J. openSNP--a crowdsourced web resource for personal genomics. PLoS One 2014;9(3):e89204 [FREE Full text] [doi: 10.1371/journal.pone.0089204] [Medline: 24647222]
28. Ball MP, Bobe JR, Chou MF, Clegg T, Estep PW, Lunshof JE, et al. Harvard Personal Genome Project: lessons from participatory public research. Genome Med 2014 Feb 28;6(2):10 [FREE Full text] [doi: 10.1186/gm527] [Medline: 24713084]
29. Haeusermann T, Greshake B, Blasimme A, Irdam D, Richards M, Vayena E. Open sharing of genomic data: Who does it and why? PLoS One 2017;12(5):e0177158 [FREE Full text] [doi: 10.1371/journal.pone.0177158] [Medline: 28486511]
30. McGuire AL, Hamilton JA, Lunstroth R, McCullough LB, Goldman A. DNA data sharing: research participants' perspectives. Genet Med 2008 Jan;10(1):46-53 [FREE Full text] [doi: 10.1097/GIM.0b013e31815f1e00] [Medline: 18197056]
31. Trinidad SB, Fullerton SM, Bares JM, Jarvik GP, Larson EB, Burke W. Genomic research and wide data sharing: views of prospective participants. Genet Med 2010 Aug;12(8):486-495 [FREE Full text] [doi: 10.1097/GIM.0b013e3181e38f9e] [Medline: 20535021]
32. Lemke AA, Wolf WA, Hebert-Beirne J, Smith ME. Public and biobank participant attitudes toward genetic research participation and data sharing. Public Health Genomics 2010;13(6):368-377 [FREE Full text] [doi: 10.1159/000276767] [Medline: 20805700]

33. Oliver JM, Slashinski MJ, Wang T, Kelly PA, Hilsenbeck SG, McGuire AL. Balancing the risks and benefits of genomic data sharing: genome research participants' perspectives. Public Health Genomics 2012;15(2):106-114 [FREE Full text] [doi: 10.1159/000334718] [Medline: 22213783]
34. Wallis JC, Rolando E, Borgman CL. If we share data, will anyone use them? Data sharing and reuse in the long tail of science and technology. PLoS One 2013;8(7):e67332 [FREE Full text] [doi: 10.1371/journal.pone.0067332] [Medline: 23935830]
35. Wicks P, Sulham KA, Gnanasakthy A. Quality of life in organ transplant recipients participating in an online transplant community. Patient 2014;7(1):73-84 [FREE Full text] [doi: 10.1007/s40271-013-0033-0] [Medline: 24194474]
36. Vahdat S, Hamzehgardeshi L, Hessam S, Hamzehgardeshi Z. Patient involvement in health care decision making: a review. Iran Red Crescent Med J 2014 Jan;16(1):e12454 [FREE Full text] [doi: 10.5812/ircmj.12454] [Medline: 24719703]
37. Prainsack B. Voting with their mice: personal genome testing and the "participatory turn" in disease research. Account Res 2011 May;18(3):132-147. [doi: 10.1080/08989621.2011.575032] [Medline: 21574070]
38. McGowan ML, Choudhury S, Juengst ET, Lambrix M, Settersten RA, Fishman JR. “Let’s pull these technologies out of the ivory tower”: The politics, ethos, and ironies of participant-driven genomic research. BioSocieties 2017 Mar 22;12(4):494-519. [doi: 10.1057/s41292-017-0043-6]
39. Frost J, Okun S, Vaughan T, Heywood J, Wicks P. Patient-reported outcomes as a source of evidence in off-label prescribing: analysis of data from PatientsLikeMe. J Med Internet Res 2011;13(1):e6 [FREE Full text] [doi: 10.2196/jmir.1643] [Medline: 21252034]
40. Brownstein CA, Brownstein JS, Williams DS, Wicks P, Heywood JA. The power of social networking in medicine. Nat Biotechnol 2009 Oct;27(10):888-890. [doi: 10.1038/nbt1009-888] [Medline: 19816437]
41. Cohn JP. Citizen Science: Can Volunteers Do Real Research? Bioscience 2008;58(3):192-197.
42. Hunter D. Participant-led health research and ethical regulation. Research Ethics 2013 Jun 14;9(2):50-51. [doi: 10.1177/1747016113489950] [Medline: 22973420]
43. Goldman RE, Kingdon C, Wasser J, Clark MA, Goldberg R, Papandonatos GD, et al. Rhode Islanders' attitudes towards the development of a statewide genetic biobank. Personalized Medicine 2008 Jul;5(4):339-359. [doi: 10.2217/17410541.5.4.339]
44. Follett R, Strezov V. An Analysis of Citizen Science Based Research: Usage and Publication Patterns. PLoS One 2015 Nov;10(11):e0143687 [FREE Full text] [doi: 10.1371/journal.pone.0143687] [Medline: 26600041]
45. Earp J, Anton A, Aiman-Smith L, Stufflebeam W. Examining Internet Privacy Policies Within the Context of User Privacy Values. IEEE Trans. Eng. Manage 2005 May;52(2):227-237. [doi: 10.1109/TEM.2005.844927]
46. Fiesler C, Lampe C, Bruckman A. Reality and Perception of Copyright Terms of Service for. New York: ACM; 2016 Presented at: 19th ACM Conference on Computer-Supported Cooperative Work and Social Computing; 27 February-2 March 2016; San Francisco p. A.
47. Open Humans. 2018. URL: https://www.openhumans.org [WebCite Cache ID 6z71RpzQg]
48. Survey Monkey. URL: https://www.surveymonkey.com [WebCite Cache ID 6z71ZToCS]
49. Emanuel EJ, Wendler D, Grady C. What makes clinical research ethical? JAMA 2000;283(20):2701-2711. [Medline: 10819955]
50. Jenkins V, Farewell V, Farewell D, Darmanin J, Wagstaff J, Langridge C, et al. Drivers and barriers to patient participation in RCTs. Br J Cancer 2013 Apr 16;108(7):1402-1407 [FREE Full text] [doi: 10.1038/bjc.2013.113] [Medline: 23511558]
51. Altman LK. Who goes first? The story of self-experimentation in medicine. New York: Random House; 1987.
52. Weisse AB. Self-experimentation and its role in medical research. Tex Heart Inst J 2012;39(1):51-54 [FREE Full text] [Medline: 22412227]
53. Fincham JE. Response rates and responsiveness for surveys, standards, and the Journal. Am J Pharm Educ 2008 Apr 15;72(2):43 [FREE Full text] [Medline: 18483608]
54. Cohen J. A power primer. Psychol Bull 1992 Jul;112(1):155-159. [Medline: 19565683]
55. Rubin D. Multiple imputation for Nonresponse in Surveys. New York: John Wiley & Sons; 1987.
56. Braun V, Clarke V. Using thematic analysis in psychology. Qualitative Research in Psychology 2006 Jan;3(2):77-101. [doi: 10.1191/1478088706qp063oa]
57. Council for International Organizations of Medical Sciences. International ethical guidelines for biomedical research involving human subjects. Bull Med Ethics 2002 Oct(182):17-23. [Medline: 14983848]
58. WHO. Standards and Operational Guidance for Ethics Review of Health-Related Research with Human Participants. Geneva: World Health Organization; 2011:1-41.
59. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. JAMA 2013 Nov 27;310(20):2191-2194. [doi: 10.1001/jama.2013.281053] [Medline: 24141714]
60. Lamberti MJ, Awatin J. Mapping the Landscape of Patient-centric Activities Within Clinical Research. Clin Ther 2017 Nov;39(11):2196-2202. [doi: 10.1016/j.clinthera.2017.09.010] [Medline: 29032849]
61. Swan M. Emerging patient-driven health care models: an examination of health social networks, consumer personalized medicine and quantified self-tracking. Int J Environ Res Public Health 2009 Feb;6(2):492-525 [FREE Full text] [doi: 10.3390/ijerph6020492] [Medline: 19440396]

62. Terry SF, Terry PF. Power to the people: participant ownership of clinical trial data. Sci Transl Med 2011 Feb 09;3(69):69cm3. [doi: 10.1126/scitranslmed.3001857] [Medline: 21307299]
63. Health Data Exploration Project. Personal Data for the Public Good: New Opportunities to Enrich Understanding of Individual and Population Health. Health Data Exploration Project. Calit2, UC Irvine and UC San Diego 2014 Mar [FREE Full text]
64. Sheeran P. Intention—Behavior Relations: A Conceptual and Empirical Review. European Review of Social Psychology 2002 Jan;12(1):1-36. [doi: 10.1080/14792772143000003]
65. Corti K, Reddy G, Choi E, Gillespie A. The researcher as experimental subject: using self-experimentation to access experiences, understand social phenomena, and stimulate reflexivity. Integr Psychol Behav Sci 2015 Jun;49(2):288-308. [doi: 10.1007/s12124-015-9294-6] [Medline: 25597036]
66. Ng JYY, Ntoumanis N, Thøgersen-Ntoumani C, Deci EL, Ryan RM, Duda JL, et al. Self-Determination Theory Applied to Health Contexts: A Meta-Analysis. Perspect Psychol Sci 2012 Jul;7(4):325-340. [doi: 10.1177/1745691612447309] [Medline: 26168470]
67. Barazzetti G, Cavalli S, Benaroyo L, Kaufmann A. "Still Rather Hazy at Present": Citizens' and Physicians' Views on Returning Results from Biobank Research Using Broad Consent. Genet Test Mol Biomarkers 2017 Mar;21(3):159-165. [doi: 10.1089/gtmb.2016.0412] [Medline: 28177781]
68. Earp JB, Anton AI, Aiman-Smith L, Stufflebeam WH. Examining Internet Privacy Policies Within the Context of User Privacy Values. IEEE Trans Eng Manage 2005 May;52(2):227-237. [doi: 10.1109/TEM.2005.844927]
69. Fiesler C, Lampe C, Bruckman A. Reality and Perception of Copyright Terms of Service for Online Content Creation. 2016 Mar Presented at: 19th ACM Conference on Computer-Supported Cooperative Work & Social Computing; 2016; Chicago.
70. Vayena E, Haeusermann T, Adjekum A, Blasimme A. Digital health: meeting the ethical and policy challenges. Swiss Med Wkly 2018 Dec 29;148:w14571 [FREE Full text] [doi: 10.4414/smw.2018.14571] [Medline: 29376547]
71. Murphy JJ, Allen PG, Stevens TH, Weatherhead D. A Meta-analysis of Hypothetical Bias in Stated Preference Valuation. Environ Resource Econ 2005 Mar;30(3):313-325. [doi: 10.1007/s10640-004-3332-z]

Abbreviations

4P medicine: predictive, preventive, personalized, and participatory medicine
IRB: Institutional Review Board
PLR: participant-led research

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Original Paper

Evaluating the Impacts of Methylsulfonylmethane on Allergic Rhinitis After a Standard Allergen Challenge: Randomized Double-Blind Exploratory Study

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Abstract

Background: The sulfur-containing compound methylsulfonylmethane (MSM) has been used as a dietary supplement for a variety of reported health benefits. Clinical observations and case studies have indicated that MSM may help alleviate allergic rhinitis; however, this effect has not been evaluated under controlled conditions.

Objective: This study aimed to determine the effects of MSM consumption on allergic rhinitis symptoms after provocation with a standardized allergen.

Methods: We recruited healthy participants with a history of allergic nasal congestion to participate in a randomized, double-blind, adaptive-design study. Participants were administered a standardized allergen in clinic to determine the presence or absence of an allergic response. Participant responses were recorded using a recognized measure of nasal patency, peak nasal inspiratory flow (PNIF), and by a visual analog scale to score the severity of their allergy-related nasal symptoms. After we collected baseline nasal responses to allergen, followed by a 1-week washout period, participants returned to the clinic and were exposed to allergen after taking an acute high dose of 12 g of MSM. We then randomly assigned participants to a lower dose of MSM (1 g, 3 g, or 6 g), which they consumed once a day for 14 days. Participants returned to the clinic for repeat assessments while again taking their assigned daily dose of MSM.

Results: All MSM treatment courses significantly reduced visual analog scale average nasal symptoms in a longitudinal comparison across all participants, with low-dose treatments decreasing symptoms by 53.72% (P=.001), and an acute 12-g dose decreasing symptoms by 22.49% (P=.03). Although the acute dose of MSM did not yield significant changes in nasal patency, low “everyday” doses significantly relieved nasal obstruction as indicated by a 17.32% (P=.02) increase in PNIF across all participants. The most effective dose across all measurements was daily consumption of 3 g of MSM, which significantly decreased all nasal symptoms (nasal obstruction, rhinorrhea, watery or itchy eyes and nose, and sneezing) and further was found to significantly (P=.01) increase PNIF.

Conclusions: The MSM study product provided significant relief of allergic rhinitis symptoms and objective nasal obstruction measurements without the occurrence of adverse events. Oral consumption of the study product may reduce the symptoms and onset of allergic rhinitis without the side effects associated with standard-care medication.

Trial Registration: ClinicalTrials.gov NCT02342483; https://clinicaltrials.gov/ct2/show/NCT02342483 (Archived by WebCite at http://www.webcitation.org/73vLKNvAp)

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KEYWORDS

methylsulfonylmethane; sulfur; allergies; allergic rhinitis; supplements

Introduction

Background

Allergic rhinitis, or nasal allergy, is an extremely common ailment that occurs when the nasal mucosa undergoes inflammation in response to inhaled allergens [1]. The prevalence of this condition ranges from 10% to 20% in the United States [2]. It is characterized by several uncomfortable symptoms: red itchy eyes; a blocked, itching, runny nose (a group of symptoms referred to as rhinorrhea); and sneezing. Other reported symptoms include throat clearing, headaches, facial pain, ear pain, itchy throat and palate, snoring, and sleep disturbances. Severe allergic rhinitis can significantly affect the patient's quality of life, sleep, and work performance [3]. Nasal allergy commonly occurs when an individual's immune system overreacts to allergens such as grass, weed, or tree pollens; house dust; mites; mold; and animal dander [4,5].

Allergic rhinitis was previously considered to be a disorder localized in the nasal passages, but emerging research indicates that the entire respiratory tract is involved. Close physiological, functional, and immunological relationships exist between the upper (nose, nasal cavity, paranasal sinuses, pharynx, and larynx) and lower (trachea, bronchial tubes, bronchioles, and lungs) respiratory tracts [6]. Although allergic rhinitis can be considered a simple nuisance in the case of mild symptoms, it has been classified as a chronic disease that should be addressed by a physician [7]. Allergic rhinitis is also associated with serious inflammatory disorders, including asthma. In fact, 80% of asthmatic patients have allergic rhinitis and 40% of rhinitis patients have asthma [8,9]. Allergic rhinitis is controlled by various palliative therapies, most commonly antihistamine medications, which often produce sedative side effects [10].

Methylsulfonylmethane (MSM), also known as dimethyl sulfone and methyl sulfone, is an organic compound containing sulfur that occurs naturally in the body, as well as in a variety of fruits, vegetables, grains, and animals [5]. Orally and topically, it is used to treat chronic and musculoskeletal pain, osteoarthritis, joint inflammation, exercise-induced muscle damage, hemorrhoids, and rosacea [11]. However, only a few studies have reported the potential benefits of MSM in treating allergic rhinitis and allergic sinusitis [12,13].

One multicenter human trial found that the consumption of 2.6 g of MSM effectively reduced symptoms of seasonal allergic rhinitis (SAR). This dose of MSM improved the frequency of upper respiratory signs and symptoms such as runny nose, nasal obstruction, and paroxysmal sneezing after a week of oral intake [13]. However, that study prompted criticism because it lacked quantification of pollen count each participant was exposed to [14]. In this study, we aimed to address the efficacy of MSM treatment using controlled standardized conditions in healthy participants with a history of SAR.

MSM is considered safe for consumption, as clinical studies have reported few, if any, side effects in a human population [13]. Moreover, in rats, MSM administered at 2 g/kg, a dose 5 to 7 times the maximum recommended dose for humans, was well tolerated and elicited no adverse events or deaths. No gross pathological lesions or changes in organ weights were observed, and renal history appeared to be normal in treated rats [12]. Similarly, oral intake of MSM also led to no adverse events in pregnant rats [15], suggesting it is safe for consumption even at high doses.

Objective

This randomized, double-blind, adaptive-design study aimed to assess the efficacy of the MSM study product in attenuating nasal provocation after exposure to standardized allergens. End points were percentage change in peak nasal inspiratory flow (PNIF) and visual analog scale (VAS) nasal symptom score in response to allergen exposure.

Methods

Investigational Product

The investigational product for this study was OptiMSM (Bergstrom Nutrition, Vancouver, WA, USA, the sponsor of this study). OptiMSM is designated "generally recognized as safe" with a letter of no questions issued by US Food and Drug Administration Center for Food Safety and Applied Nutrition (USFDA-CFSAN). Doses for study evaluation were chosen by the sponsor (1 g, 3 g, 6 g, and 12 g). The study products were provided by the sponsor and were consumed once a day, according to the randomization assignment.

Participants

We recruited study participants through online or database recruitment and screened them by telephone prior to scheduling a screening visit. We enrolled and randomly assigned healthy volunteers into the study who were between the ages of 18 and 65 years who had a history of nasal congestion in response to pollen, dust mites, cat dander, or dog dander and who scored moderate or severe in the visual analog scale (VAS) for nasal symptoms in response to an allergenic challenge at screening (V1). Pregnant or lactating women and participants with idiopathic rhinitis, atrophic rhinitis, or rhinitis medicamentosa were excluded from the study. Those taking any antihistamine or antiallergenic products underwent a 1-week washout period of these medications.

Study Design

This study was a randomized, double-blind, adaptive-design clinical trial with a duration of up to 14 days. Group allocation was placed in individually numbered envelopes to maintain blinding of all individuals. The participants, as well as the clinical staff, data management staff, and statistical analysis staff, were unaware of the study group. This study was conducted by a contract research organization (Medicus Research, Northridge, CA, USA). The study and the informed consent were approved and monitored by the MaGil Institutional

Review Board (Rockville, MD, USA) prior to the initiation of any study-related activities.

The study duration was 14 days, with a total of 3 visits: V1 (screening visit), V2 (administration of the acute dose of MSM of 12 g), and V3 (administration of varying doses of MSM of 1 g, 3 g, or 6 g; end of the study). After V2, participants were randomly assigned to receive 1 of 3 doses of MSM (1 g, 3 g, or 6 g) to consume daily for 14 days; they then returned to the clinic at V3 for repeat assessments in response to the allergen challenge.

For the initial screening visit, participants were acclimated in the room for 1 hour to allow for a washout of environmental allergens. All participants underwent the informed consent process and were screened for the presence of all the inclusion criteria and the absence of all the exclusion criteria. The screening process also included a detailed medical history, prior and concomitant medications, a physical examination, and measurement of vital signs. Participants also had laboratory assessments, including a urine pregnancy test. To determine the presence or absence of response, participants were administered an allergenic challenge consisting of the aerosolized allergens listed in Textbox 1 (supplier: Jubilant HollisterStier, LLC, Spokane, WA, USA).

In the study, the dose of allergen was set at 10,000 bioequivalent allergy units/mL, an allergen dose that has been shown to result in a substantial drop in average PNIF based on a study of Scadding et al [16].

After exposure to an allergen, participants had their PNIF measured and answered the VAS nasal symptom score questionnaire at multiple time points over 1 hour: –30 minutes (preexposure), 5 minutes (postexposure), 15 minutes (postexposure), 30 minutes (postexposure), and 60 minutes (postexposure). The allergen was administered at T0. Participants were provided with a rescue dose of medication (50 mg diphenhydramine [Benadryl]) if they continued to experience severe symptoms at T60 minutes.

After a 1-week washout period, participants returned to the clinic for V2, when they were interviewed by clinical staff to determine changes in medical history or the start of any new medications. After adverse event review and retaking of vital signs, participants were randomly assigned to 1 of the 3 test doses. Participants consumed an acute dose of the study product (MSM 12 g) 30 minutes prior to allergen exposure. At T0, the allergen was administered. Following exposure, participants' PNIF and VAS nasal symptom score were recorded at multiple time points over the following 2 hours: –30 minutes (preexposure), 15 minutes (postexposure), 30 minutes (postexposure), 60 minutes (postexposure), and 120 minutes (postexposure). At the end of V2, participants were dispensed with a 14-day supply of study product along with a daily dosing diary and a rescue medication (diphenhydramine 50 mg) to be used if they experienced severe symptoms.

Participants returned to the clinic for V3, when they were interviewed by clinical staff to determine changes in medical history and screened for adverse events. Participants were assessed for compliance by review of completed paper diaries and assessment of leftover and used study products. Participants were again exposed to allergen and received their randomized study product dose (MSM 1 g, 3 g, or 6 g). PNIF and VAS nasal symptom scores were recorded on a similar schedule to that at V2**)**. Rescue medication was offered if they continued to experience severe symptoms.

Textbox 1. Allergen exposure protocol: aerosolized allergens.

Pollen

- Tree pollen
  - Oak mix
  - Birch mix
  - Mountain cedar
  - Pecan
- Grass pollen
  - Bermuda grass
  - Kentucky bluegrass
  - Fescue, meadow
  - Johnson grass
  - Ryegrass, perennial

Dust mites

Cat dander

Dog dander

End Points

The objectives of this study were to assess the efficacy of MSM in improving nasal breathing and promoting recovery of nasal breathing, and improving "stuffy nose" symptoms after exposure to environmental allergens. The end points for this objective were percentage change from allergen exposure to each time point in PNIF and VAS nasal symptom scores (including nasal obstruction, rhinorrhea, watery eyes, itching eyes, itching nose, and sneezing).

Statistics

Parallel dual data entries were done by data management personnel across all end points. Data were validated and parallel entries were reconciled after the dual data entry process. The monitoring team compared the values on the original source documents, correcting any discrepancies found. All data elements were screened for reasonableness, and all missing, suspicious, or impossible values were referred back to the monitoring team for query generation and resolution. The database was formally locked after all suspicious entries in the database were resolved. The product assignments were then distinguished from the randomization or blinding codes and merged into the database and data tables.

We processed descriptive measures such as numbers, means, standard deviations, and standard errors of means for each numeric end point on all visits. Percentage changes were used to quantify increase or decrease of end points from baseline for each arm. On the other hand, categorical end points were presented as frequency tables, with corresponding percentages.

We performed a modified per-protocol analysis to assess the efficacy variables of the study. Participants who completed at least one postdose visit were included in the analysis. All efficacy end points were analyzed depending on the level of measurement of the end point.

For each end point in the interval or ratio scale that followed a normal distribution (or had semblance to normality), we analyzed the data using a paired *t* test for comparison between visit 1 and other time points. For nonnormally distributed data, we performed a sign test to analyze changes from each MSM product. Lastly, in longitudinal data, we measured the dependent variable at several time points for each participant and analyzed using a linear mixed model. In the analysis, the different doses of the MSM product were the factor, and the value of the efficacy variable at every visit was modeled as a function of group (response variable of interest) and of the value of the efficacy variable readings in every time point (covariate).

The linear mixed model procedure expands the general linear model so that the error terms and random effects are permitted to exhibit correlated and nonconstant variability. The linear mixed model, therefore, provides the flexibility to model not only the mean of a response variable, but its covariate structure as well. We selected categorical predictors as factors in the model. Each level of a factor can have a different linear effect on the value of the dependent variable. We selected scale predictors as covariates in the model. Within combinations of factors levels, values of covariates are assumed to be linearly correlated with values of the dependent variable. Repeated-effects variables are variables whose values in the dataset can be considered as markers of multiple observations of a single participant. Participant variables define the individual participants of the repeated measurement. In addition, the model used in the 1-way analysis of variance procedure was equivalent to fitting a linear mixed model with 1 fixed factor. All tests of hypotheses were done at alpha=.05.

To obtain comparable documentation on adverse events, the investigator asked each participant open, standardized questions at each visit. The frequency and intensity of adverse events and serious adverse events were recorded in detail, based on the participant's interviews during each visit. We grouped recorded adverse events by general type of event (body system). We assessed differences in adverse event patterns for each MSM product dose by McNemar change test.

Results

Participant Allocation

Of the 41 participants screened for this study, 18 passed the screen, and all 18 were retained through completion of the clinical trial. The 18 participants attended an initial screening visit (V1), when baseline responses to allergen exposure were recorded. At V2, all 18 participants were exposed to allergen after consumption of MSM 12 g, randomly assigned to 3 groups of 6 participants each, and then given a 14-day supply of their assigned randomized study product (MSM 1 g, 3 g, or 6 g) to self-administer once daily. At V3, participants were again assigned to consume differing amounts of MSM before and after exposure to allergen (MSM 1 g, 3 g, or 6 g; Figure 1).

Longitudinal Comparisons

An acute dose of 12 g of MSM significantly decreased the VAS average nasal symptom score by 5.95 U from screening to baseline (22.49%; *P*=.03) in longitudinal comparison between V1 and V2 (Figure 2). The specific subcategories that significantly decreased from baseline at this dose were nasal obstruction (8.02 U decrease, 17.88%; *P*=.04), rhinorrhea (10.08 U decrease, 34.99%; *P*=.004), watery eyes (11.27 U decrease, 53.18%; *P*=.001), and itching nose (18.89 U decrease, 67.23%; *P*=.001). The symptom of itching eyes was not significantly altered by the 12-g treatment, and sneezing was increased significantly after administration of allergen (12.46 U increase, 72.02%; *P*=.002; Figure 2). We observed no significant effect on PNIF after 12 g of MSM.

Longitudinal comparison between V1 and V3 across all participants produced a significantly increased PNIF with low daily MSM consumption (15.78 U increase, 17.32%; *P*=.02; Table 1). Individual low doses of MSM (1 g, 3 g, and 6 g) had variable effects on each SAR symptom when compared with baseline analysis, although each dose resulted in statistically significant decreases in at least 4 of the 8 VAS nasal symptom end points. Interestingly, when analyzed individually, only the 3-g MSM dose resulted in a significant increase in PNIF of 42.22 L/min from V1 to V3 (45.35%; *P*=.01; Figure 3).

Figure 1. Attrition chart for the study. MSM: methylsulfonylmethane; V1: visit 1, screening visit; V2: visit 2; V3: visit 3.

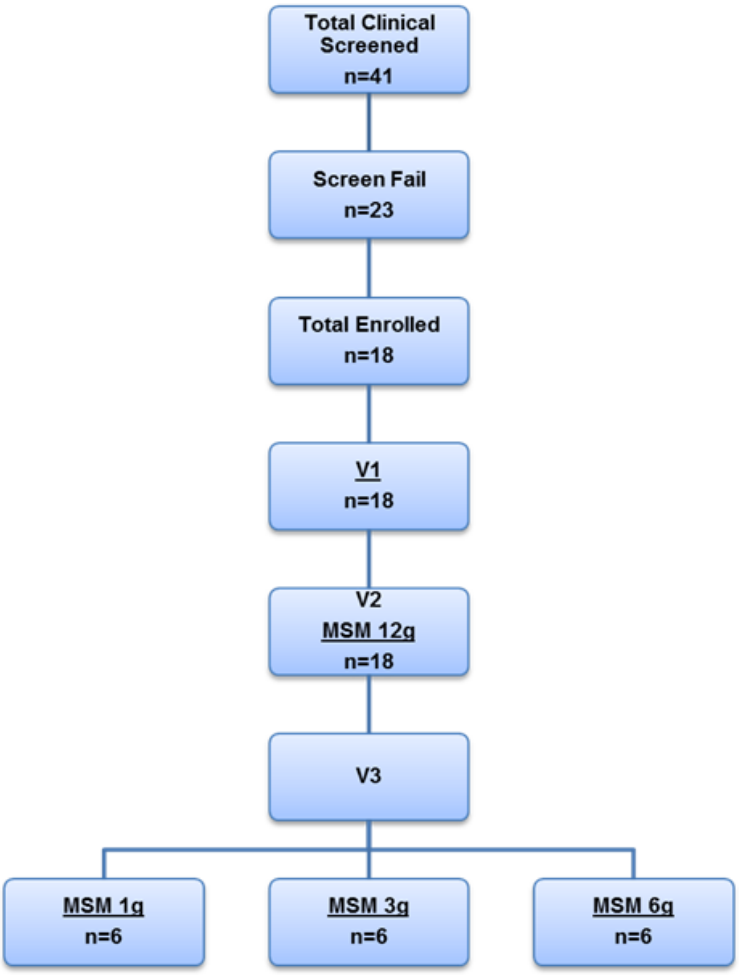


Figure 2. Methylsulfonylmethane (MSM) 12g percent change from screening. Peak nasal inspiratory flow (PNIF) and visual analog scale (VAS) nasal scores show the effects of an acute high methylsulfonylmethane dose (12 g) on patient symptoms. Significance was tested using linear mixed model analysis. *$P \leq .05$; **$P \leq .01$.

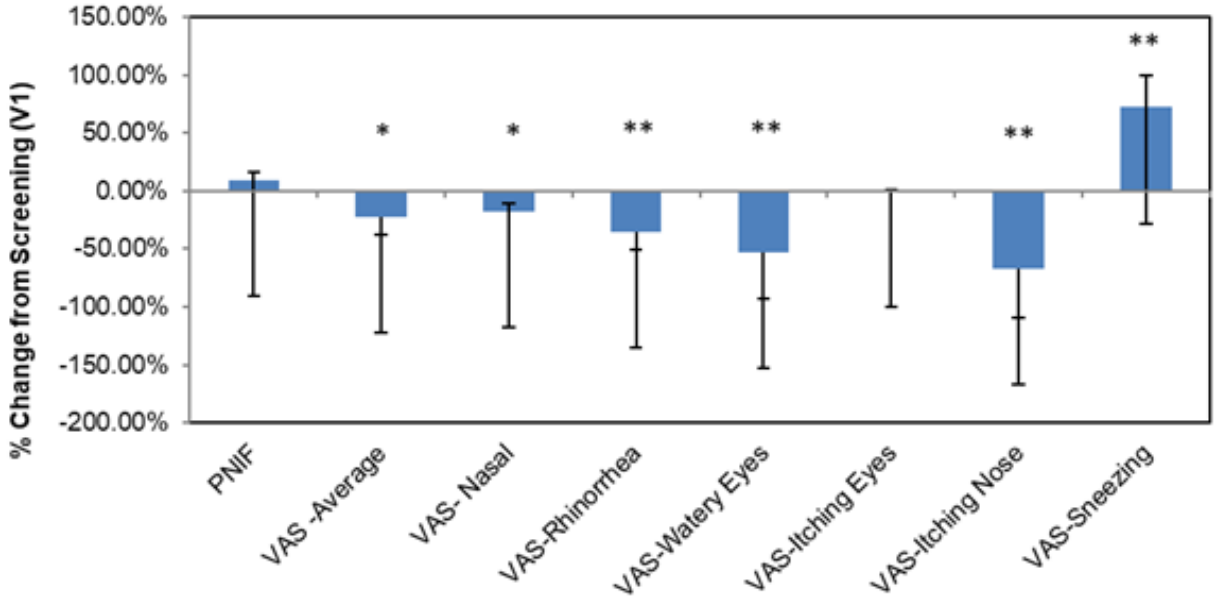
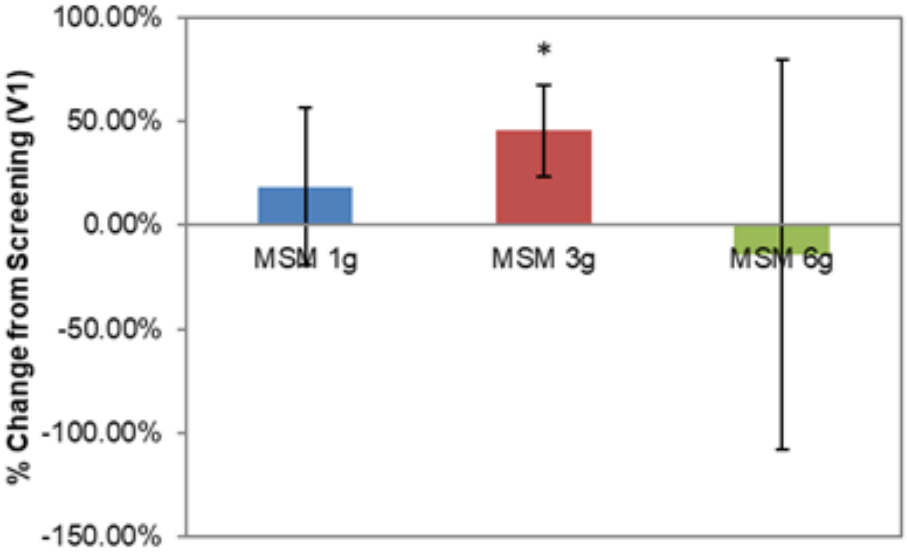


Table 1. Longitudinal (V1-V3) comparison of peak nasal inspiratory flow (PNIF) and visual analog scale (VAS) average nasal symptoms across all participants (n=18).

Measure	Visit (V)			
	1 (screening)	3 (day 14)	Percentage change (V1-V3)	*P* value[a]
Number of tests	126	112	—	—
PNIF (L/min), mean (SD)	91.1 (4.315)	106.89 (4.817)	17.32%	.02
VAS score, mean (SD)	26.47 (22.950)	12.25 (12.00)	–53.72%	.001

[a]Significance was established using the linear mixed model; significant at $P<.05$.

Figure 3. Comparison between 3 subchronic doses of methylsulfonylmethane (MSM; 1 g, 3 g, and 6 g): percentage change in peak nasal inspiratory flow from V1 (screening) to V3 (day 14). Significance was tested using linear mixed model analysis. *$P \leq .05$.



VAS average nasal symptoms decreased significantly at all doses in the longitudinal comparison between visits. Across all participants, the decrease was by 14.22 U (53.72%; *P*=.001; Table 1). VAS scores decreased by 1152 U, 18.71 U, and 12.30 U for MSM 1 g (51.49%; *P*=.03), 3 g (61.65%; *P*=.009), and 6 g (46.11%; *P*=.03), respectively, from screening to V3 (Figure 4). Analysis by symptom revealed statistically significant decreases in all dose conditions for nasal obstruction for MSM 1 g (18.38 U decrease, 41.96%; *P*=.04), 3 g (25.86 U decrease, 49.59%; *P*=.009), and 6 g (17.98 U decrease, 46.62%; *P*=.02) from screening to day 14 (Figure 5). Rhinorrhea symptoms were similarly decreased at all dose levels of MSM: 1 g (16.71 U decrease, 66.86%; *P*=.03), 3 g (18.57 U decrease, 55.71%; *P*=.04), and 6 g (12.95 U decrease, 46.10%; *P*=.04) from screening to V3 (Figure 6).

The response of the remaining SAR symptoms varied between doses. Although symptoms decreased in all dose categories, watery eyes were significantly relieved only at low doses of MSM: 1 g (13.67 U decrease, 72.66%; *P*=.02), 3 g (20.00 U decrease, 79.25%; *P*=.01), and 6 g (8.67 U decrease, 44.39%; *P*=.09) from screening to day 14 (Figure 7). Itching eyes were significantly relieved by high doses but not the lowest dose: 3 g (13.10 U decrease, 65.48%; *P*=.03) and 6 g (12.48 U decrease, 50.38%; *P*=.03) from screening to day 14 (Figure 8). Itching nose symptoms decreased only at high doses of MSM: 3 g (20.00 U decrease, 70.59%; *P*=.02) and 6 g (18.84 U decrease, 52.05%; *P*=.02) from screening to day 14 (Figure 9). Sneezing was affected only by the MSM 3-g dose, with a decrease of 14.76 U (63.92%; *P*=.04) from screening to day 14 (Figure 10).

Figure 4. Comparison between 3 subchronic doses of methylsulfonylmethane (MSM; 1 g, 3 g, and 6 g): percentage change in visual analog scale average nasal symptoms from V1 (screening) to V3 (day 14). Significance was tested using linear mixed model analysis. *$P \leq .05$; **$P \leq .01$.

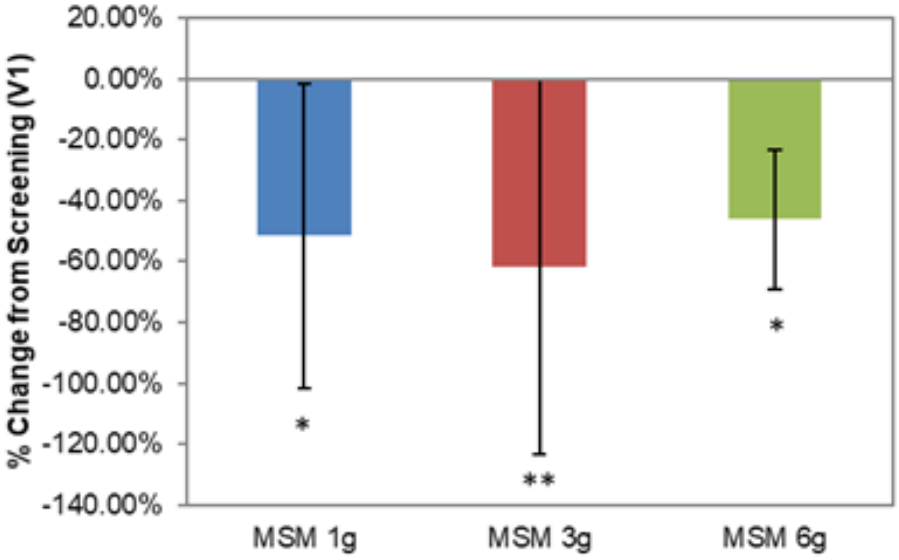


Figure 5. Comparison between 3 subchronic doses of methylsulfonylmethane (MSM; 1 g, 3 g, and 6 g): percentage change in visual analog scale nasal obstruction from V1 (screening) to V3 (day 14). Significance was tested using linear mixed model analysis. *$P \leq .05$; **$P \leq .01$.

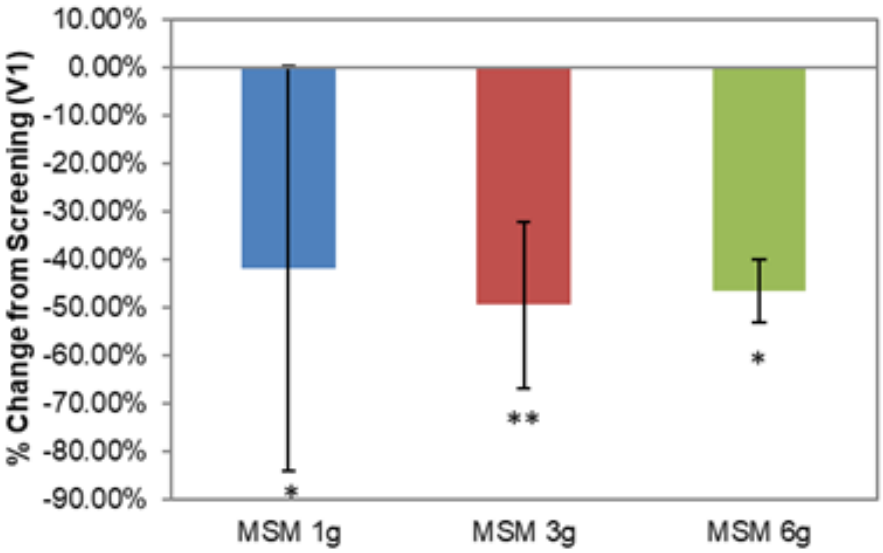


Figure 6. Comparison between 3 subchronic doses of methylsulfonylmethane (MSM; 1 g, 3 g, and 6 g): percentage change in visual analog scale rhinorrhea from V1 (screening) to V3 (day 14). Significance was tested using linear mixed model analysis. *$P \leq .05$.

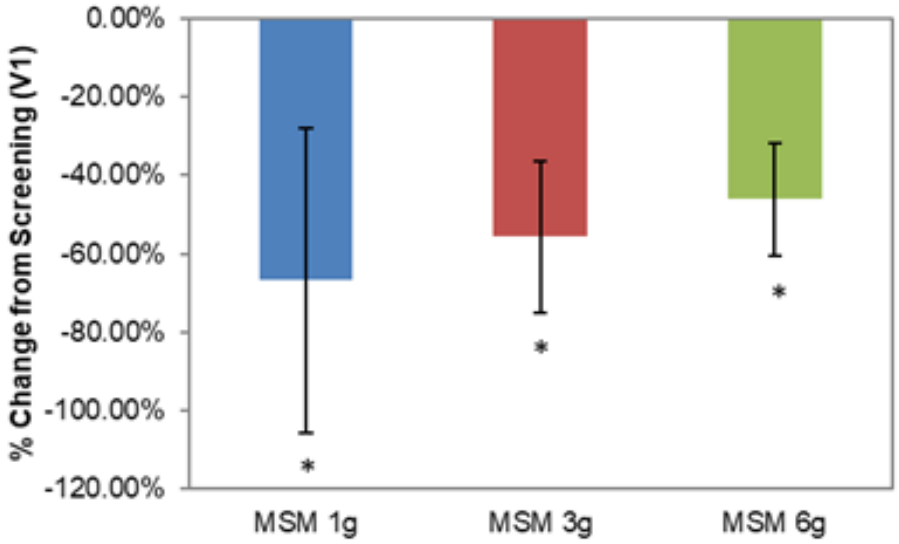


Figure 7. Comparison between 3 subchronic doses of methylsulfonylmethane (MSM; 1 g, 3 g, and 6 g): percentage change in visual analog scale watery eyes from V1 (screening) to V3 (day 14). Significance was tested using linear mixed model analysis. *$P \leq .05$.

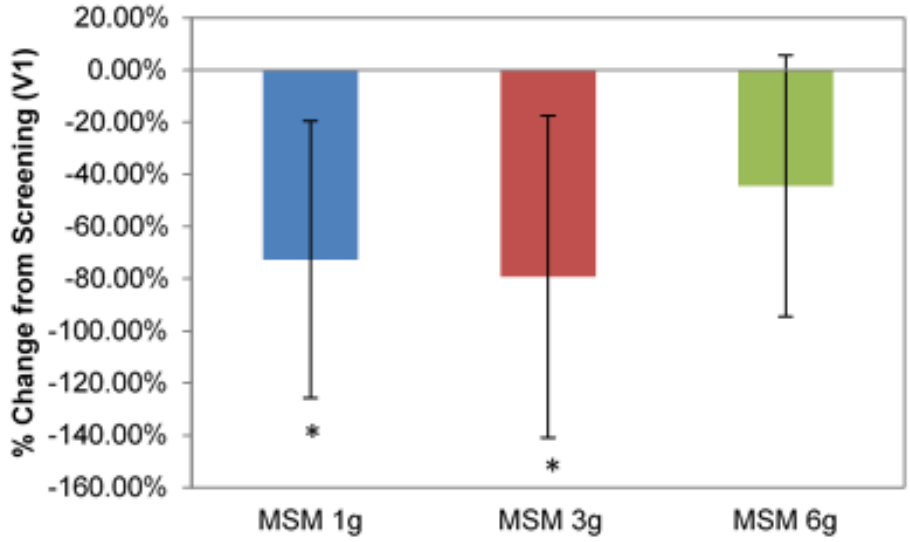


Figure 8. Comparison between 3 subchronic doses of methylsulfonylmethane (MSM; 1 g, 3 g, and 6 g): percentage change in visual analog scale itching eyes from V1 (screening) to V3 (day 14). Significance was tested using linear mixed model analysis. *$P \leq .05$.

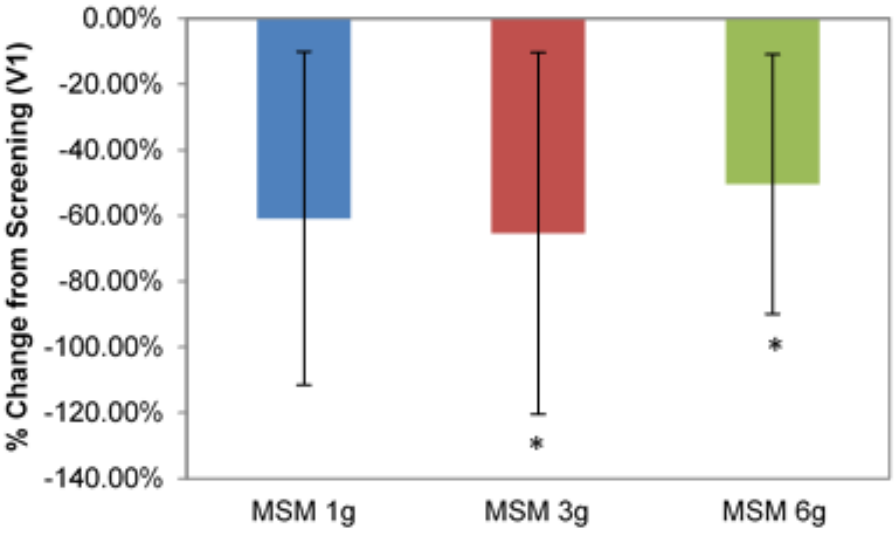


Figure 9. Comparison between 3 subchronic doses of methylsulfonylmethane (MSM; 1 g, 3 g, and 6 g): percentage change in visual analog scale itching nose from V1 (screening) to V3 (day 14). Significance was tested using linear mixed model analysis. *$P \leq .05$.

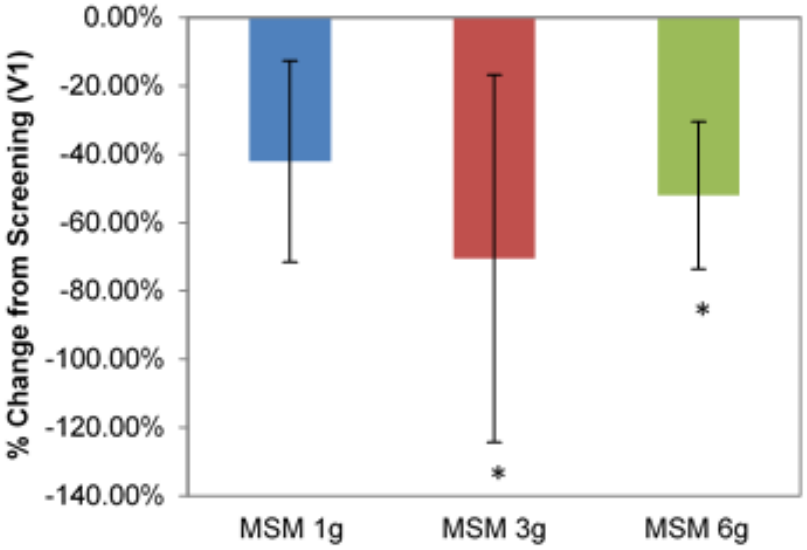
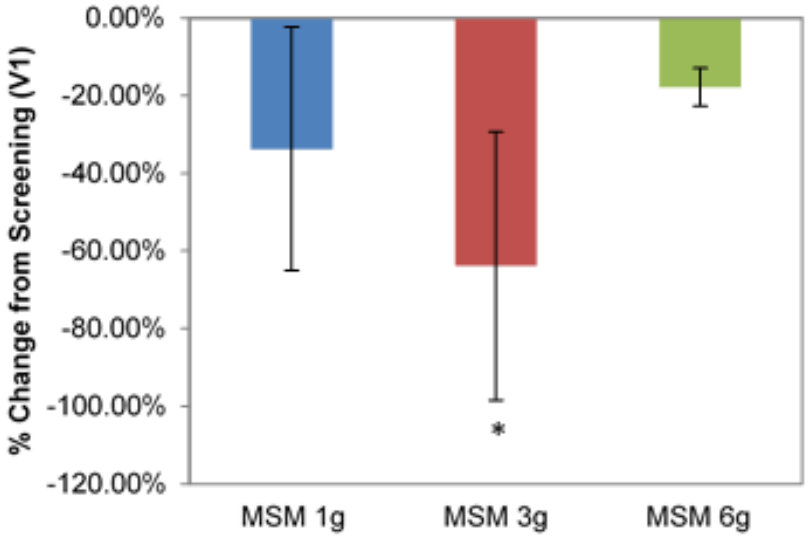


Figure 10. Comparison between 3 subchronic doses of methylsulfonylmethane (MSM; 1 g, 3 g, and 6 g): percentage change in visual analog scale sneezing from V1 (screening) to V3 (day 14). Significance was tested using linear mixed model analysis. *$P \leq .05$.



Discussion

Principal Findings

In this study, we assessed the efficacy of the MSM supplement on attenuating nasal provocation by administering a standardized allergen challenge to healthy participants to induce allergic rhinitis symptoms. Although a limited human study has been performed with MSM during exposure to allergy season [13], to our knowledge, this is the first investigation into the effects of MSM consumption on attenuating a standardized allergen designed to mimic an acute allergy attack.

Normally, the nasal cavity warms, humidifies, and filters air, which is vital for the proper functioning of the upper airway tract. These physiological functions are severely diminished by passageway obstruction due to allergen exposure [17]. Immunoglobulin E (IgE) plays a major role in mediating nasal and upper respiratory allergic response following initial allergen exposure [18]. In a typical person who has developed allergies, mast cells are coated with IgE and become cross-linked on binding of an allergen. On IgE cross-linking, mast cells in the nasal mucosa degranulate and release chemical mediators known to promote well-known symptoms, including nasal itch, nasal obstruction, watery and itchy eyes, and sneezing [19,20]. The release of preformed inflammatory mediators, such as histamine, stimulates the histamine-1 receptor on sensory nerves. Stimulation of these nerves causes vascular dilation and increased plasma leakage, which results in nasal discharge and congestion [21].

This study tested the protective effects of MSM on the allergy attack following exposure to a highly concentrated nasal allergen. The allergen challenge consisted of a standardized mixture of the most common outdoor and indoor allergens that are associated with nasal allergy. We tested several doses of MSM and compared their effect with baseline symptoms, where the allergenic challenge was presented with no MSM study product present. We assessed efficacy by comparing symptoms observed after standardized allergen exposure in the presence of MSM versus symptoms observed at baseline.

An acute high dose of MSM (12 g) was administered at the clinic 30 minutes prior to the allergenic challenge. Although PNIF was not significantly altered, the acute dose of 12 g of MSM resulted in statistically significant decreases in all nasal symptoms of allergic rhinitis, except for itching eyes. This suggests a potential improvement in quality of life via improvement in symptoms experienced by the participants. This result suggests that a 12-g dose of MSM administered just before and during allergen exposure is effective in reducing patient's stuffy nose symptoms, but it did not directly improve nasal breathing.

After the high-dose treatment visit, participants were randomly assigned to a lower daily dose (1 g, 3 g, or 6 g). They took this dose daily for 14 days, and then again 30 minutes prior to the allergenic challenge. The dosage routine was designed to mimic what might be at-home daily use of the MSM. This regimen appeared to be effective at significantly reducing most symptoms of allergic rhinitis. The MSM 3-g dose appeared most effective (consistent), significantly reducing all VAS nasal symptoms scales.

Nasal obstruction resulting from the presence of allergen or infection decreases the maximum flow of air through the nose [22]. Improvement in PNIF generally signifies improvement of nasal airway patency and corresponds to a lesser extent of nasal obstruction, which results in improved nasal breathing [23]. The results of the study suggest that, while an acute high dose (12 g) of MSM significantly improved stuffy nose symptoms of allergic rhinitis following allergen challenge, a long-term daily dose of MSM can significantly improve nasal breathing as measured by PNIF.

Our findings are consistent with those of previous MSM clinical trials. A previous multicentered, open-label trial by Barrager et al [13] assessed the safety and efficacy of orally administered MSM 2.6 g for 30 days. That study assessed environmental SAR by a seasonal allergy symptom questionnaire. Barrager

and colleagues also further monitored immune and inflammatory markers, including plasma histamine, IgE, and C-reactive protein. Upper, lower, and total respiratory symptoms were significantly reduced from baseline as early as day 7, and the improvements were maintained throughout the 30-day study duration. Interestingly, there were no significant changes in levels of IgE or histamine [13], suggesting that MSM may have an alternative mode of action besides direct alteration of IgE or histamine levels. To our knowledge, our study is the first randomized, double-blind clinical trial that presented the efficacy of the MSM product for alleviation of allergic rhinitis symptoms. Here, we showed that MSM of various doses reduced the subjective and objective symptoms of allergic rhinitis in healthy participants overexposed to standardized allergens.

MSM has been shown to have anti-inflammatory properties and is reported to block the formation of inflammasomes [24]. This is in contrast to antihistamine substances that inhibit histamine production [25] and produce soporific side effects. The sulfur component of MSM may also be used by the body to produce antibodies that can combat foreign material, particularly allergens. However, there is still no reliable information to confirm the mechanism of action of MSM [26]. Animal studies have demonstrated that the anti-inflammatory effects of MSM mitigate the abnormal immune reactions that trigger inflammation [27], suggesting that a similar mechanism may be in play. Human studies have demonstrated a positive effect of antioxidant capacity MSM, which may also play a role in the mechanism of action of this ingredient under allergic rhinitis conditions [28]. Most importantly, it has been shown that MSM produces fewer side effects than prescription medications such as antihistamines [13].

The results of this randomized, double-blind study provide preliminary evidence that several dose levels of the MSM product alleviate symptoms of nasal provocation in a population of healthy participants. While the findings are promising and have produced statistically and clinically significant positive results, larger randomized, placebo-controlled trials are warranted to confirm these findings.

Conclusion

MSM supplementation significantly alleviated participants' symptoms in response to a standardized allergenic challenge. An acute dose of MSM 12 g was highly effective at improving the stuffy nose symptoms of allergy as measured by the VAS nasal symptom scales. A dose of 3 g of MSM daily for 14 days not only decreased all scores of the VAS nasal symptoms, but also significantly improved nasal breathing as measured by PNIF. We observed no safety concerns. More research is warranted.

Conflicts of Interest

None declared.

References

1. Small P, Frenkiel S, Becker A, Boisvert P, Bouchard J, Carr S, et al. Rhinitis: a practical and comprehensive approach to assessment and therapy. J Otolaryngol 2007;36(S1):S5-S27. [doi: 10.2310/7070.2006.X002]
2. Ozdoganoglu T, Songu M. The burden of allergic rhinitis and asthma. Ther Adv Respir Dis 2012 Feb;6(1):11-23. [doi: 10.1177/1753465811431975] [Medline: 22179899]
3. Dykewicz MS, Hamilos DL. Rhinitis and sinusitis. J Allergy Clin Immunol 2010 Feb;125(2 Suppl 2):S103-S115. [doi: 10.1016/j.jaci.2009.12.989] [Medline: 20176255]
4. Radulovic S, Calderon MA, Wilson D, Durham S. Sublingual immunotherapy for allergic rhinitis. Cochrane Database Syst Rev 2010 Dec 08(12):CD002893. [doi: 10.1002/14651858.CD002893] [Medline: 21154351]
5. Tran NP, Vickery J, Blaiss MS. Management of rhinitis: allergic and non-allergic. Allergy Asthma Immunol Res 2011 Jul;3(3):148-156 [FREE Full text] [doi: 10.4168/aair.2011.3.3.148] [Medline: 21738880]
6. Small P, Kim H. Allergic rhinitis. Allergy Asthma Clin Immunol 2011 Nov 10;7 Suppl 1:S3 [FREE Full text] [doi: 10.1186/1710-1492-7-S1-S3] [Medline: 22166009]
7. Nathan RA. The burden of allergic rhinitis. Allergy Asthma Proc 2007;28(1):3-9. [Medline: 17390749]
8. Bousquet J, Schünemann HJ, Samolinski B, Demoly P, Baena-Cagnani CE, Bachert C, World Health Organization Collaborating Center for Asthma and Rhinitis. Allergic Rhinitis and its Impact on Asthma (ARIA): achievements in 10 years and future needs. J Allergy Clin Immunol 2012 Nov;130(5):1049-1062. [doi: 10.1016/j.jaci.2012.07.053] [Medline: 23040884]
9. Cruz AA, Popov T, Pawankar R, Annesi-Maesano I, Fokkens W, Kemp J, ARIA Initiative Scientific Committee. Common characteristics of upper and lower airways in rhinitis and asthma: ARIA update, in collaboration with GA(2)LEN. Allergy 2007;62 Suppl 84:1-41. [doi: 10.1111/j.1398-9995.2007.01551.x] [Medline: 17924930]
10. Braido F, Arcadipane F, Marugo F, Hayashi M, Pawankar R. Allergic rhinitis: current options and future perspectives. Curr Opin Allergy Clin Immunol 2014 Apr;14(2):168-176. [doi: 10.1097/ACI.0000000000000043] [Medline: 24535140]
11. Natural Medicines Comprehensive Database. Stockton, CA: Therapeutic Research Faculty; 2016. MSM (methylsulfonylmethane) URL: http://naturaldatabase.therapeuticresearch.com/nd/PrintVersion.aspx?id=522&AspxAutoDetectCookieSupport=1 [accessed 2018-10-04] [WebCite Cache ID 72vN9mxDD]
12. Horváth K, Noker PE, Somfai-Relle S, Glávits R, Financsek I, Schauss AG. Toxicity of methylsulfonylmethane in rats. Food Chem Toxicol 2002 Oct;40(10):1459-1462. [Medline: 12387309]

13. Barrager E, Veltmann JR, Schauss AG, Schiller RN. A multicentered, open-label trial on the safety and efficacy of methylsulfonylmethane in the treatment of seasonal allergic rhinitis. J Altern Complement Med 2002 Apr;8(2):167-173. [doi: 10.1089/107555302317371451] [Medline: 12006124]
14. Gaby AR. Methylsulfonylmethane as a treatment for seasonal allergic rhinitis: more data needed on pollen counts and questionnaire. J Altern Complement Med 2002 Jun;8(3):229. [doi: 10.1089/10755530260127925] [Medline: 12165181]
15. Magnuson BA, Appleton J, Ryan B, Matulka RA. Oral developmental toxicity study of methylsulfonylmethane in rats. Food Chem Toxicol 2007 Jun;45(6):977-984. [doi: 10.1016/j.fct.2006.12.003] [Medline: 17258373]
16. Scadding GW, Calderon MA, Bellido V, Koed GK, Nielsen N, Lund K, et al. Optimisation of grass pollen nasal allergen challenge for assessment of clinical and immunological outcomes. J Immunol Methods 2012 Oct 31;384(1-2):25-32. [doi: 10.1016/j.jim.2012.06.013] [Medline: 22759401]
17. Lin SJ, Meyers AD, Danahey DG. Medscape. New York, NY: WebMD LLC; 2015 May 14. Nasal aerodynamics URL: https://emedicine.medscape.com/article/874822-overview [accessed 2018-10-04] [WebCite Cache ID 72vNRaDjn]
18. Berger WE. Treatment of allergic rhinitis and other immunoglobulin E-mediated diseases with anti-immunoglobulin E antibody. Allergy Asthma Proc 2006;27(2 Suppl 1):S29-S32. [Medline: 16722329]
19. Verbruggen K, Van Cauwenberge P, Bachert C. Anti-IgE for the treatment of allergic rhinitis--and eventually nasal polyps? Int Arch Allergy Immunol 2009;148(2):87-98 [FREE Full text] [doi: 10.1159/000155739] [Medline: 18799888]
20. Pawankar R, Bunnag C, Chen Y, Fukuda T, Kim Y, Le LTT, et al. Allergic rhinitis and its impact on asthma update (ARIA 2008)--western and Asian-Pacific perspective. Asian Pac J Allergy Immunol 2009 Dec;27(4):237-243 [FREE Full text] [Medline: 20232579]
21. Glacy J, Putnam K, Godfrey S, Falzon L, Mauger B, Samson D, et al. Treatments for seasonal allergic rhinitis. Report no. 13-EHC098-EF. AHRQ Comparative Effectiveness Reviews. Rockville, MD: Agency for Healthcare Research and Quality; Jul 2013.
22. Pertuze J, Watson A, Pride NB. Maximum airflow through the nose in humans. J Appl Physiol (1985) 1991 Mar;70(3):1369-1376. [doi: 10.1152/jappl.1991.70.3.1369] [Medline: 2033006]
23. Papachristou A, Bourli E, Aivazi D, Futzila E, Papastavrou T, Konstandinidis T, et al. Normal peak nasal inspiratory flow rate values in Greek children and adolescents. Hippokratia 2008 Apr;12(2):94-97 [FREE Full text] [Medline: 18923655]
24. Ahn H, Kim J, Jeung E, Lee G. Dimethyl sulfoxide inhibits NLRP3 inflammasome activation. Immunobiology 2014 Apr;219(4):315-322. [doi: 10.1016/j.imbio.2013.11.003] [Medline: 24380723]
25. Ozdemir PG, Karadag AS, Selvi Y, Boysan M, Bilgili SG, Aydin A, et al. Assessment of the effects of antihistamine drugs on mood, sleep quality, sleepiness, and dream anxiety. Int J Psychiatry Clin Pract 2014 Aug;18(3):161-168. [doi: 10.3109/13651501.2014.907919] [Medline: 24673474]
26. Yacobucci KL. Natural Medicines. J Med Libr Assoc 2016 Oct;104(4):371-374. [doi: 10.3163/1536-5050.104.4.029]
27. Hasegawa T, Ueno S, Kumamoto S. Anti-inflammatory effect of methylsulfonylmethane (MSM) in mice. Jpn Pharm Ther 2005 Jan;33(12):1217-1223.
28. Nakhostin-Roohi B, Niknam Z, Vaezi N, Mohammadi S, Bohlooli S. Effect of single dose administration of methylsulfonylmethane on oxidative stress following acute exhaustive exercise. Iran J Pharm Res 2013;12(4):845-853 [FREE Full text] [Medline: 24523764]

Abbreviations

IgE: immunoglobulin E
MSM: methylsulfonylmethane
PNIF: peak nasal inspiratory flow
SAR: seasonal allergic rhinitis
VAS: visual analog scale

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Protocol

Lung Function in Users of a Smoke-Free Electronic Device With HeatSticks (iQOS) Versus Smokers of Conventional Cigarettes: Protocol for a Longitudinal Cohort Observational Study

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Abstract

Background: Chronic obstructive pulmonary disease (COPD) is a global public health problem. It is the third-leading cause of death in the world, the fourth leading cause of death in Kazakhstan, and is strongly associated with smoking. Smoking cessation reduces the severity of respiratory symptoms and COPD exacerbations. Heated tobacco products, such as HeatSticks heated by the iQOS device, a smoke-free electronic device, may serve as less risky alternatives to conventional combustible cigarettes.

Objective: The purpose of this study is to evaluate frequency of exacerbations, respiratory symptoms, physical exercise intolerance, and abnormal lung functions, as well as other parameters and comorbidities among men and women aged 40-59 residing in Almaty, Kazakhstan, who use iQOS with HeatSticks compared to smokers of conventional cigarettes.

Methods: This is a 5-year single-center cohort observational study. It includes two cohorts of participants consisting of men and women aged 40-59 residing in the city of Almaty, Kazakhstan: (1) smokers of combustible cigarettes (control group) and (2) users of iQOS with HeatSticks (exposure group). The study has baseline and periodic (ie, annual) comprehensive clinical assessments, as well as continuous COPD case-finding activities and registration of acute respiratory exacerbations over the course of the 5-year observation period. Study measures include spirometry, chest computed tomography, electrocardiography, physical exams, laboratory testing of serum for biomarkers of inflammation and metabolic syndrome, anthropometry, and the 6-minute walk test. Information about COPD symptoms will be collected using the COPD Assessment Test.

Results: Participant recruitment began December 2017, and enrollment is expected to last until late summer 2018.

Conclusions: This is the first cohort observational study in Kazakhstan to assess differences in lung function between users of the heated tobacco product, iQOS with HeatSticks, and smokers of conventional combustible cigarettes. The study results will add to knowledge on whether switching from combustible cigarettes to iQOS with HeatSticks affects respiratory symptoms and diseases, including the development and progression of COPD.

Trial Registration: ClinicalTrials.gov NCT03383601; https://clinicaltrials.gov/ct2/show/NCT03383601 (Archived by WebCite at http://www.webcitation.org/72BYoAKxa)

International Registered Report Identifier (IRRID): PRR1-10.2196/10006

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KEYWORDS

COPD; iQOS with HeatSticks; exacerbations; respiratory symptoms; CT scan; COPD assessment test

Introduction

Chronic obstructive pulmonary disease (COPD), the fourth leading cause of death in Kazakhstan, is a global public health problem. It is the third leading cause of death globally, accounting for 3.2 million deaths worldwide in 2015 [1]. In Kazakhstan, an expected 1.4 million people may have COPD based on estimations from neighboring countries [2]. COPD negatively affects the quality of life and is a major health care burden [3]. It is the third leading cause of hospital readmission within 30 days [4]. Cigarette smoke is the most common risk factor for COPD [5]. COPD is traditionally defined by airflow obstruction and includes emphysema, gas trapping, and chronic bronchitis [6]. Systemic effects (eg, on heart and muscles) and associated comorbidities (eg, heart failure, metabolic disorders, sleep apnea syndrome, and depression) may complicate the course of disease, posing challenges in the management of COPD [7-9].

Recently, we conducted a cross-sectional study of COPD among men and women aged 40-59 who currently smoke cigarettes, do not smoke, and stopped smoking 1-5 years ago [10]. We demonstrated that based on the COPD Assessment Test (CAT), respiratory symptoms are common in current smokers who have spirometric values that are generally considered to be within the normal range. We identified a relatively low percentage of participants with obstructed respiratory functions on spirometry. It was higher among current smokers (5.5%) compared to former and nonsmokers (3% among both groups). We found that 42% of current smokers had COPD symptoms based on a CAT score of ≥10—a prevalence of symptoms that was far greater than that among former smokers and controls who never smoked (17% and 12.5%, respectively). In addition, smoking cessation significantly reduced functional exercise incapacity, that is, inability to walk 450 meters within 6 minutes in the 6-Minute Walk Test (6MWT; 11% among ex-smokers compared to 16.7 % among current smokers).

Our findings agree with and extend previously published data, including studies that document exacerbation-like events in smokers without airway obstruction [11,12]. Many current or former smokers, despite normal spirometry values, have clinical symptoms and findings that are consistent with a chronic lower respiratory disease similar to COPD. In addition, these symptomatic current or former smokers with preserved pulmonary function had a higher risk of respiratory exacerbations or abnormalities on a chest computed tomography (CT) scan or shorter 6-minute walk distances than asymptomatic current or former smokers with preserved pulmonary function. The CAT is a clinically useful tool that can identify smokers at risk for exacerbations [11].

Smoking cessation reduces the severity of respiratory symptoms and slows the mean rate of lung function decline but does not eliminate the risk of progressive lung disease [13]. In our cross-sectional study, we demonstrated negative association between smoking cessation and activity limitations and positive association between smoking of combustible cigarettes and evidence of airway disease. As compared to never-smokers, current and former smokers had elevations in all components of the CAT score: cough, phlegm, chest tightness, breathlessness going up hills/stairs, activity limitation at home, confidence leaving home, sleep, and energy. At the same time, those parameters were lower among those who stopped smoking 1-5 years ago compared to those who continued smoking.

Alternative tobacco products to conventional cigarettes have come on the global market with claims of being “modified risk” tobacco products. These electronic devices heat the tobacco instead of burning it to supposedly deliver fewer toxins than cigarette smoke. These heated tobacco products include HeatSticks, a specially designed heated tobacco unit that contains tobacco heated up to 350˚C by the iQOS device. The product was developed by Philip Morris International, Inc, which claims that the vapor from HeatSticks heated by the iQOS device contains 90%-95% less harmful and potentially harmful compounds and is 90%-95% less toxic than the smoke of a reference combustible cigarette. Results of a 3-month reduced-exposure study in Japan showed that a reduction in 15 biomarkers of exposure to 15 harmful and potentially harmful compounds for the smokers who switched to a heated tobacco product for the duration of the study approaches the reduction in the same biomarkers for smokers who quit for the duration of the study [14]. Polosa et al showed that electronic cigarettes (ie, a battery-operated device that emits doses of vaporized nicotine) might improve COPD outcomes, including subjective respiratory outcomes as well as annual exacerbation rate [15]. We hypothesize that participants who use iQOS with HeatSticks will have less prevalent presence of respiratory symptoms, have better functional exercise capacity, and experience fewer exacerbations compared to those who smoke combustible cigarettes.

Methods

Study Design

The goal of this study is to evaluate whether the presence of respiratory symptoms, functional exercise incapacity, and COPD exacerbation rate across time are the same between the exposure group (users of iQOS with HeatSticks) and the control group (smokers of combustible cigarettes) through hypothesis testing.

In addition to this confirmatory goal, we would like to explore trends in spirometry results, chest CT scan results, prevalence of impaired quality of life, metabolic syndrome, abnormalities found by electrocardiography (ECG), physical exams, and serum lab tests among those who use iQOS with HeatSticks and those who currently smoke combustible cigarettes.

Exacerbation history will be collected prospectively (every 3 months) with the use of the adapted version of our proprietary SymptoMaster (Web, iOS, and Android) [16], and Medintel (Web) apps [17]. Symptoms history will be analyzed by clinical investigators. Should there be symptoms identified that are relevant to COPD, clinical investigators will approach health care organizations (serving participants in primary health care catchment area) to obtain ambulatory records of the use of antibiotics and/or systemic glucocorticoids or a health care utilization event.

Our primary confirmatory outcome variables are (1) presence of respiratory symptoms defined by CAT≥10, (2) functional exercise incapacity, and (3) exacerbation rate. The main exposure variable is smoking status (users of combustible cigarettes and users of iQOS with HeatSticks). The study groups are defined as:

1. Individuals (men and women) aged 40-59 years (inclusive) with a minimum of 10 pack-year smoking history who switched to and predominantly use the heated tobacco product iQOS with HeatSticks (exposure group). Predominant use of iQOS with HeatSticks is defined as >70% use.
2. Individuals (men and women) aged 40-59 years (inclusive) who are currently smoking combustible cigarettes with a minimum of 10 pack-year smoking history (control group)

Pack-years will be calculated by taking the average number of cigarettes smoked per day divided by 20 and multiplied by the number of years smoked.

The Global Initiative for Chronic Obstructive Lung Disease (GOLD) definition describes COPD exacerbations as an acute worsening of respiratory symptoms that results in additional therapy [18]. They are classified as mild (ie, treated with short-acting bronchodilators only), moderate (ie, treated with short-acting bronchodilators and/or oral corticosteroids), or severe (ie, patient requires hospitalization or emergency room visit). Severe exacerbations may also be associated with acute respiratory failure. Once signs of exacerbations are identified, special efforts will be made by the Kazakhstan Academy of Preventive Medicine (KAPM) clinical investigators, coordinators, and the principal investigator to establish their significance (ie, mild, moderate, or severe), and relevance to COPD.

Inclusion and Exclusion Criteria

The study's inclusion criteria comprise the following: male or female, aged 40-59 years, smoking history ≥10 pack-years (for all groups), and ability to follow study procedures. The exclusion criteria consist of the following:

- pregnant women
- legally incapable individuals
- patients with history of chronic infectious and noninfectious lung disease except asthma (eg, pulmonary fibrosis, bronchiectasis, cystic fibrosis, tuberculosis) diagnosed prior to or during the first visit to the KAPM COPD Center
- previous surgical excision of at least one lung lobe (or having undergone a lung volume reduction procedure)
- active cancer of any localization under treatment
- suspected cancer of any localization
- metallic objects in the chest
- recent eye surgery (within 6 months prior to the visit)
- episode(s) of myocardial infarction within 6 months prior to the visit or another form of acute or chronic coronary heart disease, history of heart rhythm abnormality with episode of arrhythmia within 6 months prior to the visit or long lasting that requires continuous drug therapy
- acute episode of cerebrovascular ischemic attack within 12 months prior to the visit
- chest or abdominal surgery performed within 6 months prior to the visit
- contraindications to salbutamol or refusal to inhale salbutamol
- chest radiation therapy within 12 months prior to the visit
- radiology diagnostic procedures of chest within 6 months prior to the visit
- recent (6 weeks before visit) respiratory tract infection (colds, flus), fever of any etiology with increasing temperature >37°C at the time of the visit and 2 weeks prior to the visit
- significant history of alcohol abuse or consumption of more than recommended units of alcohol per week (28 units male and 21 units female)
- positive screening test for HIV antibodies or positive screening for TB, if available at the time of first visit
- elevated blood pressure (systolic) ≥160 mmHg at the time of visit
- employees of Philip Morris International and first-degree relatives who are employees of Philip Morris International

Sample Size Calculation

Based on the results of the cross-sectional study, we demonstrated that smoking cessation alleviates activity limitations and airway disease caused by smoking of combustible cigarettes. This is evidenced by the prevalence of a CAT score of ≥10 among those who stopped smoking during the past 1-5 years at 17% compared to 42.8% among current smokers, and reduced inability to walk 450 meters within 6 minutes on 6MWT (11% compared to 16.7% among current smokers).

We hypothesize that switching from combustible cigarettes to iQOS with HeatSticks may reduce the risk of respiratory exacerbation and other COPD manifestations, somewhat similar to the effects of smoking cessation observed in the cross-sectional study.

In the cross-sectional study, duration of smoking abstinence in the second (ex-smoker) study group varied from 1-5 years. This is comparable with the length of the cohort study (5 years) that we propose. Therefore, we can use estimates of the outcome variables derived from the cross-sectional study to calculate required sample sizes that can identify statistically significant differences.

We suggest implementing a matched-pair cohort study design where a pair contains one iQOS with HeatSticks user and two conventional cigarette users matched by gender, age, education, and baseline exposure level (number of pack-year). By selecting this study design, we take into account the limited number of iQOS users from which the first (exposure) cohort is planned to be recruited.

To perform sample size calculation, we will assume that the associations we observed in the cross-sectional study between primary confirmatory outcomes and the smoking status (ex-smokers vs current combustible cigarette smokers) will be the same for iQOS users as compared to combustible cigarette smokers at the final visit after 5 years:

1. At the final visit, the odds ratio of association between the exposure and CAT score of ≥10 will equal 0.27 and a CAT ≥10 prevalence will be 42.8% in the control group.
2. At the final visit, odds ratio of association between the exposure and inability to walk 450 meters on the 6MWT will equal 0.62 and a 6MWT <450 meters prevalence will be 16.7% in the control group.
3. At the final visit, rate ratio of association between the exposure and exacerbations will equal 0.5 and annual exacerbation rate will be 0.1 in the control group based on conservative estimations from Woodruff et al [10]. We also assume that these associations will increase steadily from 1 to the above-indicated values. Sample size calculations for three primary confirmatory outcomes have been performed by simulations and the frequentist method based on the power and level of significance of a test. For each primary confirmatory outcome, we have generated data from the distribution assumed for the combustible cigarette smokers and the distribution for the iQOS with HeatSticks smokers (based on our assumptions of how their changes in respiratory symptoms prevalence, proportions of participants who walk less than 450 meters, and annual exacerbation rate might be different if switched from combustible cigarettes to iQOS with HeatSticks). We have used R [19] for simulations (1000 simulations per each primary confirmatory outcome variable) and fitting a generalized linear mixed-effects model (GLMM) on simulated data (function “glmer” in the package “lme4”). For sample size calculation, we have used a power value of 80%, two-sided significance level (alpha) 1.7% that accounts for multiple hypotheses testing, and 1:2 ratio for sample sizes of the experimental and control cohorts.

Then, we have adjusted the sample size for anticipated proportion of dropouts (taking into consideration a 10% annual dropout rate and the fact that already collected data relating to any participant who stops the study early will be analyzed). Sample size calculations are presented in Table 1.

As a result, the sample size of 1041 respondents is enough to detect significant differences in three primary confirmatory outcomes with at least 80% power. However, in addition to dropouts, we need to consider that participants may switch from one tobacco product to another, quit smoking, use several tobacco products at the same time, and the fact that a nonrandomized observational study needs to be adjusted for confounding factors. Even if most of these events do not cause subjects’ withdrawal, they lead to a decreased number of participants for further statistical analysis. Therefore, we need more participants to solve this issue. We propose recruiting 400 participants in the exposure (iQOS) cohort and 800 participants in the control (combustible cigarettes) cohort. The following sample size should allow us to achieve the confirmatory goal of the study: (1) iQOS with HeatSticks smokers (exposure group, N=400) and (2) conventional cigarette smokers (control group, N=800; total sample size=1200).

Study Procedures

Recruitment

We will select 800 current smokers and 400 users of iQOS with HeatStick based on the inclusion criteria. The recruitment strategy for smokers of combustible cigarettes and participants who use iQOS with HeatStick includes word-of-mouth communication to friends and spouses of individuals who participated in the cross-sectional study, advertisements, social media engagement (ie, Facebook, Instagram, WhatsApp chats), and outreach to community groups. In addition, we will recruit users of iQOS with HeatSticks at iQOS stores in Almaty, Kazakhstan.

To achieve comparability of comparison groups at baseline, the matched-pair cohort study design will be implemented, where a pair contains one iQOS with HeatSticks user and two conventional cigarette users. The following variables will be utilized for matching: gender, age (±3 years), education (as a proxy for socioeconomic status), and number of pack-year (±5 pack-years) as the baseline exposure level (number of pack-year).

Once potential participants who meet inclusion criteria are identified, they will undergo further medical assessment at the KAPM COPD Center to test for exclusion criteria and to start baseline comprehensive assessment.

The study will include (1) baseline comprehensive assessment at outset of the study during the enrollment period, which is expected to last for about 6 months (4^{th}quarter of 2017 to 1^{st}-3^{rd}quarters of 2018); (2) annual comprehensive assessments at 2^{nd}-4^{th}quarters of 2018-2022; (3) periodic prospective case finding and exacerbation history assessment on quarterly basis (every 3 months), semiannual, and annual basis; and (4) continuous COPD case-finding activities based on patient self-assessment and professional clinical assessment during periodic visits to KAPM dedicated primary care unit.

Table 1. Sample size calculations.

Primary confirmatory variable	Estimated value of outcome variable in exposure group	Estimated value of outcome variable in control group	Sample size exposed/ nonexposed	Adjusting sample size for anticipated dropouts
Symptomatic smokers defined by CAT ≥10	17%	42.8%	23/46	31/62
6MWT <450 m	11%	16.7%	260/520	347/694
Annual exacerbation rate	0.05	0.1	255/510	340/680

Baseline comprehensive assessment at outset of the study (4th quarter of 2017) and annual assessments (4th quarters of 2018-2020) will include the following:

- COPD assessment test
- 6MWT
- Short form-12 (SF-12) Quality of Life questionnaire
- spirometry (forced expiratory volume in 1 second [FEV1]/ forced vital capacity [FVC] bronchodilation test
- ECG
- body mass index
- CT scan of the chest
- COPD-related conditions and comorbidities identified by using our proprietary mHealth technologies: SymptoMaster and Medintel
- Stanford 25 comprehensive clinical assessment to identify clinical signs of COPD and comorbidities [20,21]
- laboratory testing for complete blood count (CBC), blood cholesterol level, high-density lipoproteins (HDL), low-density lipoproteins (LDL), triglycerides, C-reactive protein, fibrinogen, glucose
- biomarker testing for sRAGE, ICAM1, CCL20, and probably other biomarkers (to be determined based on validity and feasibility of each test)

One important feature for an efficient support tool is the ability to detect any symptom that can lead to a potential new COPD case finding and exacerbation. We will administer the CAT to identify COPD symptoms and quantify them during a stable phase of disease (>6 weeks after any exacerbation). The CAT is a validated 8-question health-status instrument with scores ranging from 0-40, with higher scores indicating greater severity of symptoms. GOLD uses a CAT score ≥10 as a threshold for more severe symptoms in consideration of treatment regimens [7].

In the context of COPD, an exacerbation is defined as a worsening of a patient's symptoms from their usual stable state. The symptoms can then be analyzed by physicians using SmartHealth algorithms to detect the potential risk of an exacerbation. We will obtain an exacerbation history prospectively (ie, every 3 months) with the use of a structured questionnaire. Exacerbations will be defined on the basis of the use of antibiotic agents, systemic glucocorticoids, or a combination of both or a health care utilization event (ie, office visit, hospital admission, or emergency department visit for a respiratory flare-up). Severe exacerbations will be defined as interactions that lead to hospitalization or an emergency department visit. Exacerbations will be managed by the participants' primary care physicians in close communication with study participants, their families, and health care organizations in their service areas of Almaty.

The inclusion of secondary endpoints (eg, lab tests, ECG, and clinical assessment) allows for generating further hypotheses for different effects of switching to iQOS. Schedule of enrollment, data collection, and assessment are shown in Tables 2 and 3.

All study participants in both cohorts will receive smoking cessation advice according to clinical standards endorsed by Kazakhstan's Health Ministry, offered throughout the study at each visit. The participants will also be offered formal professional assistance on smoking cessation. At the screening visit, in conjunction with signing the informed consent form, clinical investigators will give smoking cessation advice. It will be free of charge (paid by the sponsor) and is set out in the informed consent form. It will include psychological support to eliminate nicotine dependency, and participants will be referred to a specialist commercial medical organization in Almaty. We anticipate that some smokers and iQOS users will quit and that some smokers will switch to a reduced-risk product during the study. Quitting and switching will not be considered as reasons for early withdrawal and will be accounted for in sample size calculations.

Spirometry

Spirometry data will be collected using the combined spirometry system, BTL-08 SPIRO. All spirometry studies will be reviewed centrally to ensure quality control. Bronchodilator responsiveness will be considered positive if the subject had a ≥12% change in FEV1 or FVC above pre-bronchodilator measurements [22].

Each spirometer to be used in this study will be tested and continuously standardized with a 3.0-liter syringe. Each clinical coordinator will be certified after spirometry training. Quality assessments will be made on each study.

Smokers will be categorized for analysis using the GOLD staging system according to the results on spirometry, which will be performed before and after two inhalations of salbutamol, 0.1 µg per inhalation. Among the criteria needed to make a diagnosis of COPD are deficits in the rate at which one can forcefully exhale. Most experts consider a low ratio (<0.70) of the FEV1 to the FVC after bronchodilator use to be a key diagnostic criterion [7].

Once the diagnosis of COPD has been established, the GOLD nomenclature grades severity according to the degree to which the measured FEV1 is lower than the patient's predicted value [7]:

- GOLD stage 1 (mild disease): FEV1 ≥80% of the predicted value
- GOLD stage 2 (moderate disease): FEV1 ≥50% and <80% of the predicted value
- GOLD stage 3 (severe disease): FEV1 ≥30% and <50% of the predicted value
- GOLD stage 4 (very severe disease): FEV1 <30% of the predicted value

Assessment Test for Chronic Obstructive Pulmonary Disease

The CAT is a validated, short (8-item) questionnaire to be completed by study participants. Despite the fact that CAT is designed for patients with COPD, it can be used to measure respiratory symptoms among all participants including those who have preserved pulmonary function [10]. The CAT has a scoring range of 0-40, with the cut-off point equaling 10.

Table 2. Schedule of participants enrollment and baseline assessment, 2017-2018.

Test	Screening[a]	Baseline visit[b]
Informed consent process	X	
Review inclusion/exclusion criteria to determine study eligibility, including smoking status and iQOS use	X	
Review medical history	X	
Provide study requirements handout (explain study/visit requirements)	X	
Pregnancy test	X	X
Stanford 25 comprehensive clinical assessment		X
Spirometry (FVC[c], FEV[d], FEV1[e], FEV1/ FVC, FEF[f] 25-75, MEF[g]), bronchodilation test using salbutamol		X
CAT[h]		X
6MWT[i]		X
Short form-12 Quality of Life questionnaire		X
ECG[j]		X
Body mass index		X
Smoking status and exposures		X
Comprehensive physical assessment Stanford 25		X
Previous COPD[k] exacerbations based on use of inhaled steroids, antibiotics, inhaled bronchodilators, steroids		X
Previous COPD exacerbations based on health care visits (office visits, admissions to emergency department or hospital)		X
Previous COPD severe exacerbations based on emergency department admission or hospitalizations		X
Laboratory testing for blood cholesterol level, CBC[l] (25 parameters); HDL[m], LDL[n], triglycerides, C-reactive protein, fibrinogen, glucose, glycosylated hemoglobin		X
Biomarker testing for sRAGE[o], ICAM1[p], and CCL20[q]		X
Lung computer tomography		X

[a]Months –3 to 3.

[b]Months 0 to 3.

[c]FVC: forced vital capacity.

[d]FEV: forced expiratory volume.

[e]FEV1: forced expiratory volume in 1 second.

[f]FEF: forced expiratory flow.

[g]MEF: maximum expiratory flow.

[h]CAT: COPD Assessment Test.

[i]6MWT: 6-Minute Walk Test.

[j]ECG: electrocardiogram.

[k]COPD: chronic obstructive pulmonary disease.

[l]CBC: complete blood count.

[m]HDL: high-density lipoproteins.

[n]LDL: low-density lipoproteins.

[o]sRAGE:advanced glycosylation end-product receptor.

[p]ICAM1: intercellular adhesion molecule 1.

[q]CCL20: macrophage inhibitory protein 3a.

Table 3. Schedule of participants visits for data collection and monitoring, years 1-5.

Test	Year 1			Year 2				Year 3				Year 4				Year 5			
	Q[a]2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
Stanford 25 comprehensive clinical assessment				X				X				X				X			
Spirometry (FVC[b], FEV[c], FEV1[d], FEV1/ FVC, FEF[e] 25-75, MEF[f]), bronchodilation test using salbutamol				X				X				X				X			
CAT[g]				X				X				X				X			
6MWT[g]				X				X				X				X			
Short form-12 Quality of Life questionnaire				X				X				X				X			
ECG[g]				X				X				X				X			
Body mass index				X				X				X				X			
Smoking status, exposures				X				X				X				X			
Laboratory testing for blood cholesterol level, CBC[j] (25 parameters); HDL[k], LDL[l], triglycerides, C-reactive protein, fibrinogen, glucose, glycosylated hemoglobin				X				X				X				X			
Biomarker testing for sRAGE[m], ICAM1[n], and CCL20[o]				X				X				X				X			
Lung computer tomography				X				X				X				X			
Continuous health status monitoring, including home visits, phone, email, telemedicine, and COPD[p] Center visits as necessary	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Monitoring COPD exacerbations based on use of inhaled steroids, antibiotics, inhaled bronchodilators, steroids, health care visits (office visits, emergency department, or hospital)	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Monitoring adverse events and serious adverse events using SymptoMaster self-assessment that triggers notification	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X

[a]Q: quarter.

[b]FVC: forced vital capacity.

[c]FEV: forced expiratory volume.

[d]FEV1: forced expiratory volume in 1 second.

[e]FEF: forced expiratory flow.

[f]MEF: maximum expiratory flow.

[g]CAT: COPD Assessment Test.

[h]6MWT: 6-Minute Walk Test.

[i]ECG: electrocardiogram.

[j]CBC: complete blood count.

[k]HDL: high-density lipoproteins.

[l]LDL: low-density lipoproteins.

[m]sRAGE: advanced glycosylation end-product receptor.

[n]ICAM1: intercellular adhesion molecule 1.

[o]CCL20: macrophage inhibitory protein 3a.

[p]COPD: chronic obstructive pulmonary disease.

Computed Tomography

All study subjects will undergo inspiratory 64-channel CT scans of the chest with the following standard parameters: 0.8 mm reconstructed slice thickness, 0.4 mm slice interval, matrix size 512 x 512, range -500 to 1500, 120 kV, 40 mAs.

A trained professional research assistant will evaluate the scan for technical completeness, compliance with protocol, adequacy of inspiration, and presence of motion artifact. The stability of CT measurements for CT scanner used in the study will be monitored by monthly scanning using a custom phantom designed for this study.

While conducting this cross-sectional study, we identified an optimal quantitative CT assessment protocol by using Airway Inspector based on the Slicer computer program (Harvard University) for lung densitometry [23]. In addition to qualitative assessment of 3D lung reconstruction, Slicer software allows for quantitative measurements of lung tissue density based on Hounsfield units. Such a tool provides the opportunity for automated measurement and quantitative comparisons between study groups based on an objective emphysema scoring system.

Electrocardiography

A standard 12-lead ECG taken by Fukuda Denshi FX-8222 Cardimax will be performed for each study subject by employing strictly standardized procedures. Research staff will be trained to properly place electrodes. At least four cardiac cycles will be taken from each of 12 leads. The machine runs at 50 mm/sec. The following ECG parameters will be evaluated by a trained clinical researcher: waves and complexes, presence and description of ECG abnormalities including pathologic q-waves, ST elevation, ST depression, T-wave inversion, hypertrophy, QRS axis deviation, block, and arrhythmia. ECGs will be visually inspected for technical errors and interpreted by a qualified cardiologist. The prevalence of specific ECG abnormalities as well as grouped abnormalities will be reported for each study group. We will measure and analyze associations between COPD and ECG abnormalities, crude and adjusted by sex, age, and smoking status.

Physical Exam

Clinical investigators were trained to conduct the pulmonary (ie, percussion and inspection) exam and technique for listening to second heart sounds. Two Stanford Medicine 25 modules [20,21] will be used as study materials in hands-on sessions. The prevalence of individual pathological findings will be presented for each study group.

Anthropometry

Anthropometric measurements will include height, weight, waist circumference, heart rate, blood pressure, and pulse oximetry.

Six-Minute Walk Test

The 6MWT is a simple and effective test that measures the distance that a patient can quickly walk on a flat, hard surface in a period of 6 minutes. A 100-ft hallway is needed, and no exercise equipment or advanced training for technicians is required [24].

Laboratory Data

Blood donated by the study participants will be processed at the KAPM COPD Center for shipment, analysis, and intermittent (at -20°C) and long-term (deep freeze at -80°C) storage at HealthCity Laboratory in accordance with biobanking standards. The HealthCity Laboratory will perform the following assays: CBC, blood cholesterol level, HDL, LDL, triglycerides; glucose, hemoglobin A1C; C-reactive protein; and fibrinogen.

In addition, blood will be stored in order to perform testing for sRAGE, ICAM1, CCL20, and other potential biomarkers at a later stage. Biomarker testing will be done using enzyme-linked immunosorbent assay (ELISA) and/or aptamers analysis. Testing for other biomarkers, such as CDH1, CDH13, SERPINA7, Interleukin 16 (plasma level), and genotyping will also be considered depending on availability of the tests and their value in COPD diagnosis. We are also exploring technical capabilities for "-omics" studies, additional biomarkers, and tobacco-specific nitrosamines assay in urine.

Previously reported findings, particularly when combined with other studies of individual biomarkers, suggest a panel of blood biomarkers including sRAGE (advanced glycosylation end-product receptor), the biomarker of increased emphysema percentage in the lungs independent of gender, age, airflow limitation, body mass index, and current smoking status. Decreased ICAM1 levels correlate with increased severity of emphysema on CT scans, independent of smoking status, FEV1, and other covariates CCL20 (macrophage inhibitory protein 3a), inversely and significantly associated with emphysema. Interleukin 16 (IL-16; a multifunctional cytokine that has been associated with autoimmune and allergic diseases) is positively associated with age and body mass index and negatively associated with current smoking and emphysema in the upper lobes. An integrated "-omics" analysis in a very large cohort identified an association between decreased IL-16 and emphysema and discovered a novel IL-16 local expression quantitative trait loci (cis-eQTL) [25]. Thus, IL-16 plasma levels and IL-16 genotyping may be useful in a personalized medicine approach for lung disease.

Collecting Data Using SmartHealth Technologies

KAPM's SmartHealth technologies (SymptoMaster and Medintel) will be used to capture early symptoms of COPD and signs of COPD exacerbations and comorbidities. Our proprietary expert technology called SymptoMaster [16] will help patients establish the probable causes of the symptoms of diseases without assistance from a health care professional. Using a computer, mobile phone, or tablet, a patient inputs their symptoms into the system, which produces the most likely preliminary diagnosis. After receiving the diagnosis, a patient can refer to Medintel [17], an online library that contains information about 1000 common diseases, their causes, symptoms, ways to prevent them, and treat them. These technologies allow a patient to make an informed decision on

whether they should seek immediate medical assistance by calling an ambulance or consult a doctor on their next routine visit. SmartHealth technologies facilitate monitoring patients' conditions by clinical investigators.

Computer-Assisted Personal Interviewing

KAPM has developed an electronic data capture system in the form of its proprietary computer-assisted personal interviewing app. The app is available for tablet personal computers and will be modified to be implemented in the cohort study to collect, store, and transmit data related to a personal survey interview. The questionnaire will be designed to collect data on possible COPD risk factors including history of smoking, current smoking, level of smoking exposure (in pack-year), passive smoking, occupational and environmental hazards, including dusts, chemicals, and indoor fuel pollution. The questionnaire will contain covariates: age, gender, ethnicity, education, occupation, and self-reported morbidity. It will also include questions to address COPD exacerbations and to record the use of combustible cigarettes, iQOS with HeatSticks, electronic cigarettes, and other alternatives, as well as iQOS switch date.

Statistical Analysis and Data Management Plan

Appropriate descriptive statistics will be used to summarize required study elements overall and by cohort (eg, proportion, mean, standard error, median, and interquartile ranges). Exploratory graphical analysis will be done preliminary to numerical analysis. Histograms, two-dimensional scatterplots of raw data, will provide information on the univariate and bivariate distributions of the variables focusing on distribution of variables, relation between the variables, whether it is linear or nonlinear, etc. In addition, preliminary graphs will screen raw data by highlighting obvious data errors. Spaghetti plots, scatterplots of dependent variable scores versus the time variable with a separate line for each person, will explore likely models, especially whether effects are linear or not.

Generalized estimating equations (GEE) and GLMM will be used to assess the effect of exposure on outcome variables. Both GEE and GLMM are used to account for within-person correlation of observations due to repeated measures. GEE uncovers the population average effect of a covariate, whereas GLMM estimates the individual specific effect. For binary confirmatory outcomes, CAT score ≥10, and inability to walk 450 meters on the 6MWT, the logit transformation will be utilized as the model link function. To model the annual exacerbation rate (count data), we will use the logarithm transformation and the Poisson or quasi-Poisson distribution depending on mean-variance relationship.

Presence of the statistically significant "time by group" interaction coefficient in GEE/GLMM will be our focus. It will demonstrate that the primary outcomes in two cohorts will have been changed significantly and provide statistical evidence for the harm reduction hypotheses.

To adjust for confounders, we will examine distributions of all covariates in the exposed and control group and will use Cohen effect sizes [26] to identify whether participants' characteristics are different between groups at baseline. The impact of a potential confounder will be confirmed on whether the adjustment for the confounding variable changes the estimate of association.

We will apply a three‐stage reporting framework [27]. Model 1 will report the crude analysis (without any adjustments for confounders), Model 2 will report the semi‐adjusted analysis (including the following a priori defined covariates of gender, age, number of pack-year at base-line), and Model 3 will present the fully adjusted model (including all the covariates as in Model 2 plus those covariates that have discrepancies across two cohorts and change the estimate of association). The matching variables can be ignored in the model if we have exactly two controls for each participant in the iQOS cohort. Because of dropouts and other reasons, that will be impossible to achieve. There will be some confounder effect remaining, which means we have to include matching variables in the analysis. Model diagnostic plots will be generated to test model assumptions, for example, normality of deviance residuals.

We will also use two methods of propensity score analysis (PSA)—stratification on the propensity score and inverse probability weighting using the propensity score [28]—to adjust for confounders that may vary in study groups.

For missing data analysis, we will use missing at random assumptions. Missing values will be handled by multiple multivariate imputation in R. We will analyze five copies of the data, each with missing values imputed, in the GEE/GLMM multivariate analysis. The estimates of association will then be averaged according to Rubin's rule [29] to produce a single mean estimate and adjusted standard errors.

To address dual usage, switching, and quitting, we will use several methods. First, we will implement the intention-to-treatment strategy, that is, we will adjust only for baseline confounders and evaluate the exposure effect as if all study participants remain under the exposures at the baseline until end of follow‐up. Second, we will evaluate the exposure effect censoring switchers and quitters from the analysis. Third, particularly for dual usage, we will model two exposures, iQOS and conventional cigarette usage, as weighted sums of doses calculated in pack-years. Weights will depend on the importance of the different periods, where the closest period will have the highest weight.

Analysis will be done using R [19]. The Bonferroni correction of the significance level will be applied to account for three confirmatory hypotheses being tested in the study, so an alpha <.017 (0.05/3) will be considered significant.

Sensitivity analysis will be performed to assess consistency of the effect estimate by testing variations in underlying assumptions. First, we will assess potential biases due to unmeasured confounders or how strong should be an unmeasured confounder to explain the magnitude of the effect estimate. Second, we will consider the use of more than one cohort definition to ensure that the effect estimate is robust to the assumptions behind these definitions. For example, we will use a different cut-off for predominant use of iQOS with HeatSticks (>50%, >60%, >70%, >80%, >90%, 100%) based on averaging iQOS percentage use over time beginning from baseline. Third, there are several alternative statistical analysis

approaches to evaluate the effect estimate. We will explore whether the choice of statistical method (GEE/GLMM/PSA) will influence the effect estimate. Finally, we will search how redefining the threshold (ie, different cut-off points for binary outcomes, CAT, and 6MWT) changes the effect estimate.

All study data will be stored at the Information Technology Unit of KAPM. Data will be entered through a Web-accessible system. The questionnaire will be designed as an HTML Web form and will be placed on the server so that it can be loaded and displayed through the client browser at the time of connection. Data analysis will be done only in aggregate. All data will be used for research purposes only, and no participant will be identified when the data are analyzed, presented, or published. No individually identifiable information will be published. The Ethics Committee of KAPM approved this study on December 5, 2017.

Results

Participant inclusion began December 2017 and recruitment is expected to last until late summer 2018. When completed, the study results will be published in peer-reviewed scientific journals.

Discussion

Principal Considerations

To the best of our knowledge, this is the first longitudinal cohort observational study to demonstrate whether trends in the response variables across time differ between users of iQOS with HeatSticks (exposure group) and smokers of combustible cigarettes (control group).

We hypothesize that iQOS with HeatSticks may serve as a less risky alternative to combustible cigarettes and to other traditional tobacco products in a clinical setting. Specifically, we hypothesize that participants using iQOS with HeatSticks will have less prevalent presence of respiratory symptoms, have better functional exercise capacity, and experience fewer exacerbations compared to those who smoke combustible cigarettes.

Assuming that smokers who switch to iQOS do reduce their exposure to harmful and potentially harmful smoke compounds, our study will determine whether switching to iQOS actually reduces the development and progression of COPD, based on CT scans and conventional spirometry tests.

Limitations

This study is observational. Despite the fact that we have collected an extensive set of data on possible confounders, unmeasured confounding variables may exist. The study cannot produce definitive proof of a cause-effect relationship between the exposures and health outcomes, as with any observational medical research. Participants may leave the study for different reasons, which can compromise the validity of the study, particularly if the cohort dropout rates are different or the participants who remain in the study are different from those who drop out.

Conclusion

This is the first cohort study in Kazakhstan to evaluate differences between smoking of combustible cigarettes compared to using the heated tobacco product, iQOS with HeatSticks, and the effect on respiratory symptoms, functional exercise capacity, and exacerbation rate of COPD. The study results will add to knowledge on whether switching from combustible cigarettes to iQOS with HeatSticks affects respiratory symptoms and diseases including the development and progression of COPD.

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Authors' Contributions

The study was designed by AS, BZ, DS, IK, and EE. AS and BZ drafted the manuscript. All authors critically revised the manuscript. All authors read and approved the final manuscript.

Conflicts of Interest

None declared.

References

1. GBD 2015 Mortality and Causes of Death Collaborators. Global, regional, and national life expectancy, all-cause mortality, and cause-specific mortality for 249 causes of death, 1980-2015: a systematic analysis for the Global Burden of Disease Study 2015. Lancet 2016 Oct 08;388(10053):1459-1544 [FREE Full text] [doi: 10.1016/S0140-6736(16)31012-1] [Medline: 27733281]
2. Adeloye D, Chua S, Lee C, Basquill C, Papana A, Theodoratou E, Global Health Epidemiology Reference Group (GHERG). Global and regional estimates of COPD prevalence: Systematic review and meta-analysis. J Glob Health 2015 Dec;5(2):020415 [FREE Full text] [doi: 10.7189/jogh.05-020415] [Medline: 26755942]

3. Vogelmeier C, Criner G, Martinez F, Anzueto A, Barnes P, Bourbeau J, et al. Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Lung Disease 2017 Report. GOLD Executive Summary. Am J Respir Crit Care Med 2017 Dec 01;195(5):557-582. [doi: 10.1164/rccm.201701-0218PP] [Medline: 28128970]
4. Shah T, Churpek MM, Coca PM, Konetzka RT. Understanding why patients with COPD get readmitted: a large national study to delineate the Medicare population for the readmissions penalty expansion. Chest 2015 May;147(5):1219-1226 [FREE Full text] [doi: 10.1378/chest.14-2181] [Medline: 25539483]
5. GBD 2015 Chronic Respiratory Disease Collaborators. Global, regional, and national deaths, prevalence, disability-adjusted life years, and years lived with disability for chronic obstructive pulmonary disease and asthma, 1990-2015: a systematic analysis for the Global Burden of Disease Study 2015. Lancet Respir Med 2017 Sep;5(9):691-706 [FREE Full text] [doi: 10.1016/S2213-2600(17)30293-X] [Medline: 28822787]
6. MacNee W. Pathology, pathogenesis, and pathophysiology. BMJ 2006 May 18;332(7551):1202-1204. [doi: 10.1136/bmj.332.7551.1202]
7. Global Initiative for Chronic Obstructive Lung Disease. 2017. Global Strategy for the Diagnosis, Management and Prevention of COPD URL: https://goldcopd.org/gold-2017-global-strategy-diagnosis-management-prevention-copd/ [WebCite Cache ID 72VBTLAvG]
8. Qaseem A, Wilt TJ, Weinberger SE, Hanania NA, Criner G, van der Molen T, American College of Physicians, American College of Chest Physicians, American Thoracic Society, European Respiratory Society. Diagnosis and management of stable chronic obstructive pulmonary disease: a clinical practice guideline update from the American College of Physicians, American College of Chest Physicians, American Thoracic Society, and European Respiratory Society. Ann Intern Med 2011 Aug 02;155(3):179-191. [doi: 10.7326/0003-4819-155-3-201108020-00008] [Medline: 21810710]
9. Cebron LN, Beijers RJHCG, van der Bost B, Doehner W, Lainscak M, Schols AMWJ. The Prevalence of Metabolic Syndrome In Chronic Obstructive Pulmonary Disease: A Systematic Review. COPD 2016 Dec;13(3):399-406. [doi: 10.3109/15412555.2016.1140732] [Medline: 26914392]
10. Sharman A, Zhussupov B, Sharman D, Stambekova A, Yeraliyev S. Cross-Sectional Study of Chronic Obstructive Pulmonary Disease Prevalence Among Smokers, Ex-Smokers, and Never-Smokers in Almaty, Kazakhstan: Study Protocol. JMIR Res Protoc 2017 Jul 25;6(7):e143 [FREE Full text] [doi: 10.2196/resprot.7422] [Medline: 28743683]
11. Woodruff PG, Barr RG, Bleecker E, Christenson SA, Couper D, Curtis JL, SPIROMICS Research Group. Clinical Significance of Symptoms in Smokers with Preserved Pulmonary Function. N Engl J Med 2016 May 12;374(19):1811-1821 [FREE Full text] [doi: 10.1056/NEJMoa1505971] [Medline: 27168432]
12. Regan EA, Lynch DA, Curran-Everett D, Curtis JL, Austin JHM, Grenier PA, Genetic Epidemiology of COPD (COPDGene) Investigators. Clinical and Radiologic Disease in Smokers With Normal Spirometry. JAMA Intern Med 2015 Sep;175(9):1539-1549 [FREE Full text] [doi: 10.1001/jamainternmed.2015.2735] [Medline: 26098755]
13. Fletcher C, Peto R. The natural history of chronic airflow obstruction. Br Med J 1977 Jun 25;1(6077):1645-1648 [FREE Full text] [Medline: 871704]
14. Haziza C, de la Bourdonnaye G, Merlet S, Benzimra M, Ancerewicz J, Donelli A, et al. Assessment of the reduction in levels of exposure to harmful and potentially harmful constituents in Japanese subjects using a novel tobacco heating system compared with conventional cigarettes and smoking abstinence: A randomized controlled study in confinement. Regul Toxicol Pharmacol 2016 Nov;81:489-499 [FREE Full text] [doi: 10.1016/j.yrtph.2016.09.014] [Medline: 27693654]
15. Polosa R, Morjaria JB, Caponnetto P, Prosperini U, Russo C, Pennisi A, et al. Evidence for harm reduction in COPD smokers who switch to electronic cigarettes. Respir Res 2016 Dec 16;17(1):166 [FREE Full text] [doi: 10.1186/s12931-016-0481-x] [Medline: 27986085]
16. Symptomaster.com: Manage Your Health. URL: https://www.symptomaster.com/ [WebCite Cache ID 72VANHVTL]
17. Medintel. URL: https://medintel.kz/ [WebCite Cache ID 72VAl9VtE]
18. Global Initiative for Chronic Obstructive Lung Disease Global Initiative for Chronic Obstructive Lung Disease. Pocket guide to COPD diagnosis, management, and prevention URL: https://goldcopd.org/wp-content/uploads/2016/12/wms-GOLD-2017-Pocket-Guide.pdf [accessed 2018-09-17] [WebCite Cache ID 72VAqhbcH]
19. R Foundation for Statistical Computing. Vienna, Austria R: A language and environment for statistical computing URL: https://www.R-project.org/ [WebCite Cache ID 72VBC4HQ8]
20. Stanford Medicine 25. Pulmonary exam: percussion and inspection URL: http://stanfordmedicine25.stanford.edu/the25/pulmonary.html [WebCite Cache ID 72VCy4zqP]
21. Stanford Medicine 25. Cardiac second sounds URL: http://stanfordmedicine25.stanford.edu/the25/cardiac.html [WebCite Cache ID 72VDBPBOt]
22. Pellegrino R, Viegi G, Brusasco V, Crapo RO, Burgos F, Casaburi R, et al. Interpretative strategies for lung function tests. Eur Respir J 2005 Nov;26(5):948-968 [FREE Full text] [doi: 10.1183/09031936.05.00035205] [Medline: 16264058]
23. Fedorov A, Beichel R, Kalpathy-Cramer J, Finet J, Fillion-Robin J, Pujol S, et al. 3D Slicer as an image computing platform for the Quantitative Imaging Network. Magn Reson Imaging 2012 Nov;30(9):1323-1341 [FREE Full text] [doi: 10.1016/j.mri.2012.05.001] [Medline: 22770690]

24. ATS Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories. ATS statement: guidelines for the six-minute walk test. Am J Respir Crit Care Med 2002 Jul 01;166(1):111-117. [doi: 10.1164/ajrccm.166.1.at1102] [Medline: 12091180]
25. Bowler RP, Bahr TM, Hughes G, Lutz S, Kim Y, Coldren CD, et al. Integrative omics approach identifies interleukin-16 as a biomarker of emphysema. OMICS 2013 Dec;17(12):619-626 [FREE Full text] [doi: 10.1089/omi.2013.0038] [Medline: 24138069]
26. Cohen J. Statistical Power Analysis for the Behavioral Sciences. London, UK: Taylor & Francis, Inc; 1988.
27. Mamdani M, Sykora K, Li P, Normand SLT, Streiner DL, Austin PC, et al. Reader's guide to critical appraisal of cohort studies: 2. Assessing potential for confounding. BMJ 2005 Apr 23;330(7497):960-962 [FREE Full text] [doi: 10.1136/bmj.330.7497.960] [Medline: 15845982]
28. Austin PC. An Introduction to Propensity Score Methods for Reducing the Effects of Confounding in Observational Studies. Multivariate Behav Res 2011 May;46(3):399-424 [FREE Full text] [doi: 10.1080/00273171.2011.568786] [Medline: 21818162]
29. Rubin D. Multiple Imputation for Nonresponse in Surveys. NY, New York: Wiley, John & Sons, Incorporated; 2004.

Abbreviations

6MWT: Six-Minute Walk Test
CAT: COPD Assessment Test
CBC: complete blood count
CCL20: macrophage inhibitory protein 3a
COPD: chronic obstructive pulmonary disease
CT: computed tomography
ECG: electrocardiogram
FEF: forced expiratory flow
FEV: forced expiratory volume
FEV1: forced expiratory volume in 1 second
FVC: forced vital capacity
GEE: generalized estimating equation
GLMM: generalized linear mixed model
GOLD: Global Initiative for Chronic Obstructive Lung Disease
HDL: high-density lipoproteins
ICAM1: intercellular adhesion molecule 1
KAPM: Kazakhstan Academy ∘ f Preventive Medicine
LDL: low-density lipoproteins
MEF: maximum expiratory flow
PSA: propensity score analysis
SF-12: Short form-12
sRAGE: advanced glycosylation end-product receptor

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Protocol

Living With Inflammatory Bowel Disease: Protocol for a Longitudinal Study of Factors Associated With Symptom Exacerbations

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Abstract

Background: There has been limited longitudinal research that has comprehensively evaluated possible factors in the exacerbation of inflammatory bowel disease (IBD) symptoms with or without associated inflammation. Evolving Web-based technologies facilitate frequent monitoring of patients' experiences and allow a fine-grained assessment of disease course.

Objective: We aimed to prospectively identify factors associated with symptom exacerbation and inflammation in IBD including psychological functioning, diet, health behaviors, and medication adherence.

Methods: Between June 2015 and May 2017, we enrolled adults with IBD, recruited from multiple sources, who had been symptomatically active at least once within the prior 2 years. They completed a Web-based survey every 2 weeks for 1 year and submitted a stool sample at baseline, 26 weeks, and 52 weeks. Any participant reporting a symptom exacerbation was matched to a control within the cohort, based on disease type, sex, age, and time of enrollment; both were sent a supplemental survey and stool collection kit. Biweekly surveys included validated measures of the disease course, psychological functioning, health comorbidities, and medication use. Intestinal inflammation was identified through fecal calprotectin (positive level >250 μg/g stool).

Results: There were 155 participants enrolled with confirmed IBD, 66.5% (103/155) with Crohn disease and 33.5% (52/155) with ulcerative colitis, of whom 98.7% (153/155) completed the study. Over the 1-year period, 47.7% (74/155) participants experienced a symptom exacerbation. The results of analyses on risk factors for symptom exacerbations are pending.

Conclusions: We recruited and retained a longitudinal IBD cohort that will allow the determination of risk factors for symptom exacerbation with and without inflammation. This will increase understanding of symptom exacerbations among persons with IBD.

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KEYWORDS

Crohn disease; diet; flare; inflammatory bowel disease; survey; ulcerative colitis; Web-based

Introduction

Inflammatory bowel disease (IBD), manifesting as Crohn disease (CD) or ulcerative colitis (UC), is complex. Individuals experience gastrointestinal symptoms such as abdominal pain, diarrhea, and rectal bleeding, but they may also have fatigue or extraintestinal manifestations such as arthritis [1]. As with many chronic illnesses, the clinical impact of IBD cannot be fully accounted for with objective tests, such as endoscopy or biological markers [2]. Psychological factors and diet have been identified as contributing to symptoms and patient outcomes [3-6]. To better understand the role of biological, psychological, and lifestyle factors in the expression and course of IBD, there is a need to prospectively study these multiple domains.

People living with IBD often face episodes of increased symptom activity separated by periods of relative or absolute quiescence. We have shown that 30% of individuals with IBD who report no symptoms will become symptomatic at some time over the following year [4]. People often report a lower health-related quality of life [7] during these periods, and many may seek medical care for the management of these symptoms [8]. Importantly, not all symptoms in patients with IBD are related to active inflammation, although most IBD therapies are directed at reducing inflammation [4,9].

There has been little research exploring the causes of the development or worsening of IBD-related symptoms and what exactly it means when a patient reports a “flare.” Persons with IBD often attribute symptom exacerbation to changes in diet and stress, although there is currently little understanding of which dietary or psychological factors play a role. Symptomatic activity in IBD is generally reported in clinical studies using tools such as the Harvey-Bradshaw Index that have poor biopsychometric properties [10]. Further, current Web-based technologies allow fine-grained assessment of individuals’ disease experience in a cost-effective and efficient manner [11].

This study aims (1) to assess patients’ experiences of symptomatic activity every 2 weeks over a 1-year period; (2) to describe which specific symptoms are correlated with patient-defined IBD flares, which are correlated with inflammation measured by fecal calprotectin (FCAL), and what patients believe causes their symptom exacerbations; (3) to identify predictors of patient-reported symptom exacerbations and, separately, inflammation, including psychological characteristics (perceived stress, self-efficacy, distress, optimism, intolerance of uncertainty, and health anxiety), diet, menstrual cycle, medication, comorbidity, and substance use; and (4) to describe diet in IBD, including stability over 1 year, and whether diet changes before or after symptom exacerbation.

In this report, we describe the protocol, participant enrollment, and participant retention for the study. Having recently completed the data collection, we are ready to undertake our varied analyses, which will be the subject of future reports.

Methods

Recruitment

Participants with established IBD were recruited from a previous longitudinal cohort study [12], our provincial population-based research registry [13], regional gastroenterology clinics, posters in the hospitals and gastroenterologists’ offices, and information posted on our center’s website (ibdmanitoba.org). Diagnoses of IBD were confirmed by medical records review and by querying treating physicians directly as needed. All recruitment was undertaken using a standardized script either in person or via email.

Inclusion criteria were (1) being aged 18-75 years old; (2) being able to provide informed consent; (3) being able to complete Web-based surveys in English; (4) willing to participate in the study for 1 year; and (5) having experienced symptoms related to IBD within the past 2 years.

Exclusion criteria were (1) total colectomy, ileostomy, or colostomy; (2) inadequately characterized disease history (disease phenotype and duration); (3) taking immune-modulating medication for any condition not related to IBD; (4) cancer treatment in the last 2 years (breast cancer patients on long-term tamoxifen who were well were included); and (5) specific serious chronic diseases other than IBD (ie, insulin-dependent diabetes, cirrhosis unless currently well, dialysis-dependent renal failure, organ transplantation, HIV, dementia, lupus, and scleroderma).

Participant Retention

Reminder emails were sent at 24, 48, and 72 hours if the biweekly survey had not been completed. Telephone contact was made with participants at 72 hours if the survey was not completed. Participants received an honorarium of Can $10 for each completed survey and an additional Can $50 for successfully completing at least 80% of all surveys and 100% of requested stool specimens, to a maximum honorarium of Can $320.

Data Collection

Long surveys were administered at baseline, midpoint (week 26), and study completion (week 52), while short surveys were completed every 2 weeks. At weeks 2 and 50, the short surveys were supplemented with a food frequency questionnaire. Quarterly, supplemental surveys added detailed medication and IBD clinical investigation questions. Stool specimens were collected for FCAL measurement at baseline, midpoint, and study completion.

Participants were sent an additional survey when they reported at least moderate worsening in symptom activity, as assessed by the IBD Symptom Change Indicator (SCI). Each of these cases was then matched with a control who had not previously experienced a symptom exacerbation and was not currently experiencing an exacerbation. Controls were matched on age (within 5 years), disease type, sex, and study entry date (to control for the season). Controls answered a similar additional survey. Cases and controls were also asked to return a stool collection kit. A maximum of 5 stool samples was collected

from each participant over the year of the study (weeks 0, 26, and 52; up to 1 control; and up to 2 symptom exacerbations). Survey data were collected and managed using REDCap electronic data capture tools, hosted at the University of Manitoba [14].

Measures

The measures against which data were collected include background characteristics, health behaviors, psychological qualities, IBD symptom activity and health-related outcomes, medication, and possible triggers of symptom exacerbation. If not otherwise stated, these were measured every 2 weeks. See Multimedia Appendix 1 for a tabular representation of when each measure was administered.

Background Characteristics

Demographics

At baseline, participants reported their (1) sex; (2) date of birth; (3) marital status: single or never married, married or living as married, separated, divorced, widow(er); (4) employment status: working full time, working part-time, homemaking, attending school, both working and attending school, retired, disabled, or other; (5) ethnic background: Canadian, indigenous or Aboriginal, European, Jewish, Latina or Latino or Hispanic, Asian, African or black, other, or do not know or prefer not to answer (participants could choose all ethnicities that were applicable); (6) education: grades 1-13, apprenticeship, nonuniversity program (college, technical, business, vocational, and nursing), university program; and (7) annual household income (in Canadian dollars): <$25,000, $25,001-$50,000, $50,001-$75,000, $75,001-$100,000, $100,001-$150,000, >$150,000, or do not know or prefer not to say.

Inflammatory Bowel Disease Characteristics

At baseline, participants reported (1) IBD disease type as CD, UC, unclassified or indeterminate colitis, or do not know or not sure; (2) the year they were diagnosed with IBD; (3) their IBD-related surgeries (number, type, and year); and (4) whether they had been hospitalized for IBD over the previous 12 months.

Medical History

Participants reported at baseline whether a doctor had ever diagnosed them with any chronic condition and whether they had undergone any non-IBD surgery. Biweekly, they reported if any chronic illness (other than IBD) had worsened in the last 2 weeks or if a physician had diagnosed or treated them for any new condition, including minor illnesses or injuries (eg, sprained ankle). Menstruating women (according to the baseline report) were asked if their period had started in the last 2 weeks. At the end of the study, female participants who had not experienced menopause reported if they had become pregnant in the last year. If they had, they were asked to specify the start and end dates of the pregnancy.

Smoking Cigarettes and Drinking Alcohol

At baseline, participants reported smoking status as daily or almost daily, occasionally, former, or never. Alcohol consumption was reported as the average number of drinks per week.

Diet

Diet was assessed using the 2007 Harvard Food Frequency Questionnaire [15]. Food frequency questionnaires (FFQs) are a validated dietary assessment tool for epidemiological research [15]. The FFQ is a checklist of foods with a section for reporting how often each food item was consumed. The Harvard FFQ, with results generally stable over a year, was administered at weeks 2 and 50. Food categories included dairy, fruits, vegetables, eggs and meats, sweets and baked goods, dietary supplements, beverages, and breads, cereals, and starches.

Psychological Qualities

Kessler Screening Scale for Psychological Distress

The Kessler Screening Scale for Psychological Distress (K6) [16] consists of 6 questions about an individual's feelings over the past 2 weeks, including nervousness and hopelessness. Responses range from 1 ("none of the time") to 5 ("all of the time"); summed scores from 19 to 30 are indicative of high distress [17]. Although the K6 is sensitive to all forms of psychological distress, it does not distinguish between depression and anxiety [16].

Perceived Stress Scale

The Cohen Perceived Stress Scale (PSS) measures the perception that demands exceed personal resources to cope. The 10-item version (PSS-10) has high internal consistency and test-retest reliability as well as good construct and predictive validity [18]. The PSS-10 was collected at weeks 0, 26, and 52. The 4-item PSS-4 was collected at all other time points [18].

General Self-Efficacy Scale

This validated tool assesses self-efficacy, the belief that one can function under adversity [19]. The 10-item General Self-Efficacy Scale-10 was used at weeks 0, 26, and 52. The shorter General Self-Efficacy Scale-6 collected data at all other time points.

Health Anxiety Inventory

This 14-item measure of concerns about health was administered at weeks 0, 26, and 52 [20]. Individuals with hypochondriasis score higher than physically ill patients, individuals with anxiety disorders, and healthy controls [20].

Intolerance of Uncertainty Scale

This 12-item survey assesses a tendency toward negativity when faced with uncertain situations. Items are evaluated on a 5-point scale with endpoints of "not at all characteristic of me" and "entirely characteristic of me" [21]. Good convergent and discriminant validity as well as internal consistency have been demonstrated [22,23].

Optimism

The Life Orientation Test-Revised is the 10-item optimism survey most commonly used in health research [24]. Each item is scored on a 5-point scale from "strongly disagree" to "strongly agree" [25].

Inflammatory Bowel Disease Symptom Activity and Health-Related Outcomes

Inflammatory Bowel Disease Symptom Inventory

The newly-developed IBD Symptom Inventory (IBDSI) is a 35-item self-report measure assessing 5 symptom clusters: bowel symptoms, abdominal discomfort, fatigue, bowel complications, and systemic complications [26]. It embeds the Harvey-Bradshaw Index for CD [10] and the Powell-Tuck Index for UC [27], so these scores can be calculated from the IBDSI. The complete IBDSI was collected at weeks 0, 26, and 52. A short form of the IBDSI, with 25 items, was collected at all other measurement points.

Manitoba Inflammatory Bowel Disease Index

The Manitoba Inflammatory Bowel Disease Index, developed and validated as part of the Manitoba IBD Cohort Study [28], uses a single item to describe symptom persistence. At weeks 0, 26, and 52, participants answered, "In the past 6 months my disease has been (1) constantly active, giving me symptoms every day; (2) often active, giving me symptoms most days; (3) sometimes active, giving me symptoms on some days (for instance 1-2 days per week); (4) occasionally active, giving me symptoms 1-2 days per month; (5) rarely active, giving me symptoms on a few days in the past 6 months; or (6) I was well in the past 6 months, what I consider a remission or absence of symptoms." Active disease can be defined as experiencing symptoms constantly to occasionally (responses 1-4).

Inflammatory Bowel Disease Symptom Change Indicator

This 7-point indicator of symptom change was developed by our group based on the Clinical Global Impression measure [29]. The IBD SCI asks, "Compared to 2 weeks ago, my IBD symptoms are: (1) much improved, (2) moderately improved, (3) minimally improved, (4) no change, (5) minimally worse, (6) moderately worse, or (7) much worse." A response of "moderately worse" or "much worse" defined symptom exacerbation in this study.

Flare Certainty Indicator

At every measurement occasion except week 0, individuals were asked: "Do you consider yourself to be in an IBD disease flare?" Response options included: "I am not in an IBD flare, I am possibly in an IBD flare, I am probably in an IBD flare," and "I am definitely in an IBD flare." This scale was created by our research group for this study.

Short Inflammatory Bowel Disease Questionnaire

Disease-specific quality of life was measured using the Short Inflammatory Bowel Disease Questionnaire (SIBDQ) [30]. Use of the Inflammatory Bowel Disease Questionnaire (IBDQ), authored by Jan Irvine, MD (1994), was made under license from McMaster University, Hamilton, Canada [31]. The SIBDQ [30,32], based on the original 32-item Inflammatory Bowel Disease Questionnaire, is a 10-item scale measuring bowel, systemic, social, and emotional aspects of living with IBD. It is responsive to changes in disease activity [32].

Disability

Questions were adapted from the Canadian Community Health Survey [33] and the Sheehan Disability Scale [34]. Examples are, "How many days in the last 2 weeks did your IBD symptoms cause you to miss work?" and "How many days in the last 2 weeks did you feel so impaired by your IBD symptoms that, even though you went to work, your productivity was reduced?"

Health Care Utilization and Clinical Investigations

Participants were asked to report any hospital admissions, emergency department visits, or physician visits (clinic or office) for their IBD in the prior 2 weeks. Every 3 months they reported any clinical investigations, including colonoscopy, capsule endoscopy, flexible sigmoidoscopy, abdominal magnetic resonance imaging or computerized tomography scan, and barium x-ray.

Administrative Health Data

At enrollment, consent was given to link the data from this study with the individuals' administrative health data. Manitoba Health is the single provincial health insurance provider. All physician visits and hospitalizations since 1984 and all prescription medication dispensed since 1995 can be tracked. Administrative data will confirm the dose and quantity of dispensed IBD medications, including 5-aminosalicylates, corticosteroids, thiopurines, methotrexate, and antitumor necrosis factor agents. The Manitoba administrative prescription drug database contains records of all dispensations for the entire population and captures the date of dispensation, information about the prescriber, drug name, and the dose or quantity dispensed [35]. Hospitalizations and outpatient physician and gastroenterologist visits will be confirmed using hospital discharge abstracts and physician billing claims. As well, we will collect utilization and medication information for 1 year prior to study entry.

Intestinal Inflammation

At weeks 0, 26, and 52 and at the report of symptom exacerbation, stool specimens were collected to measure FCAL, a marker of intestinal inflammation. Recently, it has been shown that the level of FCAL in a stool sample correlates with the presence and severity of gut inflammation [36-38]. Stool collection kits were delivered and returned by courier to the IBD Clinical and Research Centre, Manitoba, Canada. FCAL levels remain stable for 7 days at room temperature. Once the kit was received at the study center, it was kept at −80˚C until analyzed with a calprotectin enzyme-linked immunosorbent assay (ALPCO, Salem, NH, USA). We obtained 2 measurements from each sample, and the average FCAL level was used for analysis. The upper limit of measurement for FCAL is 1,888 µg/g stool. Participants were considered to have active intestinal inflammation if FCAL exceeded 250 µg/g stool [39,40].

Inflammatory Bowel Disease Medications

Participants were asked to select from a list the IBD medications they currently used. They were asked about amounts (eg, mg or mL), the number of pills taken at a time, and timing (eg, 2 times per day). For each medication, participants were asked to report 1 of the following 3 options: (1) number of times the

medication was taken in the last 2 weeks, if medication was taken on an as needed basis; (2) percent of scheduled medication taken in the last 2 weeks (eg, 80%); or (3) not scheduled to take medication in the last 2 weeks. Participants were asked to report if they had stopped their IBD medication(s) in the last 2 weeks, or they could report not using any IBD medications.

Non-IBD Medications

Every 2 weeks, participants reported if they had started, stopped, or changed the dosage of any medication taken for any reason other than IBD. A full list of all prescribed and nonprescribed medications they used was collected at weeks 0, 14, 26, 40, and 52 as well as when a medication start, stop, or change was reported. Additional multiple-choice questions collected information on amounts of acetaminophen, narcotics, aspirin, and other nonsteroidal anti-inflammatory drugs taken over the 2-week period (0 pills, 1-5 pills; 6-13 pills; 14-28 pills; >28 pills).

Medication Adherence Report Scale

The tendency to take medication as prescribed was assessed with the 5-item Medication Adherence Report Scale [41,42], which asks about the propensity to avoid, forget, or stop taking medication and the tendency to alter the dose. Items were scored on a 5-point scale, with response options of "always, often, sometimes, rarely, or never," and summed, with a total score of 25 indicating complete adherence. The scale can be analyzed either continuously or categorically, with a score of ≥20 categorized as high medication adherence [43].

Triggers of Symptom Exacerbation

At baseline and study completion, participants were asked open-ended questions, followed by specific questions, about their experiences with triggers of symptom exacerbations. Specified triggers included stomach or bowel infection, other infections, overwork, sleep problems, conflict, stress, medication changes, more alcohol consumption than usual, overeating, eating certain foods, and not eating certain foods. Participants were asked, "How much has [specified trigger] been related to your IBD symptoms going from inactive to active in the past?" Response options were, "not at all, a little, moderately, quite a lot, and a great deal." A supplemental survey was sent to participants when they reported at least moderate worsening of symptoms. It asked first, "Do you believe that there was something that triggered your increase in IBD symptoms?" If yes, they were asked to specify. Cases and controls were asked about changes in diet and whether they had been overworked, stressed, down, or anxious.

Statistical Analysis

We describe the demographic and clinical characteristics of the sample at enrollment using frequencies, percentages, means, and SDs (Table 1). The frequency of individuals who reported at least moderate symptom worsening with the IBD SCI is stated.

Patient attributes, such as age, sex, baseline disease activity, and baseline level of inflammation as measured by FCAL level, will be tested for their association with adherence to the protocol. This analysis will help to inform future studies, to maximize subject participation in IBD studies that use longitudinal methods.

We will track the relationship between symptom exacerbation without active inflammation as measured by FCAL, symptom exacerbation with active inflammation, active inflammation without symptom exacerbation, and how these different combinations of symptoms and inflammation change over time. We will compare self-reported symptom exacerbation on the IBD SCI with symptom scores on the IBDSI as well as with the SIBDQ and individual items from the SIBDQ, such as fatigue and quality of sleep.

Multilevel Poisson regression will model the total number of symptom exacerbations, with and without inflammation. Model covariates will include age, sex, disease type, disease duration, baseline measures of stress, and disease activity. The model fit will be assessed using likelihood ratio statistics and penalized measures of the likelihood function, such as the Aikake information criterion [44]. Potential collinearity among the explanatory variables will be assessed using descriptive correlational analyses and variance inflation factors, where appropriate.

The trajectory of symptom exacerbations (ie, exacerbation present vs absent) over the 12-month observation period will be modeled using a mixed-effects multiple logistic regression model. The model will include both marginal (ie, average) and subject-specific (ie, random) effects, to account for the clustering of repeated observations within participants. Mixed-effects models are widely recommended for longitudinal analyses because of the opportunity to describe both within-subject and between-subject variations across multiple measurement occasions [45,46]. A random intercept for time will be included in the model, and we will explore improvements in model fit when random slopes for time and other covariates are included. Both time-varying and time-invariant covariates will be considered for model inclusion, and time-lagged covariates (eg, perceived stress in the prior 2-week period, perceived stress for all previous 2-week periods, and change in perceived stress between the baseline and prior 2-week period) will be considered. Other covariates will include K6 scores; adherence to maintenance medications; use of nonsteroidal anti-inflammatory drugs, antibiotics, and other non-IBD medications; smoking status; and most recent FCAL value. The model fit will be evaluated using the methods noted above. The intraclass correlation will be used to describe the proportion of model variation due to subject-specific effects.

We will assess diet stability in persons with IBD by comparing their responses to the FFQ at week 2 with the FFQ at week 50. More importantly, the stability in diet between those persons who reported a symptom exacerbation will be compared to those who did not report an exacerbation. Furthermore, we will determine if the frequency of foodstuff consumption differs between persons who had a symptom exacerbation but normal FCAL compared to persons who had an exacerbation with active inflammation as identified by FCAL.

Table 1. Demographic and disease characteristics of participants at baseline (N=155).

Characteristics	Value
Female, n (%)	108 (69.7)
Age, mean (SD)	42.6 (12.6)
European or Canadian ethnicity, n (%)	149 (96.1)
Urban residence, n (%)	132 (85.2)
Marital status, n (%)	
Married or living as married	97 (62.6)
Separated, divorced, or widowed	22 (14.2)
Single or never married	36 (23.2)
Education (years), mean (SD)	15.6 (3.5)
Crohn disease, n (%)	102 (65.8)
Age at diagnosis (years), median	28
Age at diagnosis (years), mean (SD)	28.6 (11.5)
Age (years), n (%)	
<17 years	23 (14.8)
17-39 years	107 (69.0)
≥40 years	25 (16.1)
Disease duration (years), mean (SD)	14.8 (10.3)
Comorbid chronic condition, n (%)	91 (58.7)
Previous IBD[a]-related surgery, n (%)	55 (35.5)
IBD-related hospitalization in the past year, n (%)	19 (12.3)
Current smoker, n (%)	28 (18.1)
Alcohol consumption >14 drinks per week, n (%)	3 (1.9)
Active disease at baseline, n (%)	
IBDSI[b] at baseline: >24 in Crohn disease, >17 in ulcerative colitis	74 (47.7)
Fecal calprotectin at baseline, >250 μg/g	71 (45.8)
Symptom exacerbation during the study, n (%)	74 (47.7)

[a]IBD: inflammatory bowel disease.

[b]IBDSI: Inflammatory Bowel Disease Symptom Index.

Among those persons who reported a symptom exacerbation, we will assess whether a change in diet occurred in the 2 weeks prior. This will be done using a supplemental food survey that asks about specific food items that were consumed “more than usual in the last 2 weeks” (eg, types of milk products, grains, fruits, and vegetables) as well as whether the change was made prior to the flare or as a response to the symptoms. This supplemental survey was administered when a participant reported a symptom exacerbation on the SCI.

With our sample size of 155 and 15 predictor variables in a regression model, with alpha=.05 and power of 80%, we can detect an effect that accounts for at least 12% of the variation in a continuous outcome measure. With a model that includes 5 predictor variables, with alpha=.05 and power of 80%, we can detect an effect that accounts for at least 8% of the variation in a continuous outcome measure.

Results

Between June 2015 and May 2017, 158 individuals were enrolled. Of this number, 3 were later withdrawn: 1 did not meet medical exclusion criteria (diabetes requiring insulin), and 2 returned their initial stool sample but did not complete a baseline survey and were lost to follow-up. Therefore, the final study population included 155 participants with IBD: 66.5% (103/155) with CD and 33.5% (52/155) with UC. Of these, 89.7% (139/155) completed the study to 52 weeks and completed at least 80% of all surveys.

Table 2. Recruitment sources for study participants.

Recruitment source	n (%)
Gastroenterology clinic	119 (76.8)
Manitoba IBD[a] Cohort Study or previous research program	22 (14.2)
Manitoba IBD Research Registry	9 (5.8)
Poster or Crohn's and Colitis Canada article	5 (3.2)

[a]IBD: inflammatory bowel disease.

Table 3. Comparison of the Living with IBD Study and the University of Manitoba IBD Epidemiology Database (UMIBDED).

Measure	Study participants (N=155)	UMIBDED (N=10,636)
Female, n (%)	108 (69.68)	5684 (53.44)
Crohn disease, n (%)	102 (65.81)	5241 (49.28)
Urban residence, n (%)	132 (85.16)	6518 (61.28)
Median age at diagnosis (years)	28	36

Over the course of the 1-year study period, 47.7% (74/155) participants experienced a symptom exacerbation and were matched to a control who had not previously reported a symptom exacerbation. There were 32 participants who had >1 exacerbation (see Table 1 for participant demographics and clinical descriptions).

Participants were recruited from multiple sources (Table 2), most from gastroenterology clinics, reflecting the requirement of symptoms related to IBD within the last 2 years. Recruitment averaged 6.4 persons per month over 24 months. When compared to the provincial population of Manitobans with IBD, according to the University of Manitoba IBD Epidemiology Database, this study enrolled a higher proportion of females, persons with CD, and persons living in an urban center (Table 3).

Discussion

By surveying persons with IBD every 2 weeks over the course of 1 year and analyzing exacerbation cases compared with matched controls, we aim to gain insight into factors associated with exacerbation and the extent to which symptoms are associated with active inflammation. Ultimately, we hope our findings can improve the care of persons with IBD by better understanding the trajectory of the disease and the factors that affect its course.

Difficulties in the past in investigating the relationship between symptom exacerbations and potential triggers have been primarily methodological. Multiple factors across biological and psychological domains have rarely been assessed concurrently or assessed frequently enough to establish a contributory role. Hence, we anticipate that our study will substantially advance clinical knowledge. Much of the research to date has relied on the retrospective survey of patients with IBD, where they are asked about the presence and the severity of symptoms along with their history of exposure to potential triggers. We have also used this method previously [4,47]. While we reported that, of all factors monitored over a 3-month period, only perceived stress was associated with an exacerbation of symptoms, the retrospective rating of symptoms and potential triggers over 3-month periods may be subject to recall bias. Recall biases may also influence how participants assessed the temporality and directionality of the relationship between triggers and symptoms. Assessments carried out at more frequent intervals allow for a more accurate assessment of the presence of triggers, the severity of symptoms, and the temporal relationship between them.

The relationship between patient symptoms and inflammation is central to disease management as most of the medication options for the treatment of IBD symptom exacerbations involve either the intensification or modification of anti-inflammatory therapies [48]. Conversely, it has been shown that persons with quiescent IBD symptoms who have evidence of ongoing inflammation may be at higher risk of developing a symptom exacerbation over the next 2 years. The measurement of FCAL may play a significant role in noninvasively studying the association between inflammation and symptom exacerbation. Determining the relationship between intestinal inflammation and symptoms could better define pathophysiologic mechanisms. Understanding the symptom-inflammation relationship would also better inform the management of symptom flares, given options of initiation or intensification of anti-inflammatory therapy or, alternatively, use of supportive symptom-directed care. Feedback to patients about the relationship between symptom presentation and measurable inflammation may also increase their confidence in using self-management approaches and knowing when to contact their physician for medical intervention.

The high retention rate of 98.7% (153/155) is a strength of our study. Staggered financial incentives [49], frequent appreciative written communication with participants as well as prompt and repeated electronic and phone call reminders may have contributed to the high retention. The use of electronic methods in this study was a strength in maintaining high participation for the entire 52 weeks as well as for having data entered into a secure, analyzable database directly by the participants as they completed their surveys.

There were some limitations to our study. Women were overrepresented, similarly to other IBD cohort studies [4,47]. FCAL is a sensitive measure of intestinal inflammation in persons with colitis but may be less sensitive in persons with small bowel CD [50].

In conclusion, we have reported the protocol and enrollment for a longitudinal study of persons with IBD reporting on their lived experiences biweekly for 1 year as well as intermittently providing stool samples to study intestinal inflammation. We believe our study will provide a unique assessment of the course of IBD. We hope to define factors that are associated with triggering a symptom exacerbation. This will help both clinicians and patients better understand how to manage IBD.

Acknowledgments

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Conflicts of Interest

CNB is supported in part by the Bingham Chair in Gastroenterology. He has served on advisory boards for AbbVie Canada, Ferring Canada, Janssen Canada, Shire Canada, Takeda Canada, Pfizer Canada, and Napo Pharmaceuticals. He has consulted with 4D Pharma and Mylan Pharmaceuticals. He has received educational grants from AbbVie Canada, Shire Canada, Takeda Canada, Janssen Canada, and Pfizer Canada and has been on the speakers' panel for Ferring Canada and Shire Canada. LET has served on advisory boards for Takeda Canada, Janssen Canada, Pfizer Canada, and Mallinckrodt, USA. The other authors have no conflicts to report.

Multimedia Appendix 1

Timetable of measure administration.

[PDF File (Adobe PDF File), 221KB - resprot_v7i11e11317_app1.pdf]

References

1. Singh S, Blanchard A, Walker JR, Graff LA, Miller N, Bernstein CN. Common symptoms and stressors among individuals with inflammatory bowel diseases. Clin Gastroenterol Hepatol 2011 Sep;9(9):769-775. [doi: 10.1016/j.cgh.2011.05.016] [Medline: 21645640]
2. Lichtenstein GR, Targan SR, Dubinsky MC, Rotter JI, Barken DM, Princen F, et al. Combination of genetic and quantitative serological immune markers are associated with complicated Crohn's disease behavior. Inflamm Bowel Dis 2011 Dec;17(12):2488-2496 [FREE Full text] [doi: 10.1002/ibd.21661] [Medline: 21391291]
3. Walker JR, Ediger JP, Graff LA, Greenfeld JM, Clara I, Lix L, et al. The Manitoba IBD cohort study: a population-based study of the prevalence of lifetime and 12-month anxiety and mood disorders. Am J Gastroenterol 2008 Aug;103(8):1989-1997. [doi: 10.1111/j.1572-0241.2008.01980.x] [Medline: 18796096]
4. Bernstein CN, Singh S, Graff LA, Walker JR, Miller N, Cheang M. A prospective population-based study of triggers of symptomatic flares in IBD. Am J Gastroenterol 2010 Sep;105(9):1994-2002. [doi: 10.1038/ajg.2010.140] [Medline: 20372115]
5. Graff LA, Walker JR, Bernstein CN. It's not just about the gut: Managing depression and anxiety in inflammatory bowel disease. Practical Gastroenterology 2011;34:11-25 [FREE Full text]
6. Hou JK, Lee D, Lewis J. Diet and inflammatory bowel disease: review of patient-targeted recommendations. Clin Gastroenterol Hepatol 2014 Oct;12(10):1592-1600 [FREE Full text] [doi: 10.1016/j.cgh.2013.09.063] [Medline: 24107394]
7. Pallis AG, Mouzas IA, Vlachonikolis IG. The Inflammatory Bowel Disease Questionnaire: a review of its national validation studies. Inflamm Bowel Dis 2004 May;10(3):261-269. [Medline: 15290922]
8. Rubin DT, Siegel CA, Kane SV, Binion DG, Panaccione R, Dubinsky MC, et al. Impact of ulcerative colitis from patients' and physicians' perspectives: Results from the UC: NORMAL survey. Inflamm Bowel Dis 2009 Apr;15(4):581-588. [doi: 10.1002/ibd.20793] [Medline: 19067414]
9. Duijvestein M, Battat R, Vande CN, D'Haens GR, Sandborn WJ, Khanna R, et al. Novel Therapies and Treatment Strategies for Patients with Inflammatory Bowel Disease. Curr Treat Options Gastroenterol 2018 Mar;16(1):129-146. [doi: 10.1007/s11938-018-0175-1] [Medline: 29411220]
10. Harvey RF, Bradshaw JM. A simple index of Crohn's-disease activity. Lancet 1980 Mar 8;1(8167):514. [Medline: 6102236]
11. Shiffman S, Stone AA, Hufford MR. Ecological momentary assessment. Annu Rev Clin Psychol 2008;4:1-32. [Medline: 18509902]
12. Lix LM, Graff LA, Walker JR, Clara I, Rawsthorne P, Rogala L, et al. Longitudinal study of quality of life and psychological functioning for active, fluctuating, and inactive disease patterns in inflammatory bowel disease. Inflamm Bowel Dis 2008 Nov;14(11):1575-1584. [doi: 10.1002/ibd.20511] [Medline: 18512245]

13. Bernstein CN, Blanchard JF, Rawsthorne P, Wajda A. Epidemiology of Crohn's disease and ulcerative colitis in a central Canadian province: a population-based study. Am J Epidemiol 1999 May 15;149(10):916-924. [Medline: 10342800]
14. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)--a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform 2009 Apr;42(2):377-381 [FREE Full text] [doi: 10.1016/j.jbi.2008.08.010] [Medline: 18929686]
15. Rimm EB, Giovannucci EL, Stampfer MJ, Colditz GA, Litin LB, Willett WC. Reproducibility and validity of an expanded self-administered semiquantitative food frequency questionnaire among male health professionals. Am J Epidemiol 1992 May 15;135(10):1114-1127. [Medline: 1632423]
16. Kessler RC, Andrews G, Colpe LJ, Hiripi E, Mroczek DK, Normand SLT, et al. Short screening scales to monitor population prevalences and trends in non-specific psychological distress. Psychol Med 2002 Aug;32(6):959-976. [Medline: 12214795]
17. Marrie RA, Zhang L, Lix LM, Graff LA, Walker JR, Fisk JD, et al. The validity and reliability of screening measures for depression and anxiety disorders in multiple sclerosis. Mult Scler Relat Disord 2018 Feb;20:9-15 [FREE Full text] [doi: 10.1016/j.msard.2017.12.007] [Medline: 29274564]
18. Cohen S, Kamarck T, Mermelstein R. A global measure of perceived stress. J Health Soc Behav 1983 Dec;24(4):385-396. [Medline: 6668417]
19. Schwarzer R, Jerusalem M. Self-efficacy measurement: Generalized Self-Efficacy Scale. In: Weinman J, Wright SC, Johnstone M. editors. Measures in health psychology: A user's portfolio. Windsor, UK: NFER-Nelson; 1995:35-37.
20. Salkovskis PM, Rimes KA, Warwick HMC, Clark DM. The Health Anxiety Inventory: development and validation of scales for the measurement of health anxiety and hypochondriasis. Psychol Med 2002 Jul;32(5):843-853. [Medline: 12171378]
21. Carleton RN, Norton MAPJ, Asmundson GJG. Fearing the unknown: a short version of the Intolerance of Uncertainty Scale. J Anxiety Disord 2007;21(1):105-117. [doi: 10.1016/j.janxdis.2006.03.014] [Medline: 16647833]
22. Carleton RN, Mulvogue MK, Thibodeau MA, McCabe RE, Antony MM, Asmundson GJG. Increasingly certain about uncertainty: Intolerance of uncertainty across anxiety and depression. J Anxiety Disord 2012 Apr;26(3):468-479. [doi: 10.1016/j.janxdis.2012.01.011] [Medline: 22366534]
23. Boswell JF, Thompson-Hollands J, Farchione TJ, Barlow DH. Intolerance of uncertainty: a common factor in the treatment of emotional disorders. J Clin Psychol 2013 Jun;69(6):630-645 [FREE Full text] [doi: 10.1002/jclp.21965] [Medline: 23381685]
24. Rasmussen HN, Scheier MF, Greenhouse JB. Optimism and physical health: a meta-analytic review. Ann Behav Med 2009 Jun;37(3):239-256 [FREE Full text] [doi: 10.1007/s12160-009-9111-x] [Medline: 19711142]
25. Scheier MF, Carver CS, Bridges MW. Distinguishing optimism from neuroticism (and trait anxiety, self-mastery, and self-esteem): a reevaluation of the Life Orientation Test. J Pers Soc Psychol 1994 Dec;67(6):1063-1078. [Medline: 7815302]
26. Sexton KA, Targownik L, Walker JR, Graff LA, Miller N, Rogala L, et al. Development of an IBD Symptom Self-Report Scale for Research and Clinical Application. Gastroenterology 2014 May;146(5):S-228-S-229. [doi: 10.1016/S0016-5085(14)60805-2]
27. Powell-Tuck J, Bown RL, Lennard-Jones JE. A comparison of oral prednisolone given as single or multiple daily doses for active proctocolitis. Scand J Gastroenterol 1978;13(7):833-837. [Medline: 364626]
28. Clara I, Lix LM, Walker JR, Graff LA, Miller N, Rogala L, et al. The Manitoba IBD Index: evidence for a new and simple indicator of IBD activity. Am J Gastroenterol 2009 Jul;104(7):1754-1763. [doi: 10.1038/ajg.2009.197] [Medline: 19455122]
29. Guy W. ECDEU Assessment Manual for Psychopharmacology. Rockville, MD: National Institute of Mental Health, Psychopharmacology Research Branch, Division of Extramural Research Programs; 1976.
30. Irvine EJ, Zhou Q, Thompson AK. The Short Inflammatory Bowel Disease Questionnaire: a quality of life instrument for community physicians managing inflammatory bowel disease. CCRPT Investigators. Canadian Crohn's Relapse Prevention Trial. Am J Gastroenterol 1996 Aug;91(8):1571-1578. [Medline: 8759664]
31. Irvine EJ, Feagan B, Rochon J, Archambault A, Fedorak RN, Groll A, et al. Quality of life: a valid and reliable measure of therapeutic efficacy in the treatment of inflammatory bowel disease. Canadian Crohn's Relapse Prevention Trial Study Group. Gastroenterology 1994 Feb;106(2):287-296. [Medline: 8299896]
32. Jowett SL, Seal CJ, Barton JR, Welfare MR. The short inflammatory bowel disease questionnaire is reliable and responsive to clinically important change in ulcerative colitis. Am J Gastroenterol 2001 Oct;96(10):2921-2928. [doi: 10.1111/j.1572-0241.2001.04682.x] [Medline: 11693327]
33. Statistics Canada. Canadian Community Health Survey (CCHS) Cycle 2. URL: http://www23.statcan.gc.ca:81/imdb-bmdi/pub/document/3226_D7_T9_V2-eng.pdf [accessed 2018-09-28] [WebCite Cache ID 72lLuEjWI]
34. Sheehan DV, Harnett-Sheehan K, Raj BA. The measurement of disability. Int Clin Psychopharmacol 1996 Jun;11 Suppl 3:89-95. [Medline: 8923116]
35. Kozyrskyj AL, Mustard CA. Validation of an electronic, population-based prescription database. Ann Pharmacother 1998 Nov;32(11):1152-1157. [doi: 10.1345/aph.18117] [Medline: 9825079]
36. Schoepfer AM, Beglinger C, Straumann A, Trummler M, Vavricka SR, Bruegger LE, et al. Fecal calprotectin correlates more closely with the Simple Endoscopic Score for Crohn's disease (SES-CD) than CRP, blood leukocytes, and the CDAI. Am J Gastroenterol 2010 Jan;105(1):162-169. [doi: 10.1038/ajg.2009.545] [Medline: 19755969]

37. Abraham BP, Kane S. Fecal markers: calprotectin and lactoferrin. Gastroenterol Clin North Am 2012 Jun;41(2):483-495. [doi: 10.1016/j.gtc.2012.01.007] [Medline: 22500530]
38. Manz M, Burri E, Rothen C, Tchanguizi N, Niederberger C, Rossi L, et al. Value of fecal calprotectin in the evaluation of patients with abdominal discomfort: an observational study. BMC Gastroenterol 2012 Jan 10;12:5 [FREE Full text] [doi: 10.1186/1471-230X-12-5] [Medline: 22233279]
39. Lin J, Chen J, Zuo J, Yu A, Xiao Z, Deng F, et al. Meta-analysis: fecal calprotectin for assessment of inflammatory bowel disease activity. Inflamm Bowel Dis 2014 Aug;20(8):1407-1415. [doi: 10.1097/MIB.0000000000000057] [Medline: 24983982]
40. Meuwis M, Vernier-Massouille G, Grimaud JC, Bouhnik Y, Laharie D, Piver E, GETAID (Groupe d'Étude Thérapeutique Des Affections Inflammatoires Digestives). Serum calprotectin as a biomarker for Crohn's disease. J Crohns Colitis 2013 Dec;7(12):e678-e683. [doi: 10.1016/j.crohns.2013.06.008] [Medline: 23845231]
41. Horne R, Hankins M. The Medication Adherence Report Scale (MARS): A new measurement tool for eliciting patients' reports of non-adherence. London, UK: The School of Pharmacy, University of London 2008.
42. Horne R, Weinman J. Patients' beliefs about prescribed medicines and their role in adherence to treatment in chronic physical illness. J Psychosom Res 1999 Dec;47(6):555-567. [Medline: 10661603]
43. Ediger JP, Walker JR, Graff L, Lix L, Clara I, Rawsthorne P, et al. Predictors of medication adherence in inflammatory bowel disease. Am J Gastroenterol 2007 Jul;102(7):1417-1426. [doi: 10.1111/j.1572-0241.2007.01212.x] [Medline: 17437505]
44. McLachlan G, Peel D. Finite mixture models. New York: John Wiley & Sons; 2000.
45. Hedeker D, Mermelstein RJ, Demirtas H. An application of a mixed-effects location scale model for analysis of Ecological Momentary Assessment (EMA) data. Biometrics 2008 Jun;64(2):627-634 [FREE Full text] [doi: 10.1111/j.1541-0420.2007.00924.x] [Medline: 17970819]
46. Hedeker D, Mermelstein RJ, Berbaum ML, Campbell RT. Modeling mood variation associated with smoking: an application of a heterogeneous mixed-effects model for analysis of ecological momentary assessment (EMA) data. Addiction 2009 Feb;104(2):297-307 [FREE Full text] [doi: 10.1111/j.1360-0443.2008.02435.x] [Medline: 19149827]
47. Targownik LE, Sexton KA, Bernstein MT, Beatie B, Sargent M, Walker JR, et al. The Relationship Among Perceived Stress, Symptoms, and Inflammation in Persons With Inflammatory Bowel Disease. Am J Gastroenterol 2015 Jul;110(7):1001-1013. [doi: 10.1038/ajg.2015.147] [Medline: 26077178]
48. Bolge SC, Waters H, Piech CT. Self-reported frequency and severity of disease flares, disease perception, and flare treatments in patients with ulcerative colitis: results of a national internet-based survey. Clin Ther 2010 Feb;32(2):238-245. [doi: 10.1016/j.clinthera.2010.02.010] [Medline: 20206781]
49. Galea S, Tracy M. Participation rates in epidemiologic studies. Ann Epidemiol 2007 Sep;17(9):643-653. [doi: 10.1016/j.annepidem.2007.03.013] [Medline: 17553702]
50. Inokuchi T, Kato J, Hiraoka S, Takashima S, Nakarai A, Takei D, et al. Fecal Immunochemical Test Versus Fecal Calprotectin for Prediction of Mucosal Healing in Crohn's Disease. Inflamm Bowel Dis 2016 May;22(5):1078-1085. [doi: 10.1097/MIB.0000000000000728] [Medline: 26891256]

Abbreviations

CD: Crohn disease
FCAL: fecal calprotectin
FFQ: Food Frequency Questionnaire
IBD: inflammatory bowel disease
IBDSI: Inflammatory Bowel Disease Symptom Index
K6: Kessler Screening Scale for Psychological Distress
PSS: Perceived Stress Scale
SCI: Symptom Change Indicator
SIBDQ: Short Inflammatory Bowel Disease Questionnaire
UC: ulcerative colitis

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Protocol

A Patient Registry for the Management of Uterine Fibroids in Canada: Protocol for a Multicenter, Prospective, Noninterventional Study

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Abstract

Background: Uterine fibroids are the most common benign tumor in women. Among those with fibroids, approximately 30% become symptomatic, with abnormal uterine bleeding, pelvic pain, and bulk symptoms. Despite the high prevalence of fibroids, little information is available regarding symptoms, treatment choices, and outcomes for patients.

Objective: A Canada-wide patient registry was established to understand the real-world practice. This registry included patient presentation and treatment preferences, health care provider attitudes, and clinical outcomes in the management of symptomatic uterine fibroids.

Methods: This study is a prospective, noninterventional, observational patient registry. It will include women diagnosed with uterine fibroids and being managed for symptoms. Participant inclusion criteria were (1) at least 18 years of age, (2) premenopausal with a confirmed diagnosis of uterine fibroids, and associated symptoms, and (3) initiating treatment (drug intervention, procedure intervention, or a combination of both) or watchful waiting. Patients (or legal representative) must understand the nature of the project and provide written informed consent before enrollment. Participant exclusion criteria were (1) they have known or suspected clinically significant pelvic pathology not associated with uterine fibroids, and (2) they are undergoing an emergency hysterectomy at the initial visit. Outcomes will be evaluated in the context of routine clinical practice.

Results: Participant recruitment of this registry began in July 2015. This study currently has a total sample of 1500 patients.

Conclusions: This registry, a first in Canada, will accumulate evidence on the risks and benefits of watchful waiting, and medical and procedural interventions. It will contribute to enhancing access to treatment options for patients.

Trial Registration: ClinicalTrials.gov NCT02580578; https://clinicaltrials.gov/ct2/show/NCT02580578 (Archived by WebCite at http://www.webcitation.org/6yax4Hpvr)

International Registered Report Identifier (IRRID): RR1-10.2196/10926

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KEYWORDS

Canada; leiomyoma; registries

Introduction

Uterine fibroids (UF) are benign, monoclonal, hormone-sensitive, smooth muscle tumors that represent the most common solid pelvic tumor in women [1-3]. They affect 20% to 40% of women during their reproductive years [4]. Despite their prevalence, very little is known about the etiology of the disease, burden of illness, and quality of life associated with the condition. Although most patients with UF are asymptomatic, UF can cause heavy and prolonged menstrual bleeding, pelvic pressure or pain, bulk symptoms, and reproductive dysfunction. Patients with UF show increased use of analgesics, sanitary products, and health care resources. There are more physician visits, increased absenteeism, and a decline in energy, and overall activities, including sexual activity [5]. Apart from epidemiologic data, the natural history of UF is poorly understood.

In addition to the palpation of an enlarged irregular uterine contour on pelvic examination, ultrasonography is used to confirm the diagnosis of UF [6]. Recently magnetic resonance imaging (MRI) has gained popularity, but the cost and access to this technology prohibit routine screening. In a uterus with fewer than 5 lesions, ultrasonography appears to be equally effective as detection by MRI and virtually identical for assessing their size and location [7]. However, when the number of lesions is higher, MRI exceeds the technical limitations of ultrasound in precise fibroid mapping and characterization.

A significant issue in the field of fibroid identification is the necessity for differentiating fibroids from other pathologies such as adenomyomas and uterine neoplasms. Although uncommon in women less than 40 years old [8], these conditions require the differential diagnosis with fibroids because the treatment options and prognosis may differ [9]. Patterns of use and accuracy of diagnostic imaging of UF have not been studied systematically in the publicly funded Canadian health care system.

Treatment options for UF patients should ideally address 3 goals: (1) relief of signs and symptoms, (2) sustained reduction in fibroid size, and (3) retention or enhancement of fertility if desired. At the same time, treatment should also aim to improve quality of life, minimize side effects, be convenient for patients, and target UF directly [10]. Medical, procedural, or combined treatment options are available for patients with symptomatic UF. However, there were no medications to treat these women in Canada until 2013 when ulipristal acetate (UPA) was approved.

UPA has shown to be more effective than placebo [11] and as effective as the injectable gonadotropin-releasing hormone agonist leuprolide acetate [12] for treating UF symptoms. Leuprolide acetate received Health Canada indication for preoperative improvement of anemia in symptomatic UF women in 2017 [13]. The uptake, long-term clinical and patient-reported outcomes, efficacy, safety, as well as the pharmacoeconomics of indicated and off-label treatment options for these patients in Canada, have yet to be determined.

In the past 15 years, there has been only 1 completed registry for patients with UF who have undergone uterine artery embolization [14]. In the United States, the COMPARE-UF trial is underway [15]. A Canadian prospective patient registry provides the opportunity to address many unanswered questions, particularly the management patterns and outcomes associated with different treatments for UF and patients' preferences for, and satisfaction with, managing UF symptoms.

With this background in mind, the objectives of this study are to (1) enhance the understanding of the natural history of symptomatic UF, (2) understand Canadian provider and patient preferences for managing symptomatic UF, (3) examine factors that have an impact on the uptake of UF treatment options and compliance with therapy, (4) examine the effectiveness and efficiency of UF treatment options across ethnicities in real-world practice in Canada, and (5) provide real-world data characterizing long-term clinical and patient-reported outcomes, including effectiveness and safety, associated with different UF management options.

Methods

Overall Study Design and Plan

The CAnadian women wiTh Uterine fibroids REgistry (CAPTURE) is a prospective, observational cohort study (NCT02580578) that will include women who have been diagnosed with symptomatic UF. Outcomes will be evaluated as part of routine clinical practice. The target study population will include patients with a diagnosis of UF from 20 study sites across Canada. Participating physicians will not be required to perform any medical procedure that is outside their normal clinical practice. Serious and nonserious adverse drug reactions (ADRs) will be followed up as per local standard of care and as expected in an observational research study. Similarly, both serious and nonserious adverse events (AEs) during and following procedural intervention will be reported. Each study site was responsible for local ethics review board approval as per their institutional policy.

Participants

Approximately 1000 patients will be enrolled from 20 Canadian investigational sites, including both academic and community practices. Inclusion criteria for the study are premenopausal women at least 18 years of age with confirmed diagnosis and symptoms associated with UF that are being observed (watchful waiting), currently being treated, or initiating treatment (drug intervention, procedure intervention, or a combination of both). All patients (and the patient's authorized legal representative) should understand the nature of the project and provide written informed consent before or at the initial study visit. Exclusion criteria for the study are known or suspected significant pelvic pathology not associated with UF and patients undergoing an emergency hysterectomy at the initial visit.

Withdrawal of Participants

Participation in this registry is voluntary, and patients may withdraw at any time and for any reason. Once the patient informs the site staff that she wishes to withdraw her participation, a "Withdrawal from registry" form will be

completed with the date and reason. The patient will be informed that all data collected up to that point will be used in the analysis. From that point on, the patient will no longer be contacted for the registry, and no further data on that participant will be collected.

Participants Lost to Follow Up

Efforts will be made to keep patients in the registry for at least 24 months. A patient will be considered to have missed a study visit after all efforts have been made by site personnel to contact the patient to reschedule within 1 month of the missed appointment. If a patient has missed a follow-up visit, all efforts should be made to reach the patient to ensure that subsequent follow-up visits are completed.

Study Visits

The visit schedule is comprised of 4 study visits (baseline, 3- to 6-month, 12-month, and 24-month; Table 1) and pre-, intra-, and postoperative visits for patients undergoing procedural interventions (Table 2).

Baseline Visit

The baseline visit will involve (1) obtaining informed consent, (2) checking for inclusion/exclusion criteria, (3) collecting demographic information, (4) obtaining a medical history, and (5) assessing patient current health status. This will be followed by patient assessments that involve questions on UFs using the EuroQol 5-Dimensions 5-Levels (EQ-5D-5L) survey, the Uterine Fibroid Symptom and Quality of Life (UFS-QOL) questionnaire, the Aberdeen Menorrhagia Severity Scale (AMSS) questionnaire, and evaluation for concomitant medications and history of previous procedural interventions.

The EQ-5D-5L [16] is a validated 5-question survey with a visual analog scale used to measure health outcomes that provides a simple descriptive profile and a single index value for health status. The UFS-QOL [17] is a validated 37-question disease-specific symptom and health-related quality of life questionnaire for UF. It has been used extensively in studies to assess the impact of the disease in patients and treatment options in randomized clinical trials. The AMSS questionnaire is a validated 15-question survey that evaluates the severity and effect of bleeding that occurs during and between menses. There are 7 baseline questions for UF patients asking about the purpose of their visit and what outcome they are hoping to achieve.

If deemed eligible for registry participation, the patient will return for a visit in 3 to 6 months. When available, imaging and other test results (biopsies, blood work) will also be documented.

Table 1. Schedule of events of the CAPTURE study at baseline and scheduled visits.

Examinations	Scheduled follow-up visits			
	Baseline	3- to 6-month[a]	12-month[a]	24-month[a]
Signed informed consent form[b]	✓	—	—	—
Inclusion/exclusion criteria	✓	—	—	—
Demographics	✓	—	—	—
Medical history	✓	—	—	—
Fertility wishes	✓	✓	✓	✓
Blood work (hemoglobin)[c]	✓	✓	✓	✓
Gynecologic symptoms	✓	✓	✓	✓
Ultrasound of fibroids	✓	✓	✓	✓
Type and location of fibroids	✓	—	—	—
Endometrial biopsy[c]	✓	—	—	—
Planned/updated management plan	✓	✓	✓	✓
UFS-QOL[d]	✓	✓	✓	✓
Bleeding assessment[e]	✓	✓	✓	✓
EQ-5D-5L[f]	✓	✓	✓	✓
Concomitant medications	✓	✓	✓	✓
Adverse events	—	✓	✓	✓

[a]Visits can be performed by telephone or in clinic; however, an in-person visit is preferred.

[b]Must be obtained from patient prior to study enrollment.

[c]To be captured if available.

[d]UFS-QOL: Uterine Fibroid Symptom and Quality of Life questionnaire.

[e]Tool for assessment is the Aberdeen Menorrhagia Severity Scale questionnaire.

[f]EQ-5D-5L: EuroQol 5-dimensions 5-levels survey used to measure health status.

Table 2. Schedule of events of the CAPTURE study at procedural intervention and hysterectomy.

Examinations	Procedural intervention[a]			Hysterectomy
	Preoperative	Intraoperative	Postoperative	1-year follow up
Signed informed consent form	—	—	—	—
Inclusion/exclusion criteria	—	—	—	—
Demographics	—	—	—	—
Medical history	—	—	—	—
Fertility wishes	—	—	—	—
Blood work (hemoglobin)[b]	✓	—	—	—
Gynecologic symptoms	—	—	—	✓
Ultrasound of fibroids	✓	—	—	—
Type and location of fibroids	—	—	—	—
Endometrial biopsy	—	—	✓	—
Planned/updated management plan	✓	—	—	—
UFS-QOL[c]	✓	—	✓	✓
Bleeding assessment[d]	✓	—	✓	—
EQ-5D-5L[e]	✓	—	✓	✓
Concomitant medications	✓	—	—	—
Adverse event	✓	✓	✓	—

[a]Procedural intervention is not mandatory in the registry, and data will be collected if physician and patient decide on a procedural intervention to address symptoms associated with uterine fibroids.

[b]To be captured if available.

[c]UFS-QOL: Uterine Fibroid Symptom and Quality of Life questionnaire.

[d]Not required if patient undergoes hysterectomy procedure. Otherwise the tool for assessment is the Aberdeen Menorrhagia Severity Scale questionnaire.

[e]EQ-5D-5L: EuroQol 5-dimensions 5-levels survey used to measure health status.

Visits at Three to Six Months, Twelve Months, and Twenty-Four Months

These visits can be performed in the clinic or via telephone; however, an in-person visit is preferred. Participants will be evaluated for updates and an assessment of the management plan, and for ADRs (if medication was prescribed at the previous visit). Also, patient questionnaires (EQ-5D-5L, UFS-QOL, and AMSS) will be administered. Follow up will occur after the baseline meeting at 3 to 6 months, 12 months, and 24 months.

Preoperative Visit

This visit will only occur if the patient and physician agree on a procedural intervention. During this visit, participants will be evaluated for updates and an assessment of the management plan, and for ADRs (if medication was prescribed at the previous visit). Also, patient questionnaires (EQ-5D-5L, UFS-QOL, and AMSS) will be administered.

Intraoperative Visit

This visit will only occur if the patient and physician agree on a procedural intervention. During this visit, information on the procedure performed and the AEs will be obtained. Specific details on the type of procedure, route, and surgical times will be recorded. Intraoperative description of outcomes, including morcellation (if performed), will be documented. In the case of myomectomy, fibroid cleavage planes and density (subjective) of the fibroids will be obtained as well.

Postoperative Visit

This visit will only occur if the patient and physician agree on a procedural intervention. During this visit, information on AEs following the procedure, pathology, and patient questionnaires (EQ-5D-5L, UFS-QOL, and AMSS) will be recorded.

Hysterectomy Postoperative Follow Up

If a patient undergoes a hysterectomy, a follow-up visit will occur 1 year after the hysterectomy (in addition to the postoperative visit). This follow up will replace all remaining scheduled follow-up study visits. Information on postoperative symptoms, overall satisfaction, UFS-QOL-Hysterectomy, and EQ-5D-5L will be obtained. Once this follow up is completed, the patient will be deemed to have completed all study visits.

Unscheduled Visits

Unscheduled visits (other than the prescribed appointments) are any unexpected visits, including emergency assessments or changes to care plans. Participants will be assessed for the reason of the visit, update and evaluation of the management plan, and ADRs (if medication was previously prescribed).

Pregnancy Follow Up

If an unplanned pregnancy occurs with hormonal medical therapy during this study, a serious AE will be recorded. Also, the "Pregnancy follow up" form will be completed to capture baseline pregnancy information. If the patient consents to be followed up on the outcome of the pregnancy, then postdelivery follow-up information will be collected once available. No study visits will be completed during the pregnancy. Following delivery, the patient will resume the study visit schedule until completion.

Assessment of Clinical Efficacy and Safety

This is a patient registry that tracks the routine practice and management of patients with UF in Canada. The physician will collect data at the initial and follow-up visits between 3 to 6 months, 12 months, and 24 months. Also, if a procedural intervention is performed, pre-, intra-, and postoperative data will be captured. Patients will be asked to complete the EQ-5D-5L, UFS-QOL, and the brief bleeding questionnaires as per the visit schedule outlined in Tables 1 and 2.

Duration of Study

The duration of the study will be 2 years from the recruitment of the final patient, which occurred in February 2018. It is expected that the last visit of the final patient will occur in February 2020.

Statistical Methods

The analysis will include all patients enrolled in the study who have been entered into the database.

Statistical Analysis

The goal of this study is to establish a registry of Canadian patients with symptomatic UF. We have recruited a sample of 1500 patients to help describe the management of UF in this population.

Initially, exploratory data analysis will summarize all variables of interest by reporting means and standard deviations for continuous variables, and frequencies (percentages) for categorical variables. Analysis of variance will be used to compare continuous variables between treatment groups of interest. Chi-square tests will be used to compare categorical variables between the 2 groups. A linear mixed model will be employed to examine the association between treatment groups while adjusting for other covariates of clinical interest. These variables include demographics, UF history, comorbidities, medications, and medical tests (both current and previous).

The model will include a time-by-treatment-interaction term to determine whether treatments have improved quality of life relative to other treatment groups. Furthermore, a random effect will be included at the patient level to incorporate correlation arising from the repeated measures design of the study.

Since this is an observational registry, missing data and drop-outs (ie, early study termination) are expected. Statistical techniques will be used to examine the missing data (including logistic regression) and, if feasible, multiple imputations will be used to make any adjustments.

Additionally, where imputation techniques are not adequate, sensitivity analysis will be employed. All parameter estimates, confidence intervals, and *P* values will be reported from the model, and a 2-sided significance level of .05 will be used.

The original terms used by participating physicians to identify ADRs will be coded using the Medical Dictionary for Regulatory Activities (MedDRA). The MedDRA system organ class and preferred term will be used to present the number and percentage of patients with ADRs, the drug relationship, seriousness, and intensity of ADRs. Chi-square tests will be employed to compare the number of ADRs between groups of interest.

Data Management Process

Overall coordination of the registry will be led by a steering committee that includes 6 academic gynecologists and 1 community gynecologist. Committee responsibilities include establishing the registry database and protocol, appointing a scientific committee for data analysis and interpretation, and governing the dissemination of the registry findings through a publication plan. All members of the steering committee have a vote on decision making, with the Chair providing a deciding vote in the event of a tie. The study sponsor, Allergan Canada, does not have a vote or seat on the steering committee but will facilitate meetings.

All study data will be captured on HealthDiary, which is a Web-based electronic data-capture system. Data will be managed by the Applied Health Research Center (AHRC), a service unit within the HUB Health Research Solutions and fully integrated with the Li Ka Shing Knowledge Institute of St. Michael's Hospital, Toronto, Ontario, Canada. The AHRC is a full-service clinical research coordinating center staffed with highly trained individuals including statisticians, methodologists, research coordinators, contract and finance managers, and research informatics specialists. The facility will serve as the data management center. It has managed large randomized trials, cohort studies, and patient registries across provincial and international borders, ensuring privacy regulations using state-of-the-art, Web-based, data management software. The center will be responsible for developing the electronic case report form (eCRF), conducting data management, and issuing and clarifying queries with the participating sites. The research database includes automated edit and logic checks to assist with the data management activities. Data entry screens and edit checks will be tested with mock patient data and removed from the database before beginning the study. In addition to programmed edit and logic checks, manual data verification, and consistency checks will be performed to ensure valid, relevant, and complete data for analysis.

Medical history and concomitant medical conditions/diseases will be coded according to MedDRA. Data handling procedures, including edit check specifications, data entry guide, authorized corrections, coding instructions, and locking procedure, will be detailed in the study data management plan.

Data Quality Assurance

The database will be secured and enable quality control to be performed at the time of data entry. Quality control will focus on value ranges and missing data. Any discrepancies that occur during eCRF data entry will be flagged in real time by the system and will be saved until addressed by the data entry personnel.

In compliance with Good Clinical Practice and regulatory requirements, the sponsor, a third party on behalf of the sponsor, health regulatory agencies, or research ethics boards may conduct quality assurance audits at any time during or following the study. The participating investigator must agree to allow auditors direct access to all project-related documents, including source documents, and must agree to allocate their time and the time of their project staff to the auditors to discuss findings and issues.

Results

Participant recruitment for this registry began in July 2015. The registry has recruited 1500 patients, with the first patient enrolled in the second half of 2015. Patient follow up will occur for up to 2 years, with the last patient visit occurring in 2020. It is anticipated that national/industrial funding will be available to continue this initiative beyond 2020 based on the information generated from this registry.

Discussion

Importance of the CAPTURE Registry

Despite the prominence of UF and their detrimental effects on patient health, little is known about many aspects of the condition, including the etiology of the disease, the natural history of UF, the impact of UF on fertility and pregnancy outcomes, and the effectiveness of UF treatments in real-world clinical practice. There are virtually no well-designed, long-term, epidemiologic studies published in this disease area. The evidence on the comparative long-term effectiveness of treatment options is also of poor quality. The Agency for Healthcare Research and Quality (AHRQ) has published reviews on the state of the evidence for the management of UF in 2001 and 2007. A more recent review was published by Singh and Belland [10] outlining clinical data on the medical and surgical management of UF along with a treatment algorithm to assist health care professionals.

Our literature search for established UF registries revealed only 1 in the past 15 years called the FIBROID Registry. This was a multicenter, prospective, longitudinal study of the short- and long-term outcomes of uterine artery embolization [14]. Despite the lack of data on the management of UF, the future of obtaining real-world data in this area appears promising. In addition to this registry in Canada, registries in both the United States and Europe have been announced or are currently underway. In the second half of 2014, the Patient-Centered Outcomes Research Institute and AHRQ announced that the Duke University School of Medicine's Department of Obstetrics and Gynecology and the Duke Clinical Research Institute will lead a 5-year patient registry to evaluate the effectiveness of different treatment strategies for UF patients.

In Canada, there is a lack of documented data characterizing the UF patient population, treatment options, and outcomes associated with women who have UF. Also, no data exist regarding patient preference and satisfaction related to their management. Moreover, with the introduction of UPA—the first Health Canada-approved medication for the treatment of UF—an evaluation of effectiveness and safety is desirable. It should be noted that UPA is undergoing a clinical investigation in the United States and is currently not approved. In Europe, a prospective, observational, noninterventional study is ongoing to document real-world data related to current treatment patterns and outcomes associated with UPA in patients with symptoms associated with UF. This registry is collecting valuable real-world data in Canada on the medical and procedural management of UF to address these issues.

Potential Limitations

This registry has some limitations. The instruments used at different visits are self-reported, which may result in reporting bias. The noninterventional design can lead to selection bias as well as confounding. Finally, failure to follow up and the expected attrition of the participants at subsequent visits following recruitment could impact on the sample size, thus limiting the external validity.

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Authors' Contributions

The members of the CAPTURE Registry Steering Committee are as follows: Dr Philippe Laberge (Chair), Dr Sari Kives, Dr Nicholas Leyland, Dr George Vilos, Dr Joshua Polsky, and Dr Liane Belland. The members of the CAPTURE Publications Committee are the first author (MAB), Dr Ally Murji, and Dr Olga Bougie.

Conflicts of Interest

MAB has participated in advisory boards for Allergan Canada and AbbVie. PJ is an employee of Allergan. SSS has participated in advisory boards, as a primary investigator, and presented continuing medical education events sponsored by Allergan Canada, Bayer Pharma, and AbbVie.

References

1. Baird DD, Dunson DB, Hill MC, Cousins D, Schectman JM. High cumulative incidence of uterine leiomyoma in black and white women: ultrasound evidence. Am J Obstet Gynecol 2003 Jan;188(1):100-107. [Medline: 12548202]
2. Bulun SE. Uterine fibroids. N Engl J Med 2013 Oct 03;369(14):1344-1355. [doi: 10.1056/NEJMra1209993] [Medline: 24088094]
3. Zimmermann A, Bernuit D, Gerlinger C, Schaefers M, Geppert K. Prevalence, symptoms and management of uterine fibroids: an international internet-based survey of 21,746 women. BMC Womens Health 2012 Mar 26;12:6 [FREE Full text] [doi: 10.1186/1472-6874-12-6] [Medline: 22448610]
4. Wallach EE, Vlahos NF. Uterine myomas: an overview of development, clinical features, and management. Obstet Gynecol 2004 Aug;104(2):393-406. [doi: 10.1097/01.AOG.0000136079.62513.39] [Medline: 15292018]
5. Vilos G, Vilos A, Ferrazzi S. Symptomatic uterine fibroids (UFs) are common in premenopausal Canadian women and lead to reduced quality of life (QoL) across multiple domains. J Obstet Gynecol Can 2014;36(Suppl 1):S26.
6. Vilos GA, Allaire C, Laberge P, Leyland N. The management of uterine leiomyomas. J Obstet Gynaecol Can 2015 Feb;37(2):157-178. [doi: 10.1016/S1701-2163(15)30338-8] [Medline: 25767949]
7. Dueholm M, Lundorf E, Hansen ES, Ledertoug S, Olesen F. Accuracy of magnetic resonance imaging and transvaginal ultrasonography in the diagnosis, mapping, and measurement of uterine myomas. Am J Obstet Gynecol 2002 Mar;186(3):409-415. [Medline: 11904599]
8. Vercellini P, Viganò P, Somigliana E, Daguati R, Abbiati A, Fedele L. Adenomyosis: epidemiological factors. Best Pract Res Clin Obstet Gynaecol 2006 Aug;20(4):465-477. [doi: 10.1016/j.bpobgyn.2006.01.017] [Medline: 16563868]
9. Farquhar C, Brosens I. Medical and surgical management of adenomyosis. Best Pract Res Clin Obstet Gynaecol 2006 Aug;20(4):603-616. [doi: 10.1016/j.bpobgyn.2006.01.012] [Medline: 16563872]
10. Singh SS, Belland L. Contemporary management of uterine fibroids: focus on emerging medical treatments. Curr Med Res Opin 2015 Jan;31(1):1-12. [doi: 10.1185/03007995.2014.982246] [Medline: 25365466]
11. Donnez J, Tatarchuk TF, Bouchard P, Puscasiu L, Zakharenko NF, Ivanova T, PEARL I Study Group. Ulipristal acetate versus placebo for fibroid treatment before surgery. N Engl J Med 2012 Feb 02;366(5):409-420. [doi: 10.1056/NEJMoa1103182] [Medline: 22296075]
12. Donnez J, Tomaszewski J, Vázquez F, Bouchard P, Lemieszczuk B, Baró F, PEARL II Study Group. Ulipristal acetate versus leuprolide acetate for uterine fibroids. N Engl J Med 2012 Feb 02;366(5):421-432. [doi: 10.1056/NEJMoa1103180] [Medline: 22296076]
13. AbbVie Corporation. Product Monograph. Lupron Depot. Leuprolide acetate for depot suspension. 2017. URL: http://www.abbvie.ca/content/dam/abbviecorp/ca/en/docs/LUPRON_DEPOT_ENDO_PM_EN.pdf [WebCite Cache ID 6yZhWmsSd]
14. Myers ER, Goodwin S, Landow W, Mauro M, Peterson E, Pron G, FIBROID Investigators. Prospective data collection of a new procedure by a specialty society: the FIBROID registry. Obstet Gynecol 2005 Jul;106(1):44-51. [doi: 10.1097/01.AOG.0000165827.66541.dd] [Medline: 15994616]
15. Stewart EA. Uterine fibroids. Lancet 2001 Jan 27;357(9252):293-298. [doi: 10.1016/S0140-6736(00)03622-9] [Medline: 11214143]
16. EuroQol. EQ-5D-5L. 2017. URL: https://euroqol.org/eq-5d-instruments/eq-5d-5l-about/ [accessed 2018-04-10] [WebCite Cache ID 6yZhfVbqO]
17. SIRFoundation. Uterine Fibroid Symptom Health-Related Quality of Life Questionnaire (UFS-QOL). 2017. URL: https://www.sirfoundation.org/clinical-research2/clinical-research3/ufs-qol/ [accessed 2018-04-08] [WebCite Cache ID 6yZhrtmu5]

Abbreviations

ADR: adverse drug reaction
AE: adverse event
AHRC: Applied Health Research Center
AHRQ: Agency for Healthcare Research and Quality
AMSS: Aberdeen Menorrhagia Severity Scale
CAPTURE: CAnadian women wiTh Uterine fibroids REgistry
eCRF: electronic case report form
EQ-5D-5L: EuroQol 5-dimensions 5-levels
MedDRA: Medical Dictionary for Regulatory Activities
MRI: magnetic resonance imaging
UF: uterine fibroids

UFS-QOL: Uterine Fibroid Symptom and Quality of Life questionnaire
UPA: ulipristal acetate

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Protocol

Simulation Modeling for Psychiatric Service Planning: Protocol for a Mixed-Methods Study

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Abstract

Background: Mental health service managers must take into account multiple factors when making decisions about the best way to deliver care to clients across increasingly larger service areas. This task is made more difficult by the lack of evidence and tools historically available to inform these decisions. In recent decades, the increasing availability of epidemiological and service use data for mental illness has solved the problem of evidence, but there still exists a challenge to make these data easily accessible and understandable for managers.

Objective: This study aims to develop a simulation modeling tool to allow managers to explore various service configurations in virtual reality, enabling predictions to be made about the cost and quality of care.

Methods: This is a longitudinal, mixed-methods case study, comprising overlapping intervention and evaluation phases. In partnership with senior managers of a mental health program, the researchers will develop a series of simulation models in Arena to address key strategic issues facing the service. Thematic and content analyses of semistructured interviews, meeting observations, and document analysis will be used to evaluate the process of model implementation and the outcomes for both researchers and managers. The study is being conducted in Australia.

Results: Data collection has been ongoing since late 2013. To date, 3 prototype simulation models have been developed and presented to senior managers, and 18 evaluation interviews have been conducted. The project is expected to conclude in late 2018.

Conclusions: Findings of this study have the potential to shape decision making in mental health service delivery, by providing key examples of how to integrate patient data using simulation modeling. In addition, the results will provide key insights into how researchers and consultants can effectively implement simulation modeling in real-world health care organizations.

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KEYWORDS

decision making; health care; health services administration; mental health; protocol; mixed-methods; modeling; simulation

Introduction

The health care sector is characterized by complexity, where balancing the demands of multiple stakeholders in geographically disparate areas makes the task of service-wide strategy planning extraordinarily difficult [1,2]. In mental health, this is exacerbated by the heterogeneity of illness severity, persistence, treatment response, and treatment need, as well as the multitude of entry points and patient pathways through the mental health system [3].

In the clinical space, this complex environment is managed through the use of evidence-based practice [4] and clinical simulations to provide staff with decision-making experience in a low-risk environment [5]. In health care management, mechanisms for evidence-based decision making are much less ubiquitous. Instead, managers have traditionally relied on personal knowledge and experience to make small incremental service changes within a quality improvement framework [6]. Unfortunately, the inherent risks of the "try it and see" approach make it unsuitable for the large-scale service reforms currently being called for in the Australian mental health sector [7]. Thankfully, ongoing improvements in technology and electronic patient records have created a fertile environment for the translation of decision support tools from other sectors, including that of simulation modeling.

Simulation models are simplified abstractions of real systems, often created on a computer. They allow users to predict future states by tracking changes in the system over time, with these changes determined by attributes assigned to individuals or entities (agent-based modeling), time-specific state transitions (Markov models), events (discrete event simulation), or system flows (system dynamics) [8]. Simulation modeling is claimed to improve the rationality of decision makers and therefore improve decision quality [9], by allowing problem boundaries and alternatives to be explored safely and inexpensively [10,11].

However, little direct evidence is provided to support these claims of improved decision making outcomes. This is due to a general lack of reporting on the implementation of simulation models, with multiple reviews of health care simulation highlighting this as a key problem facing the literature [12-18]. Indeed, a recent review of mental health care simulation found only 10 papers reporting basic details of model implementation [8]. While this lack of reporting may reflect publication bias, it more likely reflects the difficulty in implementation, including the time and financial costs associated with increasing model complexity to match the clinical complexity of the health care environment. However, it is this very complexity that calls for the use of simulation and the transparent reporting of implementation.

Hence, this paper aims to describe the protocol for the development and implementation evaluation of a simulation model depicting the real-world activities of an Australian public mental health service (MHS).

The primary aims of this study are (1) to develop a sophisticated health care management decision support tool and bring it into practical use by managers of MHS as they go about service reform and redevelopment and (2) to evaluate the effectiveness of this decision support tool in improving the process and outcome of strategic decision making by MHS managers.

Methods

Study Design

The intervention and evaluation follow an iterative, mixed-method design. The intervention and evaluation timelines are staggered, but intentionally overlap, to allow evaluation results to inform refinements to the intervention in the latter stages of the study. The intervention was designed and overseen by GNM, and the evaluation was designed and conducted by KML.

Intervention Design

The intervention has 4 major phases: (1) development of a conceptual framework for the simulation model; (2) integration with simulation software; (3) validation of the model; and (4) implementation of the model within the MHS (Figure 1). In the first phase, we will analyze the components and functionalities of a mental health system and develop the architecture of a generic framework for the simulation model so that it can be embedded into any commercially available simulation modeling tool. In the second phase, we will embed the framework into Arena simulation software (a widely used modeling tool). The third phase will involve extensive validation of the model using data from the MHS. In the final phase, the model will be implemented as a decision-making tool within the MHS. The tasks in the phases will occur in parallel with some overlap between phases to provide a mechanism for each component to benefit from the outcomes of the progressive development and evaluation.

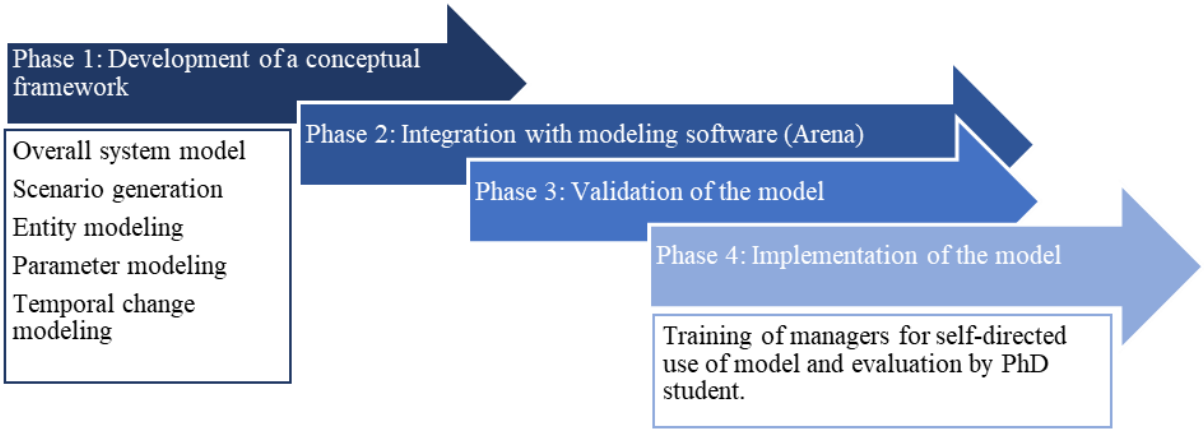
Evaluation Design

The evaluation design is a longitudinal, mixed-method case study that parallels the intervention. The analysis focuses on 2 levels: outcome and process.

Outcome will be measured by changes in mental models, reflecting increased decision process agreement and increased similarity to the rational decision-making model [19]. In addition, the outcome will be measured by researcher and participant perceptions of the intervention success, behavioral change, and cognitive change, as extracted by the thematic analysis from exit interviews.

The process will be assessed by group changes in behavioral and linguistic patterns during the intervention workshops, reflecting increased similarity to the features of good group decision-making processes [20]. These observations will be triangulated against participants' self-report of workshop success extracted by an evaluation questionnaire.

Figure 1. Intervention design.



Study Setting

The research was conducted with the cooperation of the senior leadership group (SLG) of a major public MHS in Australia. The MHS provides government-funded inpatient and community mental health services across the age spectrum, with different, but overlapping, catchment areas for Early in Life Mental Health Services (<25 years), adult, and aged (<65 years) services. There are 3 operational service groups, Early in Life Mental Health Services, community services, and bed-based services, and 3 primary hospital sites, which were added to the organizational chart in 2016. The MHS employs approximately 800 staff members who provide approximately 250,000 client contacts per year, at a total cost of Aus $125 million, 8.0% of the health provider's operating expenditure.

Strategic decision making for the MHS lies with the SLG. Members of the group attend monthly meetings as representatives of their clinical specialty (psychiatrists, psychologists, allied health, and nurses), operational units, administrative units (finance and human resources), and allied research/university groups. The membership of the SLG includes the Chief Investigator (CI) and an Associate Investigator of the intervention project, who brokered access to the group.

Recruitment

At the start of the evaluation project, off-the-record interviews were conducted by KML with organizational gatekeepers (ie, MHS managers who were also investigators on the project) to gain a basic understanding of strategic decision making in the MHS. In addition, the Executive Director invited the evaluator (KML) to brief participants on the project (October 2013) and informally observe a senior leadership meeting (November 2013).

The SLG emailing list was then used to invite participants to workshops and interviews; this ensured that data were collected only from active decision makers and members of the SLG. All participants were contacted at least 3 times for each data collection point, unless they had previously withdrawn from the study. All communication regarding meeting scheduling was logged, including cancellations and rescheduling. Signed consent was obtained from all participants during their first in-person contact with the study. The project was approved by the Human Research Ethics Committee of the partner MHS, with approval being valid from December 5, 2013 to January 9, 2019.

Adaptations to Recruitment

Owing to instability in the membership and meeting schedule of the SLG during 2014-15, participant access for interventions and their evaluation became limited. There was also marked organizational staff turnover, with 9 managerial departures, 8 internal promotions, and 4 external hires. Only 6 of the recruited participants remained in the senior management group for the duration of the project.

For the intervention, engagement became reliant on the interests of individual participants, with ad-hoc one-on-one and small group discussions replacing workshops and presentations with the entire SLG. These interactions were facilitated by the dual membership of the CI as both a researcher and participant.

For evaluation, the scope of the project was expanded to include the experiences of the researchers in responding to this environment. Hence, all researchers who were actively involved in the project between 2014 and 2016, defined by attendance at a minimum one project meeting, were invited to participate in interviews in 2017. Furthermore, research team meeting minutes and notes were retrospectively added to the data analysis, with the consent of the research team and the appropriate ethics amendments.

Intervention

Phase 1: Development of a Conceptual Framework

In the first phase, we will analyze the components of a mental health system and develop a generic framework for the simulation model. Subphases will be (1) scenario generation;

(2) entity modeling; (3) parameter modeling; (4) temporal changes modeling; and (5) output.

Scenario Generation

Participants will be consulted to determine the scenarios to be modeled. However, 3 general model scenarios are planned: (1) policy change affecting the structure of services; (2) population distribution changes; and (3) organizational innovation in the delivery of care models.

Entity Modeling

The main entities of this model are patients, staff, services, and resources (eg, budget allocation), with their interactions representing the activities of an actual health care system. A priority-based queuing model [21,22] will be adopted to allocate services based on patient severity and need. A patient will be allocated for a set of services within a selected service component where a particular service is provided by a set of staff members who use a set of resources.

Parameter Modeling

Parameter modeling consists of 2 components, namely, calculation and prediction. During the model building phase, this module will calculate arrival and transition rates and the length of stay using the observational data for a given scenario. During the validation and predictive assessment phases, the values of the above parameters will be predicted taking into consideration the expected changes and the data for validation.

Temporal Changes Modeling

The temporal changes that mainly influence the mental health system are demographics and technological changes. Demographic changes largely result from changes in birth and migration rates and will be projected from data available through the Australian Bureau of Statistics.

Output

For assessing the impact of a service component or policy option in terms of health gain, we plan to use 2 quantitative measures: quality-adjusted life year (QALY) and disability-adjusted life year (DALY).

QALY is an outcome measure for evaluating the burden of disease. It takes into account both the quantity and the quality of the extra life provided by a health care intervention or policy option and is calculated as the product of the life expectancy and the quality of the remaining years. While QALY is useful for cost-effectiveness analysis, weights used in calculation are not linked to a particular disease, condition, or disability, but are rather based on an individual's health state.

DALY is a measure of disease burden that captures both morbidity and mortality effects for a wide range of disorders and interventions and the baseline information for the health status in Australia is readily available [23]. The DALY incorporates disability weight that assigns different weights at different ages; and disability weight values for particular mental health disorders and different categories (eg, mild and severe) are available in the literature.

The model will allow end users to choose either of the measures through a graphical user interface. Apart from QALY and DALY, impacts on blocking rate and resource utilization will be investigated, and specific illness outcomes could be considered, depending on the focus of the scenario chosen.

Phase 2: Integration With Arena

A specialist in modeling will build a simulation model in Arena [24], a widely used discrete-event simulation tool. It will include different modules that represent process, entity, queue, and others elements. The output of the simulation model will be used to create custom statistics, a built-in feature in Arena. Once developed, it will require minimal effort by MHS managers to upload instances of a particular entity or update them as required, offering flexibility and the capacity for managers to use the system autonomously.

Phase 3: Validation of the Model

The data collected from the MHS will be divided into 2 sets. One will be used for model building, while the other will be used for validation, the 2 sets being mutually exclusive. To test quantitatively how adequately the model represents the actual system, within the service components of a particular scenario, we will compare the model output with actual historical (ground truth) values. For this, the values of model output parameters (eg, changes in QALYs, waiting time, and resource utilization) will be compared with their respective ground truth values through a statistical goodness-of-fit test (eg, chi-square test). Similarly, to test the model for predictive performance, the output of the model in response to the validation data will be quantitatively compared with their corresponding ground truth values (known because the validation set is also part of the available historical data). Strong agreement between the model output and the corresponding actual values will assure the model's accuracy in emulating the actual system.

Phase 4: Implementation of the Model

The project will also involve the provision of training to MHS managers in the use of the simulation modeling tool to guide decision making regarding the configuration and resourcing of MHS. Such training and the availability of the simulation model will enable MHS managers to adopt new approaches to service management, with their decision making being underpinned by much stronger evidence than is currently available.

Adaptations to the Intervention

To capitalize on participant interest stimulated by the October 2013 project briefing, a program logic modeling (PLM) workshop was scheduled during the SLG meeting in December 2013, with a follow-up workshop scheduled for July 2014. The aim was to generate inputs for the creation of the simulation models (phase 1 of the project) and to continue participant engagement in the project. The PLM workshops were facilitated by an experienced external contractor. In the first workshop, participants were prompted to identify strategic issues challenging the MHS and their consequences for the organization, staff, and consumer. The second workshop aimed to validate the outputs of the previous workshop and confirm the organizational structure of the MHS prior to integration with the modeling software.

Evaluation

Process Change

Research on problem structuring methods and group model building claim that the process is often more influential than the final model in the decision making of users [25,26]. The development of PLM as a significant element of the project allowed this claim to be tested.

Immediate changes in decision-making process will be evaluated through the observation of participants' interactions during simulation workshops and a pilot self-report survey on workshop effectiveness. Survey questionnaire items were derived from a frequency analysis of the claimed benefits of PLM in journal papers [27-31], focusing on the PLM methodology and evaluation. The literature search yielded a list of 39 nonunique descriptors. The content analysis of these descriptors revealed 4 overarching categories—clarity, communication, action, and buy-in. Items were selected for face validity and based on the prevalence of categories in the literature. Hence, clarity (6 items) and communication (4 items) were more heavily represented than action and buy-in (2 items each). This yielded 14 items rated on a Likert scale (5=*strongly agree* and 1=*strongly disagree*; Multimedia Appendix 1).

Mental Model Change

The primary outcome of interest is a change in the strategic decision making of the SLG to incorporate greater amounts of evidence. This will be captured by comparing the decision-making mental models of SLG members pre- and postintervention, within the group (similarity), and to an ideal standard (ie, rational decision making and accuracy). Mental model similarity and accuracy are both predictive of increased group performance [32,33].

To extract mental models of current decision-making, participants were asked, "If a new staff member arrived today, what would you tell them about how decisions get made by the management team?" They will then be prompted with statements such as "and before that?" or "after that?" Concept maps of current decision-making processes were created during the interview and validated against interview transcripts. To assess the test-retest reliability of the elicitation method, during the exit interview, participants were again asked, "If a new staff member arrived today, what would you tell them about how decisions get made by the management team?."

Adaptations to Evaluation

Adaptations to the intervention necessitated an adaptation to the evaluation. Of most impact was the lack of group meetings or workshops, meaning that group processes were no longer able to be directly studied through observation or questionnaire. The *ad-hoc* nature of meetings with participants exacerbates the lack of structured data collection, necessitating a greater reliance on the document analysis and interview content in the analysis stages.

The document analysis includes business plans, strategic documents, meeting minutes, and other documentation relevant to the decisions addressed by the study. Documents were released by the MHS Office of the Executive Director and the CI. These documents were used to establish a decision-making context and track the development of decisions prior to the initiation of this project. Furthermore, public document sources that provide participant demographics information, organizational information, and government policy information were accessed when required.

Interview content was also expanded to include more open-ended reflections from participants and researchers on the project, discussing topics of expectations, learning, and possible external factors affecting the implementation (Tables 1 and 2).

Table 1. Semistructured interview questions for researchers.

Topic	Example questions
Background	Firstly, can you share any reflections on the project in general?
Project evaluation	What were your original plans and expectations for the project? How well do you think the reality met your expectations?
	How do you think the organisational change at the MHS[a] affected the project?
	What has this project achieved?
	Do you believe that we have affected change at the MHS? How? Why?
	Finally, if you could describe the project in one word, what would it be?
Lessons learned	What were the strengths and weaknesses of our approach? What would you change for next time?
	What have you, personally, learnt/gained from this project?
	Has this project changed the way you understand: … mental health? …modelling? …strategic decision making? …research projects?
	If you could provide one piece of advice for another group doing similar work, what would it be?

[a]MHS: mental health service.

Table 2. Semistructured interview questions for managers.

Topic	Example questions
Background	So, we last talked about this time in 2014, two years ago [remind them of the timeline]. So I just wanted to get your thoughts and feelings on the last two years in the mental health service (MHS)?
Organizational change	You predicted [insert prediction] about the period of change in the MHS. To what extent has your expectation been met?
	What are your predictions for the future of the SLG[a]?
Mental models	And how about now? Do you have a sense of a decision-making process for the MHS? What is that? Were there any intermediate models?
	Who makes strategic decisions for the MHS at the moment?
Evaluation of current SLG performance	If you could describe your feelings about the SLG in one word, what would it be?
Simulation project evaluation	I also wanted to get a sense of how the modelling project sat within all of this organisational change. How relevant was the modelling project to you as a member of the SLG?
	What were your expectations for the project [refer to 2014 interview transcripts]? Were they met?
	Has your personal decision-making practice changed? How? Why?
	If you could describe your feelings about the simulation project in one word, what would it be?

[a]SLG: senior leadership group.

Data Collection and Management

All evaluation data collection was conducted by KML to maintain the separation between the researchers conducting the intervention and the evaluation of the intervention.

A total of 18 interviews were audiorecorded and transcribed verbatim, with 1 participant refusing a recording of the exit interview, instead of allowing note-taking. All audiorecordings, notes, and documentation were imported into the qualitative data analysis software NVivo 10 for analysis [34].

Field notes were kept by KML documenting the time, date, general content, and personal emotions and thoughts associated with contact with participants.

To maintain a close relationship to the data and participants, study data are stored in an identifiable format in password-protected files and folders on password-protected computers located at the core administration site. These can only be accessed by the research staff. The study data will be stored for a minimum of 7 years, after which these may be confidentially destroyed.

Analyses

All evaluation analyses will be conducted by KML, with an external senior qualitative researcher providing guidance and analysis checks where required.

Mental Models

The content analysis of the interview transcript was used to review and refine the interview diagram into a concept map. Each individual's content map was transcribed into a matrix formation with an arbitrary distance of 1, and input into the network analysis software JPathfinder [33,35] for quantitative analysis. Participants' individual models were compared with each other in a pairwise fashion, generating a matrix of similarity values (Pathfinder r). This range was used to represent the overall group model similarity.

Group-level concept maps will be created manually by combining all current concept maps, noting agreement by the count of participants who mentioned each concept or a similar construct. This procedure will be repeated for the second time-point. Group-level mental models at each time-point will then be compared against each other to assess any changes over the intervention period.

Linguistic Coding Framework

Linguistic coding will be used to assess the process effects of the PLM workshops. Initial codes were derived from the literature on the benefits of problem structuring methods and group model building [36-38] and then matched to concept descriptions and behavioral examples (Table 3). Transcripts of the group discussions will be assessed for similarity to ideal behavior as defined by the literature, for example, equal participation among participants [38].

Table 3. Behavioral coding examples for PLM workshops.

Coding variable	Behavioral or linguistic cue
Problem exploration	"But we don't know…" "We need to know…"
Discussion of alternatives	"What about…" "Or we could…"
Participation	Pattern of speaking duration by gender, role, and over the course of the workshop
Voice	Interjections Speaker participation relative to seniority
Information sharing	"In our service…" "From my point of view…"
Clarification of meaning	"What do you mean?" "I mean that…" "Do you agree?"
Agreement	"I agree" "Yes"
Disagreement	"No" "I don't agree"

Thematic Analysis

Participant and researcher interviews will be analyzed using thematic analysis. Open coding will be used to explore the data prior to an iterative process of thematic refinement involving member checks and the exploration of alternative interpretations. These interpretations will be presented to participants, providing them with the opportunity to provide further comment. Furthermore, the researcher-participants will be involved in the written publication of the analysis, ensuring shared ownership of the project evaluation and recommendations.

Results

The project was funded in 2012 and recruitment was completed in October 2016. Sixteen managers participated in at least one data collection (see Table 4 for a summary of participation patterns). Three researchers participated in interviews with the evaluator (KML), with another 2 providing written responses to question prompts.

Table 4. Sample participation patterns across data collection points to date.

Participant	Workshop 1 (N=8)	Interview 1 (N=9)	Workshop 2 (N=8)	Interview 2 (N=9)
1	✓	✓	✓	✓
2	✓	✓	✓	✓
3	✓	✓	✓	✓
4	✓		✓	✓
5		✓	✓	✓
6	✓	✓		
7		✓	✓	
8		✓	✓	
9		✓		✓
10	✓			✓
11	✓			
12	✓			
13		✓		
14			✓	
15				✓
16				✓

Primary data collection has been completed. Data analysis is currently under way, with parallel member checking ongoing. The first results are expected to be submitted for publication in late 2018.

Discussion

This research protocol outlines the implementation and evaluation of simulation modeling in the planning of MHS in Australia. As a case study, this research design has both advantages and limitations. The iterative design of the intervention allows easy adaptation to the changing organizational context; however, this comes at the cost of clear data points for quantitative evaluation. This is addressed by favoring a qualitative case study approach for evaluation, at the cost of generalizable findings. However, given the lack of reporting on simulation implementation in the past, such deep access and analysis provide a unique opportunity to understand the realities of translational research in this area.

While the methods used allow for feedback from senior staff, which includes direct-care staff and a consumer representative, the organizational level of the modeling intervention does not readily allow for the incorporation of other direct feedback from consumers, family members, or nonmanagerial staff. However, following the completion of the project, we expect that the modeling system will be a valuable decision support tool to be used by MHS managers, which will be integrated into the process of decision making around service configuration and allocation of resources within the MHS. This provides the potential for future follow-up studies measuring the intervention impact for patients, families, and nonmanagerial staff.

The challenges faced by the project thus far, especially the instability of the health care context, are not unusual. Hence, lessons from this research have the potential to improve the implementation of future research projects, providing greater evidence-based service planning for the mental health sector in Australia.

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Authors' Contributions

GNM was responsible for the design of the intervention. KML was responsible for the design of the evaluation.

Conflicts of Interest

None declared.

Multimedia Appendix 1

Workshop evaluation questionnaire.

[PDF File (Adobe PDF File), 28KB - resprot_v7i11e11119_app1.pdf]

Multimedia Appendix 2

ARC Grant Assessor Reports.

[PDF File (Adobe PDF File), 117KB - resprot_v7i11e11119_app2.pdf]

References

1. Weiner J, Boyer E, Farber N. A Changing Health Care Decision-Making Environment. Human Relations 2016 Apr 22;39(7):647-659. [doi: 10.1177/001872678603900704]
2. Thakur R, Hsu S, Fontenot G. Innovation in healthcare: Issues and future trends. Journal of Business Research 2012 Apr;65(4):562-569. [doi: 10.1016/j.jbusres.2011.02.022]
3. National Mental Health Commission. Contributing Lives, Thriving Communities - Review of Mental Health Programmes and Services. 2014 URL: http://www.mentalhealthcommission.gov.au/our-reports/our-national-report-cards/2014-contributing-lives-review.aspx [accessed 2018-08-03] [WebCite Cache ID 71NtqgYoO]
4. Brownson RC, Allen P, Duggan K, Stamatakis KA, Erwin PC. Fostering more-effective public health by identifying administrative evidence-based practices: a review of the literature. Am J Prev Med 2012 Sep;43(3):309-319 [FREE Full text] [doi: 10.1016/j.amepre.2012.06.006] [Medline: 22898125]

5. Cook DA, Hatala R, Brydges R, Zendejas B, Szostek JH, Wang AT, et al. Technology-enhanced simulation for health professions education: a systematic review and meta-analysis. JAMA 2011 Sep 07;306(9):978-988. [doi: 10.1001/jama.2011.1234] [Medline: 21900138]
6. Slovensky DJ, Morin B. Learning through simulation: the next dimension in quality improvement. Qual Manag Health Care 1997;5(3):72-79. [Medline: 10168374]
7. Department of Health and Ageing. Fourth national mental health plan: an agenda for collaborative government action in mental health-. 2009. URL: http://www.health.gov.au/internet/main/publishing.nsf/content/9A5A0E8BDFC55D3BCA257BF0001C1B1C/$File/plan09v2.pdf [WebCite Cache ID 71NtvDbUu]
8. Long KM, Meadows GN. Simulation modelling in mental health: A systematic review. Journal of Simulation 2017 Dec 06;12(1):76-85. [doi: 10.1057/s41273-017-0062-0]
9. McCaughey D, Bruning NS. Rationality versus reality: the challenges of evidence-based decision making for health policy makers. Implement Sci 2010 May 26;5:39 [FREE Full text] [doi: 10.1186/1748-5908-5-39] [Medline: 20504357]
10. Jun JB, Jacobson SH, Swisher JR. Application of Discrete-Event Simulation in Health Care Clinics: A Survey. The Journal of the Operational Research Society 1999 Feb;50(2):109-123. [doi: 10.2307/3010560]
11. Gogi A, Tako AA, Robinson S. An experimental investigation into the role of simulation models in generating insights. European Journal of Operational Research 2016 Mar;249(3):931-944. [doi: 10.1016/j.ejor.2015.09.042]
12. England W, Roberts S. Applications of computer simulation in health care. 1978 Presented at: Proceedings of the 10th conference on Winter simulation; December 4-6, 1978; Miami Beach, FL.
13. Wilson JCT. Implementation of Computer Simulation Projects in Health Care. The Journal of the Operational Research Society 1981 Sep;32(9):825-832. [doi: 10.2307/2581399]
14. Lehaney B, Hlupic V. Simulation modelling for resource allocation and planning in the health sector. Journal of the Royal Society of Health 2016 Sep 07;115(6):382-385. [doi: 10.1177/146642409511500611]
15. Fone D, Hollinghurst S, Temple M, Round A, Lester N, Weightman A, et al. Systematic review of the use and value of computer simulation modelling in population health and health care delivery. J Public Health Med 2003 Dec;25(4):325-335. [Medline: 14747592]
16. Brailsford SC, Harper PR, Patel B, Pitt M. An analysis of the academic literature on simulation and modelling in health care. Journal of Simulation 2017 Dec 19;3(3):130-140. [doi: 10.1057/jos.2009.10]
17. van Sambeek JRC, Cornelissen FA, Bakker PJM, Krabbendam JJ. Models as instruments for optimizing hospital processes: a systematic review. Int J Health Care Qual Assur 2010;23(4):356-377. [doi: 10.1108/09526861011037434] [Medline: 20535906]
18. Forsberg HH, Aronsson H, Keller C, Lindblad S. Managing health care decisions and improvement through simulation modeling. Qual Manag Health Care 2011;20(1):15-29. [doi: 10.1097/QMH.0b013e3182033bdc] [Medline: 21192204]
19. Shrivastava P, Grant JH. Empirically derived models of strategic decision-making processes. Strat. Mgmt. J 1985 Apr;6(2):97-113. [doi: 10.1002/smj.4250060202]
20. DeChurch LA, Mesmer-Magnus JR. The cognitive underpinnings of effective teamwork: a meta-analysis. J Appl Psychol 2010 Jan;95(1):32-53. [doi: 10.1037/a0017328] [Medline: 20085405]
21. Jones DW. An empirical comparison of priority-queue and event-set implementations. Commun. ACM 1986 Apr;29(4):300-311. [doi: 10.1145/5684.5686]
22. Sanders P. Fast priority queues for cached memory. J. Exp. Algorithmics 2000 Dec 31;5:7. [doi: 10.1145/351827.384249]
23. Haby MM, Carter R, Mihalopoulos C, Magnus A, Sanderson K, Andrews G, et al. Assessing Cost-Effectiveness - Mental Health: introduction to the study and methods. Aust N Z J Psychiatry 2004 Aug;38(8):569-578. [doi: 10.1111/j.1440-1614.2004.01420.x]
24. Rockwell Automation. Arena. 2010. URL: https://www.arenasimulation.com/ [accessed 2018-10-09] [WebCite Cache ID 7339wm7SL]
25. Scott RJ, Cavana RY, Cameron D. Recent evidence on the effectiveness of group model building. European Journal of Operational Research 2016 Mar;249(3):908-918. [doi: 10.1016/j.ejor.2015.06.078]
26. Ford D, Sterman J. Expert knowledge elicitation to improve formal and mental models. Syst. Dyn. Rev 1998;14(4):309-340. [doi: 10.1002/(SICI)1099-1727(199824)14:4<309::AID-SDR154>3.0.CO;2-5]
27. Fanaian M. Evaluation in Logic Model. In: Research Bites. Sydney: Primary Health Care Research Network, The University of New South Wales; 2004.
28. McCawley P. The Logic Model for Program Planning and Evaluation. 2002 URL: https://www.cals.uidaho.edu/edcomm/pdf/cis/cis1097.pdf [accessed 2018-08-03] [WebCite Cache ID 71NuEC84V]
29. Taylor-Powell E, Henert E. Developing a logic model: Teaching and training guide. 2008 URL: https://fyi.uwex.edu/programdevelopment/files/2016/03/lmguidecomplete.pdf [WebCite Cache ID 71NuJu75O]
30. WK Kellogg Foundation. Logic Model Development Guide. 1998. URL: https://www.wkkf.org/resource-directory/resource/2006/02/wk-kellogg-foundation-logic-model-development-guide [accessed 2018-08-03] [WebCite Cache ID 71NtUyGMJ]
31. Gugiu PC, Rodríguez-Campos L. Semi-structured interview protocol for constructing logic models. Eval Program Plann 2007 Nov;30(4):339-350. [doi: 10.1016/j.evalprogplan.2007.08.004] [Medline: 17905433]

32. Edwards BD, Day EA, Arthur W, Bell ST. Relationships among team ability composition, team mental models, and team performance. J Appl Psychol 2006 May;91(3):727-736. [doi: 10.1037/0021-9010.91.3.727] [Medline: 16737368]
33. DeChurch L, Mesmer-Magnus J. Measuring shared team mental models: A meta-analysis. Group Dynamics: Theory, Research, and Practice 2010 Dec;14(1):1-14. [doi: 10.1037/a0017455]
34. QSR International Pty Ltd. Nvivo qualitative data analysis Software. 2012. URL: https://www.qsrinternational.com/nvivo/home [accessed 2018-10-09] [WebCite Cache ID 7339Mjk2C]
35. Interlink. JPathfinder. 2017. URL: https://interlinkinc.net/ [accessed 2018-10-09] [WebCite Cache ID 733982Wjj]
36. Vennix JAM. Building consensus in strategic decision making: System dynamics as a group support system. Group Decis Negot 1995 Jul;4(4):335-355. [doi: 10.1007/BF01409778]
37. Vennix J, Scheper W, Willems R. Group model-building: what does the client think of it. 1993 Presented at: 11th International Conference of the System Dynamics Society; unknown; Cancun, Mexico.
38. Franco LA. Forms of conversation and problem structuring methods: a conceptual development. Journal of the Operational Research Society 2017 Dec 21;57(7):813-821. [doi: 10.1057/palgrave.jors.2602169]

Abbreviations

CI: chief investigator
DALY: disability-adjusted life year
MHS: mental health service
PLM: program logic modeling
QALY: quality-adjusted life year
SLG: senior leadership group

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